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A

PRACTICAL TREATISE

ON

DISEASES OF THE KIDNEYS

AND

URINARY DERANGEMENTS

LEEDS & WEST-RIDING
MEDICO-CHIRURGICAL SOCIETY

BY

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PREFACE.

The object of the present volume is to present the student and practitioner with a clear, concise, and systematic account of urinary pathology and therapeutics, based upon the latest ascertained facts, and supported by the best authorities. For this purpose, I have endeavoured to make myself acquainted with the recent literature on the subject; more especially the contributions made to our Societies, and the discussions resulting therefrom. Throughout I have endeavoured to put prominently forward the characters upon which the diagnosis of the various renal and urinary diseases is founded, and their treatment indicated.

I have to thank my friends, Dr. Green, Professor Greenfield, Dr. Frederick Roberts, Dr. Lindsay Steven, and Mr. Godlee for the use of illustrations from their works, and must also record the obligation I am under to my friend and colleague, Dr. James Anderson, for the chapter on Abnormalities of the Kidney, which his ex-

tensive anatomical knowledge peculiarly fitted him to supply.

My former work, on the "Morbid Conditions of the Urine dependent on Derangements of Digestion," being out of print, I have incorporated such portion of it as seemed desirable in the present volume, so that it will not be issued again in a separate form.

Queen Anne Street, London.
July, 1885.

LEEDS & WEST RIDING
MEDICO-CHIRURGICAL SOCIETY

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LEEDS & WEST RIDING
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DISEASES OF THE KIDNEY

AND

MORBID CONDITIONS OF THE URINE.

CHAPTER I.

General Symptomatology of Kidney Disease.

When kidney disease exists, its presence is generally indicated by certain qualitative changes in the urine secreted, and which in themselves are usually sufficient to enable us to arrive pretty conclusively at an opinion regarding the nature of the disorder. In addition to the altered character of the urinary secretion, diseases of the kidney are attended by other symptoms, partly objective, and partly subjective in character; such as those which relate to painful sensations in the organs themselves, or depend on alterations in their size and position, or are connected with disturbance of function in other organs. These symptoms, though not in themselves always sufficient, in the absence of a careful clinical examination of the urine, to determine the presence or the nature of renal disease, not only materially aid us in coming to a conclusion that these organs are the seat of disease and thus lead us to direct our inquiries more specially in that direction, but they also enable us in obscure and mixed cases to effect a differential diagnosis, and also to ascertain with a greater positiveness the stage the disease has reached, by a consideration of the changes wrought in the body generally, than

could be possible by a mere dependence on the results obtained by an examination of the urine. And as in conducting a clinical examination we always pass from the general to the special, it will be advantageous to gain an insight into the nature of the general symptoms before we undertake the task of investigating those changes in the urinary secretion attendant on diseases of the renal organs.

1. **Pain** is a symptom of kidney disease, which is subject to considerable variation, both as regards its site and intensity; for whilst there are few diseases of the kidney which are entirely unaccompanied by uneasy sensations in the neighbourhood of the organ, still pain is undoubtedly a more marked symptom in some forms than in others. Thus, for instance, inflammatory affections of the substance of the kidney may exist without the patient making any complaint of pain, even when closely questioned on the subject; at most only a feeling of weight or dragging in the loins. In other cases the pain complained of is so intense that the patient is unable to bear the slightest pressure over the loins or flank. The same variability in the degree of pain is noticeable when the organ is invaded by new growths, or becomes the seat of calculous deposit. (Curnow, *Path. Soc. Trans.*, vol. xxiv., p. 148). The explanation of the variability of this symptom is that the substance proper of the kidney is but indifferently supplied with nerves of common sensation, whilst these are freely distributed over the surface of the capsule, and around the pelvis of the organ. Thus it happens in inflammatory affections of the kidney, unless there is much swelling and tumification of the substance of the kidney, causing stretching and tension of the capsule, pain may not be experienced. Again with renal calculi, a

large mass which gradually destroys by its pressure the whole of the kidney substance may exist and yet give rise to little or no pain, whilst firmly imbedded, whereas a small fragment of gravel falling into the pelvis of the kidney will excite the most distressing paroxysms.

There are two characteristics of pain arising from kidney disease which require notice, the first is its paroxysmal character. This may be accounted for by the fact that the kidneys are more or less over-laid by the ascending colon on the right, and the descending colon on the left, and pain is likely to be occasioned when these portions of the bowel become overloaded with fæces, or distended with flatus, and thus press on a diseased kidney; as the contents of the colon are continually shifting, we can readily see how it is relief may suddenly follow intense pain in the renal region. Another reason for the paroxysmal nature of the pain in kidney disease is the occasional passage down the ureter of blood clots, and urinary deposits, which give rise to sharp and temporary colic.

The other character of renal pain is that it is often reflected. Morgagni was the first to call attention to this fact. It most frequently occurs in cases of renal calculus, and as this reflected pain is usually felt at the neck of the bladder, it happens that attention is drawn to the bladder rather than the kidney. Sometimes the pain instead of being reflected to the bladder, is felt in the groin, or down the spermatic cord, or down the inner side of the thigh. Cases of persistent pain in the heel, or foot, are recorded, which on the urine being examined led to the discovery of pus and blood-corpuscles in the urine, undoubtedly caused by the presence of a calculus in the kidney of the same side as the foot affected.

Attacks of pain of neuralgic character affecting the region of the kidney are not infrequently complained

of, especially in persons who have resided in malarial districts. In 1878 the late Dr. Murchison gave me the particulars of a peculiar form of neurosal attack which he designated as a "renal storm" and which had frequently occurred in a patient suffering from aortic regurgitation. The attack commenced with excruciating pain over the region of the right kidney, exactly like renal colic, but there was no sickness or retraction of testicle, and the urine passed during and after the attack was perfectly normal, nor was there any jaundice or anything to suggest the pain was due to biliary calculus, after lasting some hours it passed off as suddenly as it came on, With reference to this case I may mention the remarks made by Dr. Habershon (*Diseases of the Liver*, p. 13) with regard to the neuralgic pain sometimes met with in organic disease of the heart and which is referred to as being situated deeply behind the first part of the duodenum. "It is," he says, "severe, almost like that from gall-stone, but it is without jaundice or other symptoms of calculus, it is not connected with the stomach, for it is not affected by food, but paroxysmal and recurring sometimes with great regularity." In 1880 a man, aged 47, applied as an out-patient at the London Hospital solely on account of severe paroxysmal attacks of pain, which, commencing at the angle of the epigastric region where it joins the right hypochondrium, passed downwards into the right lumbar region. No disease of the liver or kidney could be detected, and the urine was perfectly normal. On examining the chest, however, we found the left ventricle considerably hypertrophied, the result of aortic regurgitation. This case was probably similar to that mentioned by Murchison and those alluded to by Habershon.

2. **Enlargements of the Kidney.**—Owing to their situation at the back of the abdominal cavity, the kidneys

cannot be felt by palpation when of ordinary size; or at the most, in thin subjects only the upper border of the right kidney in front can be made out. It is only therefore when considerable enlargement takes place that a physical examination of the abdomen can lead us to form a definite conclusion. But even when considerable enlargement exists, the difficulty of diagnosis is great, not only in determining differentially between enlargement of other organs of the abdominal cavity, such as the ovary, the spleen, the concave surface of the liver, &c.; but also when the tumour is correctly referred to the kidney, to distinguish the nature of the disease. In order therefore to make a successful diagnosis three points have to be attended to. (1) An accurate knowledge of the anatomical relations of the renal organs; (2) a systematic method of conducting the physical examination to which must be added a tactile skill acquired by constant practice; and (3) a thorough consideration of the general symptoms.

Anatomical Relation. The kidneys are situated at the back of the abdominal cavity, behind the peritoneum from which they are separated by a layer of cellulo-adipose tissue. They rest upon the lower portion of the diaphragm, on the fascia covering the quadrati lumborum and transversalis muscles and towards their inner side on the psoas muscles, The left kidney as nearly as possible lies between a line drawn outwards from the level of the 11th dorsal spine and a similar line drawn from the level of the 2nd lumbar spine, whilst the hilum corresponds to the level of the 1st lumbar spine, and is nearly two inches from the middle line of the body. The right kidney is placed at a slightly lower level than the left, being from half an inch to three quarters of an inch below the limits given above. The anterior relation of the kidneys are, however, of the greatest importance in diagnosing renal tumours, since owing to the

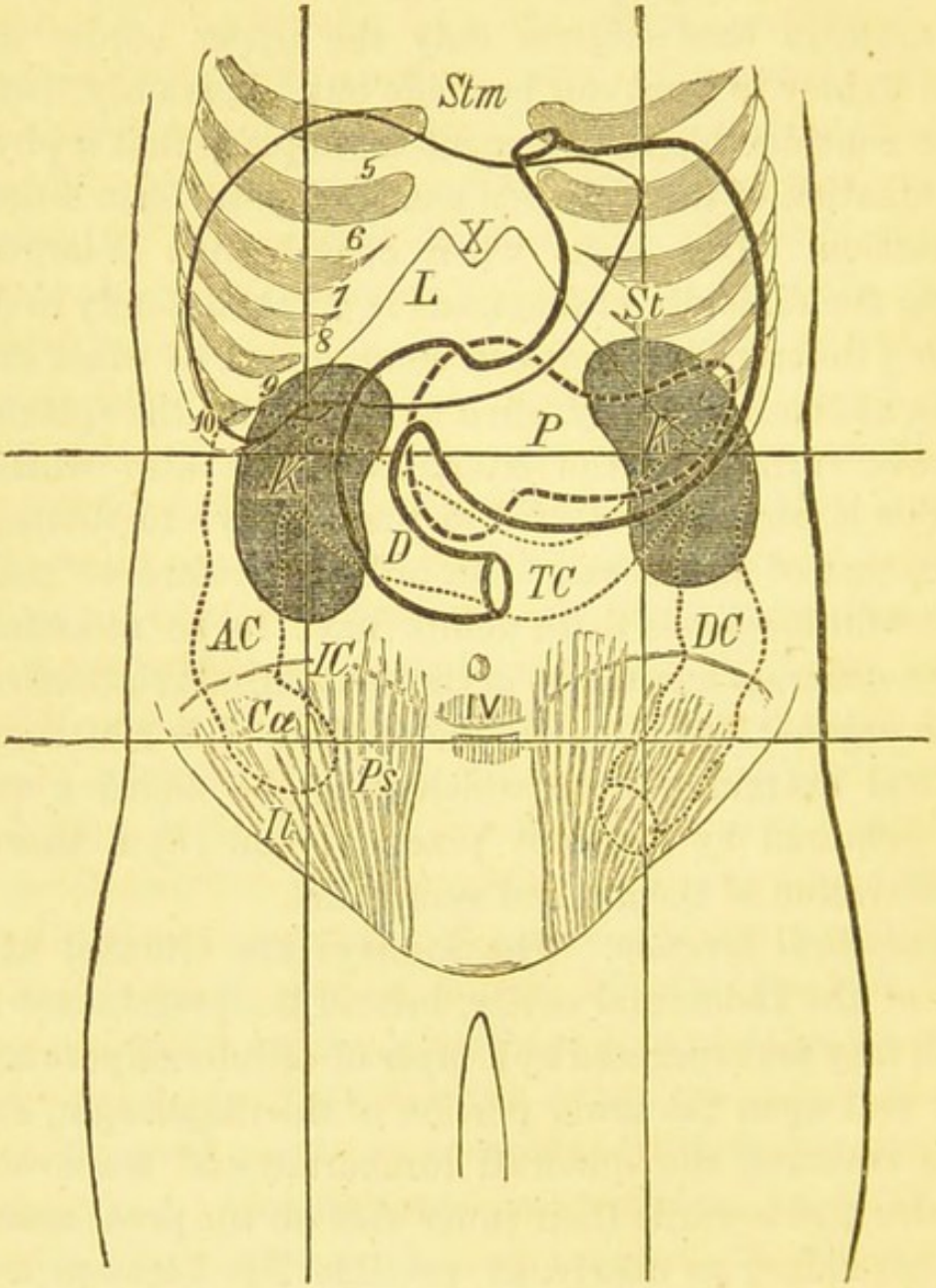


FIG. 1.—Anatomical Relations of the Kidneys, by Mr. Godlee.

Stm Sternum.
X Xiphoid Appendix.
5, 6, 7, 8, 9, 10 } Rib Cartilages.
IV 4th Lumbar Vertebra.
IC Iliac Crest.
Ps Psoas.
Il Iliacus.

L Liver — outlined thus ——
St Stomach, D Duodenum } „ „ ——
P Pancreas „ „ - - - -
Cæ Cæcum, AC Ascending Colon, TC Transverse Colon, DC Descending Colon } „ „ .....
K, K } Right and Left Kidneys.

solidity of the structures at the posterior aspect, the existence of a tumour is not so easily detected by manipulation as by gentle pressure on the anterior or lateral surface. Moreover a solid tumour occupying the loins and flank may be generally referred to the kidney, but when it comes to the front we have to take into consideration the possibility of its being caused by enlargement of other organs. The kidney on each side occupies a part of the hypochondriac, epigastric, umbilical, and lumbar regions as shown in fig. 1. The right kidney, which, as stated above, naturally lies at a lower level than the left, has its lower border corresponding to a line drawn just above the upper level of the umbilicus, whilst the left is about half an inch higher. The upper border of the inner edge of the right kidney also extends rather more into the umbilical region towards the middle line than does the left. The right kidney is in relation by its upper border with the supra-renal capsule and the under surface of the right lobe of the liver. The ascending colon covers the anterior surface, whilst the cæcum just lies below the lower border. The inner border at its upper end is just covered by the duodenum and head of the pancreas. The left kidney at its upper border is in contact with the supra-renal capsule and the spleen. Its anterior surface is covered at the upper end by the tail of the pancreas which intervenes between it and the lower border of the stomach, whilst the middle and lower portion of its surface is covered by the descending colon, which however it must be remembered crosses it rather obliquely from above downwards, and from without inwards. This is important for in large renal tumours of the left side, the descending colon is to be felt crossing rather than covering the kidney.

The manner of examining for enlargement of the kidney is as follows, the patient being in bed or on a sofa, has his knees well drawn up so as to flex the thighs

upon the trunk. If the tumour is on the right side, the left hand is to be passed along the margin of the false ribs till it reaches the space between them and the crest of the ilium; then with the right hand the wall of the abdomen is to be greatly depressed, and the intestine pushed aside, by the tips of the fingers, as much as possible. When the right hand is well over the anterior kidney region, pressure is made in the loins by the fingers of the left hand so as to push the kidney as far forwards as possible against the right hand. In this way an enlarged kidney can usually be diagnosed, but if any doubt exists, a reference to the general symptoms will as a rule determine the point satisfactorily. Thus for instance, the mobility of the tumour on deep inspiration, the presence or absence of abnormal conditions of the urine, &c.

The following points should be borne in mind in distinguishing renal tumours from enlargements of other organs.

(1) *From Enlargements of the Liver;* by the tumour being more or less covered by intestine; by the relation of the tumour to the ribs, which instead of passing under them, dips down as it were so that the fingers can be placed between their margin and the tumour that the tumour is not affected by the ordinary movements of respiration; that there is generally some marked morbid condition of the urine; that the enlargement is not accompanied with jaundice.

(2) *From Enlargements of the Cæcum or Colon;* by the absence of any special intestinal disturbance; that it does not disappear after the employment of purgatives. A perinephritic abscess is distinguished from a fæcal abscess, by its more rounded and oval form, by its deeper situation, by the frequent occurrence of an œdematous condition of the skin in the region of the loins, by a lower degree of fever and with more marked remissions.

(3) *From Enlarged Spleen;* by the tumour being more rounded than a splenic enlargement, which often presents a defined edge which is notched. By not projecting so far forward anteriorly as a splenic tumour does; by being covered more or less by the transverse colon; by its not being influenced by the respiratory movements.

(4) *From Ovarian Tumours;* the history points to the enlargement having first commenced in the lumbar region; by the tumour being felt in the loin as well as in front; by the colon more or less covering the tumour, by the negative information gained by vaginal examination.

As a general rule renal tumours are usually most prominent in the back and flank, but instances do occur where the enlargement is directed more towards the anterior wall of the abdomen, increasing however always from behind forwards. This variation in situation depends of of course on the part of the kidney affected and the nature of the disease. Thus in perinephritis, or enlargement of the kidney from numerous cysts, the tumour will be found distinctly occupying the loins, whilst in rapidly growing fungoid disease or collections of pus within the cavity of the kidney, the enlargement may often be best felt between the ribs and the median line above the umbilicus. These points however will call for special attention when each special form of renal tumour, and its differential diagnosis is dealt with.

3. **Derangements of the Circulatory System.**—In those affections of the kidney known collectively as Bright's disease, marked changes occur in the circulatory system, which by their results at once draw attention to the morbid processes going on in the renal organs. These are dropsy, pulse of high tension, hypertrophy of the left ventricle, and hæmorrhages from mucous surfaces. These conditions however are not combined in every form of Bright's

disease. Thus dropsy is the special clinical feature of the inflammation of the kidney which eventuates in the large white kidney; whilst a pulse of high tension, with hypertrophy of the left ventricle is characteristic of the granular and contracted kidney. There are exceptions, it is true, to this general statement, for a slight degree of dropsy is often noticeable towards the end in cases of granular kidney, when the hypertrophied ventricle at last becomes weakened, and the blood pressure throughout the systemic system falls from its previous high tension. On the other hand, high tension of pulse, and a certain degree of hypertrophy of the left ventricle, is undoubtedly observed in those cases in which a white large kidney has become contracted (small pale granular kidney). Still the fact remains that dropsy is characteristic of the inflammatory form, and a pulse of high tension and hypertrophy of the left ventricle of the more purely chronic variety. The reasons for this as well as the occasional exception will now be discussed.

(1) *Dropsy.*—Text-books on medicine tell us that whenever the balance between the two processes, transfusion of the nutritive plasma from the blood-vessels and its re-absorption by the lymphatics and veins, is disturbed, the quantity of fluid, which is always present in small quantity in the tissues, becomes increased, and thus leads to dropsical accumulations. It is thus manifest that dropsy may be referred either to pressure in the arterial system, or to obstruction of the venous circulation. The typical form of a dropsical accumulation due to venous obstruction, is of course that which follows on cirrhosis of liver, when the radicles of the portal venous circulation are compressed by the contraction of the connective tissue elements surrounding the lobules. In heart disease, especially of the mitral valve, and of the right side of the

heart, the dropsy in the first instance is due to venous congestion, brought about by the impeded return of blood to the right side of the heart by the inferior vena cava, and this almost invariably commences about the ankles and feet. Though as the kidneys become affected, as they do in all protracted cases of valvular disease of the heart, the dropsy assumes the form due to increase of arterial pressure. The dropsy then of cardiac and hepatic disease, because it affects the particular branch of the venous system which is obstructed, is essentially a *local* dropsy, whilst as we shall now see, the dropsy resulting from kidney disease is a *general* effusion. This is brought about in the following way. In that form of kidney disease which is generally accompanied by dropsy, the secretion of water by the kidneys is lessened considerably, whilst the quantity of water ingested to supply the needs of the body remains the same, consequently the volume of blood in the arterial system is increased, so that the serum passes into the tissues in consequence of this increased pressure, whilst no doubt its poorness in albuminous constituents, owing to the withdrawal of these substances from the blood by the urine, renders its passage through the walls of the vessels more easy. This makes plain what was previously stated, that general dropsy distinguishes the acute forms of Bright's disease from the more chronic. For in the acute form the amount of urine secreted is considerably diminished, whilst in the latter owing to the high arterial tension, as manifested by the pulse and the hypertrophied condition of the left ventricle, the urinary secretion is abundant and even copious. As soon however as the left ventricle ceases to increase and its tissue to undergo degenerative changes, then the amount of urine diminishes and a certain amount of dropsy occurs, though never to such an extent as is observable in the early stages

of the inflammatory form. Thus general dropsy becomes a distinct feature of acute and sub-acute nephritis, whilst it is comparatively a rare event in chronic interstitial nephritis.

Thus, according to a statement of Dr. George Johnson, in twenty-six cases of the large white kidney, dropsy was found in twenty-four, while in thirty-three cases of contracted kidney, dropsy was observed only in fourteen cases. In speaking however of general dropsy as being thus symptomatic of one form of Bright's disease, the student must be warned against taking the presence of general dropsy as conclusive of primary, or even of disease of the kidneys at all. In speaking of the dropsy of heart disease, it was pointed out that at first it was due to venous congestion, and that it was only when the kidneys became affected, and began to undergo atrophic changes, that the œdema became general. Here the history of the case would help us to arrive at a right conclusion, for if the œdema began at the legs and then became general, we should have no hesitation in saying that the cardiac was the primary, and the renal the secondary lesion. Again in certain cases of tricuspid regurgitation we may be misled especially when the venous circulation in the neck is much affected, so that coincident with the swelling of the legs the eyelids become puffy. A little discrimination will show however that there is no puffing of the trunk, nor do the hands swell, whilst albumin will be probably absent from the urine. In one case, however, I have seen the whole body, face, trunk, and limbs enormously swollen, and yet the kidneys were healthy. In this case a large aortic aneurism so pressed on the right auricle, as greatly to retard the blood flowing through the superior as well as the inferior cava. Mediastinal tumours might produce a similar effect, but such

cases as these are rarities, whilst the evidence of the existence of a large intra-thoracic growth would lead one to suspect compression of the cava, and hence that the dropsy was due to venous congestion than to increase of the arterial pressure. Cases of myxœdema may be mistaken for general dropsy, they can however be distinguished by the firmer character of the œdema, the peculiar mental sluggishness, the muscular slowness of movement, the spade like enlargement of the hand, and the absence, or if present, only of a small trace, of albumin in the urine, which characterise them.

Renal dropsy may set in suddenly in the course of nephritis. This most commonly happens in the acute form, though it not infrequently occurs that patients, who are suffering from the chronic variety and who have previously only exhibited a slight puffiness, will become suddenly and extremely swollen after exposure to cold. As a rule, however, it comes on more gradually and does not at first attract the patient's attention, and is perhaps first discovered by the physician who on examining the patient finds the pressure of the stethoscope gives rise to decided pitting. Or what very commonly happens is that patients come to us, complaining that when they wake in the morning their eyelids are partially closed, or the hand on the side they have been lying is swollen. From this slight œdema to an extreme condition of anasarca the gradation is variable. It is rare, however, for effusion into the serous cavities to occur during the early stages, unless the patient has been exposed to cold, though in prolonged cases it happens sooner or later as a natural sequence. When that somewhat rare event œdema of the glottis occurs, it is generally attributable to exposure to severe cold, and then it may come on in quite an early stage. When the renal disease shows signs of amendment, either when acute by a ten-

dency to recovery ; or in the chronic form by amelioration under treatment, or from the increased tension in the vessels from commencing hypertrophy of the left ventricle, the first symptom is an increased flow of urine, and this speedily followed by a corresponding decrease of the general anasarca. Indeed patients are often alarmed at the prodigious diuresis, and rapid disappearance of their swelling, imagining that their disease has taken an unfavourable turn. Often considerable relief to the dropsical distension is afforded by spontaneous diarrhœa, a method of relief the physician endeavours to encourage by the administration of hydragogue medicine, but which nevertheless should be administered with caution in the chronic form of the disease, when the patient is weakened by a long continued disease, the diarrhœa in these cases being sometimes incontrollable.

With regard to the chemical qualities of the transuded fluid, it will be plain from what has been said of the causes of dropsy, that it consists of blood serum more or less dilute, the degree of dilution being in direct proportion with the degree of hydræmia and the loss of albumin. Thus if we take the specific gravity of normal blood serum at 1·025-28, we find the specific gravity of dropsical fluid ranges form 1·005 to 1·020 according to the amount of solid matter present. The proteids consist of sero-albumin, paraglobulin and fibrinogen, and range from 0·4 to 6 per cent. On standing sometimes after being withdrawn from the body, fine flakes of fibrin are deposited. Urea is generally present varying in amount from extremely minute quantities to the same percentage as that found in the urine. Thus in one interesting case where about a pint and a half of anasarcous fluid together with the twenty-four hours' urine passed by the patient, I found the percentage composition nearly equal, so that supposing the

fluid transuded in the body to have been equal in amount to the twenty-four hours' urine, the quantity of urea passed out of the circulation into the two fluids would nearly have reached the normal excretion, the urine in this case containing as it did rather less than half the normal amount. Traces of glucose are sometimes found in dropsical effusions of the peritonæal cavity. Serous effusions are likewise distinguished by containing more albumin and solid matter generally than are found in the exudations from the subcutaneous tissue.

(2) *Cardio-vascular Changes.* Chronic renal affections are usually associated with morbid changes in other organs of the body. But no change is so marked as that which occurs in the vascular system during the development and progress of the granular kidney. The changes particularly referred to, are hypertrophy of the left ventricle, thickening of the walls of arterioles, and atheromatous conditions of the arteries.

On feeling the pulse of a patient suffering from this granular degeneration of the kidneys we find it tense and bounding—the high tension being remarkably persistent, the artery remaining full both during the systole and diastole. On examining the heart, we find its action increased and heaving; whilst the area of precordial dulness, if no emphysema of the lungs is present to mask it, is increased, the apex beat being at the same time displaced a little outwards to the left. The heart sounds are loud, and there is often accentuation of the second sound heard over the aortic cartilage. These conditions never fail to present themselves during the height, or as it is called the *status* of the disease, though during the earlier period they may escape recognition, and in the later, the active hypertrophy of the heart's muscles gives place to fatty degeneration, so

that the heart sounds become soft and faint, and the pulse feeble and compressible.

The question now arises, to what are we to attribute this pulse of high tension and hypertrophy of the left ventricle?

According to Dr. George Johnson, who first drew attention to the thickened condition of the small arteries in chronic Bright's disease (*Medico-Chirurgical Transactions*, vol. xxxiii.), it is due to an impure state of the blood. In consequence, he says, of the degeneration of the kidney, the blood is morbidly changed; the minute arteries throughout the body resist the passage of this abnormal blood, containing as it does in excess urinary excretory matter, and being also deficient of some of its own normal constituents. As a consequence of this resistance, the internal longitudinal and the external circular muscular fibres of the small arteries are considerably increased, and the external fibrous coat of the vessels is also thickened; whilst with these changes the left ventricle of the heart becomes simultaneously hypertrophied.

Sir W. Gull and Dr. Sutton on the other hand maintain (*Medico-Chirurgical Transactions*, vol. lv.), that the thickening is due to a "hyalin-fibroid" formation in the walls of the minute arteries throughout the body, and a hyalin-granular change in the corresponding capillaries; that this change occurs chiefly outside the muscular layer, but also in the tunica intima of some arterioles, whilst the muscular layer of the affected vessels is often atrophied in a variable degree. They also maintain that the kidney disease does not give rise to this vascular change, since whilst it may be found in cases when the kidney is much contracted, it may be met with in kidneys but little affected, and even healthy. They therefore hold that these changes are due to a general morbid state, and are the primary and essen-

tial condition, when found co-existing with granular kidney, though extensive degeneration of the kidney may occur without their development. They also explain the cardiac hypertrophy as arising from the impediment caused by the diminished elasticity of the arterial walls, from the deposition of this "hyalin-fibroid" material in their walls, the heart having to contract with greater force to carry on the circulation.

It will be seen from the foregoing statement that the points in dispute are sharply defined. Dr. Johnson maintaining that the change in the small arteries and the left ventricle are simultaneous, and are a secondary consequence to the renal obstruction. Whilst Sir W. Gull and Dr. Sutton contend that the thickening of the arterioles is due, not to muscular hypertrophy, but to "hyalin-fibroid" formation in their walls, and that the hypertrophy of the heart, is not simultaneous with the change in the vessels but consequent upon them, whilst these changes are primary to the morbid state of the kidney. It is difficult to harmonize

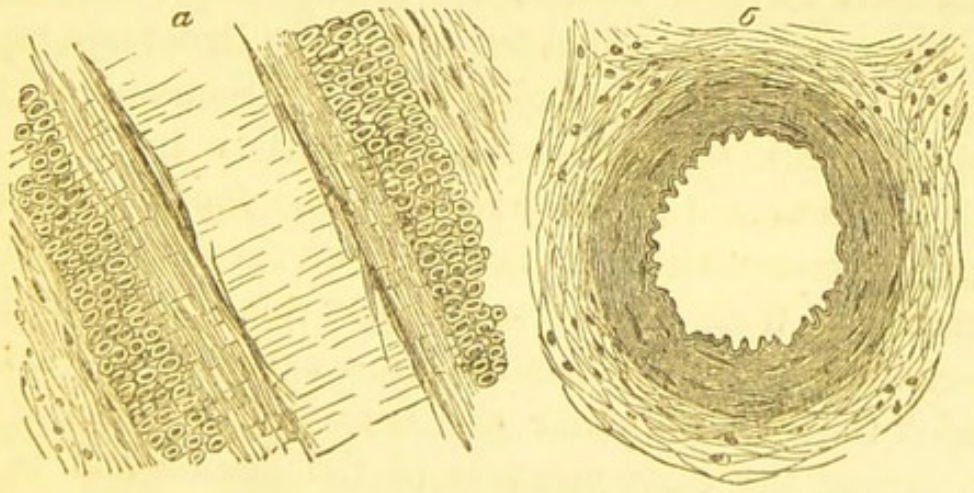


FIG. 2.—Thickened Arteries from Granular Kidneys. (*a*) Longitudinal, (*b*) Transverse Sections (Green's *Pathology*).

views so directly opposite as to questions of fact. With

regard to the thickening of vessels, subsequent observers have confirmed the statement of both parties, and have described the hypertrophy of the circular and longitudinal fibres as seen by Johnson, as well as the hyalin-fibroid changes described by Gull and Sutton. Indeed Dr. Saundby in a valuable communication (*Pathological Society's Transactions*, Vol. XXXI), has shown that in two vessels taken from the same kidney, one had well marked fibroid changes, with little or no hypertrophy, in its walls, whilst the other was almost entirely made up of muscular fibres; "near the inner margin, however, some fibres of elastic tissue were recognised, and some of the cells in the neighbourhood were more like connective spindle cells, than muscular fibres, whilst a few were round and oval, suggestive of the probability of a transition taking place." Dr. Saundby thinks that Gull and Sutton only err in denying the existence of the hypertrophy of the muscular coat, which though not constant is quite common, and he also thinks that some of their drawings were made from vessels like the second one described, but that owing to some imperfections in their histological manipulation they gave only blurred and indistinct features to the structures represented. Concurring entirely with Dr. Saundby in this matter, I think that the relative proportion in which the two conditions will be observed, will be found to depend on closer examination on the stage of the disease and its character. With regard to the part relatively played by hypertrophy and the fibroid-hyaline substance, I venture to think that the muscular elements will be found in excess during the early progress of the disease and at its height, and that the fibroid changes will be found in cases of longer standing, since we know that long continued arterial tension is favourable to the development of fibroid changes, and these probably when they supervene, replace or obliterate the muscular elements.

These cardio-vascular changes are observed in both forms of granular kidney, the pale and the red, but they develope in a different manner in each; (*a*) in the pale granular kidney, the result of acute or sub-acute inflammation, they are not observed in the early stage, whilst the kidneys are still large and tolerably smooth, but they gradually develope as the process of contraction goes on, though even in advanced stages the cardiac hypertrophy and vascular tension rarely reaches the high grade observable, often at a very early period, in red granular kidney. In the pale granular kidney the vascular changes are brought about in the following way, whilst the kidneys are still large and smooth, the quantity of water eliminated by them is extremely scanty, consequently, if the same amount of water be ingested daily, the volume of blood in the system is increased and the arterial pressure augmented throughout the body. In order to secure a sufficient secretion of urine, increased cardiac force is required. This is often not sufficient, and the over distended vessels relieve themselves by exuding their aqueous serum into the tissues (dropsy), a condition which varies inversely with the amount of urine secreted. For if by means of digitalis we supply the deficient cardiac power, and by diuretics stimulate the renal function, the dropsy diminishes *pari passu* with the increased flow of urine. The good effects resulting from the administration of digitalis in these cases point strongly to the fact, that increased cardiac action is required, and which nature under favourable conditions herself supplies. For as these cases progress we find after a time the area of cardiac dulness increasing, the pulse acquiring a higher degree of tension, the excretion of urine becoming more copious, whilst the tendency to dropsy diminishes. In this form of chronic Bright's disease, then, I think the cardio-

vascular changes may be said to fairly follow on the disease of the kidney, and are not due to a general morbid state, they however never attain a very high grade in this form of contracting kidney.

(*b*) But with the case of the typical small red granular kidney the case is very different. Here at the very onset apparently, we meet with considerable hypertrophy of the left ventricle and a hard tense pulse, sometimes without any material change in the urinary secretion to lead us to suppose there is anything amiss with the kidneys, although in the generality of cases there is increased secretion, and a trace of albumin, but the latter is not infrequently absent at an early period, and the only symptoms we have often for months, is powerful cardiac action, hard pulse, and an abundant secretion of urine. As the case goes on, we find albumin appears, sometimes intermittently if not present before, and increasing if it has been, hyalin casts begin to make their appearance and then we recognise the full character of the renal affection. But there is also another point, these patients at quite an early period, sometimes before the full development of the renal symptoms, at all events as soon as they are observed, are generally found to be the subjects of extensive atheromatous degeneration. Now it can hardly be argued, that all these vascular changes are the result of the disease in the kidneys, and are caused by the retention in the blood of urinary matters that ought to be eliminated. For even if we admit that cardiac hypertrophy and arterial tension are but rarely noticed before the renal changes make themselves manifest, we cannot with the evidence before us hesitate in coming to the conclusion that they run at least a *simultaneous* course, and that the cardio-vascular changes associated with the typical red granular kidney, are due to a

general morbid state which is the primary and essential condition. With regard to the nature of the morbid state that induces these changes in the vessels and in the kidneys, they may I think be referred to one or other of the following conditions either singly or combined. (*a*) *Increased tissue metabolism* or long continued over stimulation, from the ingestion of a highly nitrogenised diet, or the excessive use of alcohol. (*b*) *Toxic agencies* as caused by gout or rheumatism, either hereditary or acquired, or by an extraneous poison such as lead. (*c*) *Nervous influences*, these may act by leading to early textural decay by direct influence, as from the exhaustion caused by over-work, anxiety, etc. They may be also of a reflex character, chronic irritation of the kidney structure leading to cardio-vascular hypertrophy. This supposition is the more probable since Dr. Dickinson, and subsequently others, observed cardio-vascular changes to occur under the irritation produced by the presence of renal calculi, and it is not improbable that the irritation caused by the long continued secretion of highly acid urine, may have the same effect (see Gouty Nephritis).

In addition to the above mentioned changes in the heart and vessels in granular disease of the kidney, chronic arterial inflammation leading to an atheromatous condition of the vessels, is to be constantly observed. The causes that produce it are, as Dr. Moxon has stated, due to the increased strain thrown on the vessels by the long continued arterial tension, though perhaps in some measure aided by the impaired condition of nutrition generally. Owing to this arterial degeneration, accompanied by the forcible action of the hypertrophied left ventricle, hæmorrhages are of frequent occurrence, hence cerebral apoplexy is a common termination of a case of granular disease of the kidney; whilst hæmorrhages of a less formidable

nature, as epistaxis, hæmorrhage into the retina, from bowels and lungs, and ecchymoses under the skin are of frequent occurrence. When hæmorrhages occur to any extent and are repeated at frequent intervals, the prognosis becomes very grave indeed, but I cannot agree with the statement of Bartel, that every case of well established hæmorrhagic cachexia does not survive more than a few weeks after the commencement of the bleedings. I have known patients with granular kidneys survive for a considerable period after severe and repeated epistaxis; and even after an extensive cerebral hæmorrhage, their lives being prolonged by the enforcement of almost absolute rest, and the employment of a non-nitrogenous diet and complete abstinence from alcohol.

A reference to the derangements of the circulation in diseases of the kidney would not be complete without an allusion to the vascular condition which, according to Dr. Pavy, is the key to the explanation of the saccharine condition of the urine in diabetes. Dr. Pavy is of opinion that diabetes is due to a failure of the assimulative function of the liver, which instead of storing up glycogen, allows it to pass off as sugar to the blood. He has shown that venous blood is favourable, and oxygenated blood is unfavourable to the storing up of glycogen. Now no organ in the body is supplied with venous blood in like manner to the liver, so, in correspondence, nowhere does glycogen exist to a like extent. But under circumstances of vaso-motor paralysis, affecting the vessels of the chylo-poietic viscera, blood unduly charged with oxygen sometimes reaches the liver by the portal vein, thus inducing glycosuria. In confirmed cases of diabetes the vaso-motor paralysis may be general, and Dr. Pavy points to the bright red appearance of the tongue, so often noticed in severe cases of diabetes, as an evidence of this hyperæmic

condition, the idea suggesting itself that the blood is flowing through the organ without being properly deprived of its arterial character. The peculiar florid injection of the capillary vessels of the face, sometimes observed in severe cases of diabetes, is probably due to the same cause.

4. **Derangements of the Nervous System.**—Many symptoms indicative of disturbance of innervation manifest themselves in relation to both acute and chronic diseases of the kidneys, and which may be considered as belonging to either of the three following conditions, uræmia, acetonæmia, neuralgia.

(1) *Uræmia* is a clinical collective name used to describe very various functional disorders of the nervous system which are sometimes acute and sometimes chronic.

Acute Uræmic attacks may occur in the chronic stage of Bright's disease as well as in the acute. Their characteristic features are powerful epileptiform convulsions and coma. As a general rule the attacks commence with a series of epileptic fits quickly succeeding each other, and as these pass off a comatose condition succeeds. In others the attack is ushered in by a violent single convulsion which in some cases is followed by a noisy delirium which after lasting some hours suddenly passes into a profound coma. Cases occasionally occur, however, in which the patient passes into deep coma without its being preceded by convulsions. Acute uræmic attacks may come on suddenly without warning but generally there is some previous indication of the coming storm. The patient complains of headache; the pulse often becomes remarkably retarded: there is dimness of vision perhaps temporary blindness (*uræmic amaurosis*), without any ophthalmoscopic indications and which passes off as quickly as it comes on. If the urine has been examined daily we find shortly before the attack that the quantity secreted is considerably diminished as is

also the amount of solid matter excreted. In the attack itself in addition to the rapidly recurring convulsive seizures, we find that sensibility is diminished, whilst reflex irritability is increased, the pulse previously retarded becomes small and very rapid, the temperature rises to a considerable degree, even occasionally to hyperpyrexia. In the coma there are occasional convulsive movements and twitchings, the teeth are ground, and the fæces, and the urine if the latter is secreted at all, are passed involuntarily. Recovery even from this formidable condition is not at all unusual under proper management, and patients may continue to live on for years without the recurrence of uræmic poisoning in an acute form.

Chronic uræmia is distinguished from the acute form by the fact that the convulsive attacks rarely assume the character of violent epileptiform seizures, nor does the patient pass at once into a state of deep coma. When once established the symptoms of chronic uræmic intoxication may continue for many days or weeks, or may never be completely absent till the patient dies. The chief symptoms are twitching of certain groups of muscles. Headache, chiefly occipital and often of a neuralgic character. Intolerable itching of the skin. Vomiting, especially of a morning, on rising before food is taken, the vomit being frequently of low specific gravity and of alkaline reaction, accompanied with troublesome hiccup. Asthmatic paroxysms, chiefly occurring at night, and accompanied with extremely rapid pulse, and often with anginal pains over the region of the heart and in the epigastrium. The sleep is greatly disturbed, often preceded by distressing jactitation, whilst the rest is broken by dreams during which the patient grinds his teeth and often gives utterance to moans and cries of anguish. Local motor and sensory paralyses also are frequently complained of. The vision is also more or less impaired,

and the ophthalmoscope generally reveals hæmorrhage into the retina and other changes (*vide* fig. 3, p. 35), though uræmic amaurosis does occur without these been present. The connection subsisting between these nervous symptoms and diffuse inflammation of the kidney was early admitted, though considerable difference of opinion has been since expressed with regard to their causation. The views that have been brought forward may be conveniently considered as expressing the chemical theory and the mechanical theory respectively.

The chemical theory was originally suggested by Christison and was based on the supposition that a considerable accumulation of urea occurred in the blood. Subsequent experiments have shown that considerable quantities of urea injected into the vessels of animals do not induce convulsions of a uræmic character, unless the animals are nephrotomised, besides which clinical experience teaches us that large accumulations of urea may occur in the blood without the occurrence of uræmia. These facts struck Frerichs at an early stage of the controversy, and he brought forward the view that though urea itself might be innocuous, or fail to induce convulsions of a uræmic character, yet if converted into ammonium carbonate in the system its poisonous action at once declared itself. He based this theory of "ammonæmia" on the following arguments, viz., that in the breath of patients suffering from kidney disease ammonia can be demonstrated, and that ammonia is also found in the contents of the stomach, the bile and other secretions; and that injections of ammonia into the veins of animals induce convulsions and stupor. To this it has been objected, that the presence of ammonia in the breath and secretions is no evidence of the decomposition of urea in the blood, but simply that the urea is transuded

to the mucous surfaces where it undergoes conversion into ammonium carbonate. In chronic Bright's disease there is no doubt that urea is found on the mucous surfaces; even in health it is even supposed to be present, since the most rational explanation of the formation of potassium sulpho-cyanate in saliva, is that which attributes it to the decomposition of urea in the mouth and and the union of the cyanogen with potassium sulphate. Moreover, analyses have failed hitherto in giving satisfactory proof of the presence of ammonium carbonate in the blood of animals poisoned with urea, or nephrotomised, or in the blood of persons dying from acute or chronic Bright's disease. Some observers have attributed the symptoms to other chemical substances, either present in excess, or of abnormal character. Thus D'Espine has found an increase of potash salts in the blood of scarlet fever uræmia, and has suggested that the symptoms are due to the well known poisonous action of potassium in excess. This view was originally suggested by Voit, who thought the potassium salt was yielded by a retrograde metamorphosis of muscular tissue in Bright's disease. Schiffer and Brieger have brought forward the view that uræmic convulsions are the result of the formation in the blood of alkaline ptomaines. These suggestions, though plausible in themselves, are not supported with sufficient evidence to allow as yet of positive criticism, though they suggest a field for valuable research.

The mechanical theory was originally proposed by Traube it is based on the following propositions; (*a*) that in chronic Bright's disease there always exists a diluted state of the blood serum; (*b*) that uræmic convulsions are almost invariably associated with that form of kidney disease characterized by hypertrophy of the left heart and tension of the aortic system; (*c*) that in all cases in which

the brain had been examined after death, he had been able to confirm the existence of a more or less considerable œdema of that organ together with marked bloodlessness From these considerations he assumes that the phenomena of an uræmic attack depend on an œdematous effusion of the brain brought about by increased pressure acting on diluted and watery blood serum. The objections urged against this view may be thus summarized:— (*a*) Uræmic convulsions though these do not occur in chronic nephritis till cardio-vascular changes appear, often accompany acute nephritis, a condition then closely resembling that of a nephrotomised animal; viz., a general poisoning of the body with excretory materials. (*b*) That the chronic nephritis associated with high arterial tension, is attended with a profuse secretion of urine, and the blood in this condition is not hydræmic, and also that while the high tension is maintained, œdema is not observed in this form of chronic nephritis. (*c*) That the form of chronic nephritis which is generally associated with œdema is usually unattended with uræmic attacks. In addition to these considerations, Cohnheim and others have objected to Traube's view on experimental grounds.

The view that I am disposed to take of this disputed question is that considering the complex nature of the symptoms we term uræmic, we must not look for an explanation of them merely as regards the retention of a poisonous agent in the blood, or to a localized œdema of the brain, but to a general condition of the whole system. If we nephrotomise an animal, for example, there is not merely an accumulation of the urinary constituents in the blood, but there is also a general accumulation of the excretory products in the tissues of the body. Thus Hoppe Seyler examined both the blood and tissues

of a patient who died of acute uræmia, and found that whilst the blood contained 1·27 parts of urea per 1000, the muscles contained 1·59 parts of kreatin. Oppler (*Virch. Archiv*, Bd. 21, s. 260) also found a large quantity of kreatin, as well as leucin, in the muscles of nephrotomised animals, and argues from this, as well as from Hoppe Seyler's cases, that the result of the stoppage of the kidney functions is, for enormous quantities of decomposition products to arise and accumulate in the muscles, and he considers himself justified in coming to a conclusion that the nervous centres are similarly affected, and that alterations of chemical composition are brought about in them. Schottin has shown that the relation of the extractive substances to the albumin of the blood serum are very considerably changed in chronic renal disease, for whereas in health they are as 5 to 100 respectively, in a case of degenerated kidneys he found them as 40 to 100. Another point to which attention may be drawn is the fact that in uræmia attended with suppression of urine, a considerable amount of acid is retained in the system (equal certainly to two grammes of oxalic acid daily), and even in chronic Bright's disease diminished alkalinity takes place, for Garrod has pointed out that, as in gout and in collapsed cholera, the blood in chronic albuminuria often approaches the neutral point. Now when we reflect on the grave constitutional disturbances that follow on attempts to reduce the alkalinity of the blood in animals, and the diminished power of oxidation that follows on such reduction we can see how this condition reacts on the tissues already overcharged with the products of arrested metabolism. Especially is this the case with the nervous system which resents more rapidly and distinctly than any other organ disturbances of its nutrition.

(2) *Acetonæmia*:—Closely allied to uræmia is the comatose

condition which so often terminates cases of diabetes, more especially those occurring in young subjects and of an acute character. Since acetone, or an acetone yielding substance, is frequently found in the urine of these cases, the coma is supposed to be due to poisoning of the blood by this substance. Considerable doubt, however, exists as to the real nature of this coma and the agency by which it is brought about. Free acetone has not as yet been discovered in the blood, though there is little doubt that this body can be obtained from the urine. Indeed recent researches show that the peculiar mahogany-red coloration with ferric chloride, and the iodoform reaction, sometimes developes in urine apparently healthy, as if acetone, or acetone yielding substances, might be present in small quantities under normal conditions. It has also been shown to exist in very appreciable amounts in other morbid conditions besides diabetes, (Windle, *Liverpool Medico-Chirurgical Journal*, Jan. 1884), (Riess, *Zeit. f. Klin. Med.*, Bd. vii. Suppl. 1883), and this is especially noticeable in cases of anæmia. The introduction, experimentally, of large quantities of acetone, or of acetone yielding substances, such as ethyl diacetate, and aceto-acetic acid, into the bodies of animals seems to be followed by no ill effects (Frerichs, *Zeit. f. Klin. Med.*, Bd. vi. 1883), and large quantities 10 to 15 grammes, may be taken before the urine gives the peculiar reaction of acetone. The question therefore arises whether diabetic coma is due to its sudden and excessive formation and accumulation in the blood, or whether we must regard diabetic coma as due to other causes. In the first place it is important to distinguish especially the form of coma, and limit it to one characterized by certain special features. Probably all cases of diabetes die more or less in a comatose state, but the acute diabetic coma has

certain distinguishing symptoms which cannot fail to attract attention. In the first place its onset is sudden commencing with sharp epigastric pain and gastric disturbance, sometimes actual vomiting, which vomit has been observed in some cases to contain blood; in a few cases purging has been noticed. Almost coincidently the patient is seized with dyspnœa of a peculiar panting irregular character, "air hunger;" then sets in a condition of restlessness which often passes into delirium of noisy character. Almost suddenly the restlessness and delirium cease and the patient falls into deep coma. The temperature at the onset is usually below the normal; the pulse irregular at first, becomes on the supervention of coma extremely weak, rapid and thready. The odours of acetone may be present throughout, but usually diminishes markedly from the onset of the attack. Many of the symptoms above enumerated have a close parallelism with those that are attendant on death in acute yellow atrophy, phosphorus poisoning, or poisoning by the injection of acids experimentally into the blood, whilst the post-mortem changes bear out this parellelism to a further extent, since in some of the cases of acute diabetes recorded, fatty degeneration more or less intense, together with a lactescent condition of the blood seem allied to the acute fatty changes produced by phosphorus poisoning, or poisoning by oxalic acid, sulphuric acid, bile acids, etc. These considerations certainly seem to warrant us in regarding the acute forms of diabetic coma as due to a toxic agent; and that this agent to be of an acid nature, probably, derived from alcoholic fermentation of the glucose in the blood. Nor does the fact that acetone is found in the urine when no sugar is present, invalidate this view, since it is probable that small quantities of acetone or of acetone yielding products are constantly being formed in the stomach during the

process of vinous fermentation of the saccharine and amylaceous constituents of the food, and absorbed into the blood, indeed in some forms of dyspepsia especially in those caused by alcoholism, the odour of acetone can oftentimes be detected in the breath. Under ordinary circumstances, however, the acetone thus absorbed is speedily destroyed in the blood; but occasionally and especially in conditions of anæmia when oxidation is but feebly conducted, the substance is not completely destroyed and some portion of it appears in the urine. In diabetes the acetone yielding substance is probably present in the blood to some extent in all cases, and if as is now most generally held, this substance is aceto-acetic acid it accounts for the highly acid reaction of the urine so characteristic of the disease. When the quantity formed is not excessive and the kidneys maintain their functional activity the substance is eliminated without causing any disturbance in the body, since we know by experiments on animals, that considerable quantities can be ingested without evil results; but when excessive quantities are formed, or what perhaps is more likely, when the kidney functions fail, an excessive quantity is suddenly accumulated in the blood then toxic symptoms immediately manifest themselves. This failure of kidney function may be brought about simply by exhaustion consequent on long continued over activity of function from the secretion of a urine loaded with abnormal material (glucose), besides containing excess of urea and water.

When the poisoning is acute, and the amount of the toxic element very great, then on post-mortem examination we find the maximum of fatty changes, the lactescent condition of the blood, the fat emboli and the acute fatty changes in the hepatic cells and in the muscular fibres. When the process is less acute, then we meet with fatty

changes of a less pronounced character, and which may escape recognition unless diligently looked for. With regard to the nature of the acetone yielding substance as it exists in the blood, a difference of opinion still exists, it is probable, however, that it is aceto-acetic acid and not ethyl diacetate as first supposed, the reasons, chemical and clinical, for this assumption I have already given (*Path. Soc. Trans.*, 1883, p. 331). This substance, however, does not probably exist in a free state in the blood, but is probably combined with an alkaline base, most likely soda. As aceto-acetate of soda it is conveyed to the kidneys and other mucous surfaces, in the capillaries of which it probably undergoes decomposition into alcohol and acetone, though as far as the urine is concerned some portion of it passes through as acetic acid, since many diabetic urines undoubtedly contain a considerable amount of this acid. Minkowski and Külz have also discovered an acid, resembling pseudo-oxybutyric acid in diabetic urines.

In addition to death by acute coma, a fatal termination sometimes occurs very suddenly without any evidence of previous intoxication, rather through sudden failure of the heart, syncope, than by coma. This condition together with others relating to the post-mortem appearances in the bodies of persons dying of diabetes will be referred to in the chapter set aside for the consideration of that disease.

(3) *Neuralgia.*—Severe attacks of neuralgia are not at all uncommon in patients suffering from chronic renal disease, especially that form associated with cardio-vascular changes and is another evidence of how profoundly the nutrition of the nervous centres is affected. A common form is severe racking pain in the occipito-cervical region; whilst visceral neuroses are frequently complained of, the chief being anginal seizures, occurring generally at night-time, associated with attacks of dyspnœa (renal

asthma), and racking pains commencing in the epigastrium and shooting down into the abdominal and pelvic regions. In diabetes the patient often suffers from similar neuralgic seizures, the most common of which are those especially affecting the stomach and liver. These pains vary in intensity in different cases, in some they amount to no more than a gnawing feeling like the cravings of hunger, but in others the attacks are excruciating, "like having the liver forcibly compressed and twisted out of you" as a patient once expressed it to me. Diabetic patients also suffer greatly from lumbar and sciatic pains. Of the latter there are two kinds, one following the course of the nerve from the hip to the ankle, the other being deeper, seated apparently in the bone, generally limited to the region of the hip, but sometimes extending down the whole length of the femur. The pain has been spoken of as if the bone was being crushed or bruised. These sciatic pains have been alluded to by some recent writers as if they were a newly discovered clinical feature, but although not prominently noticed by some of the later authors who speak of them as radiating lumbar pains, still the distinction between lumbar pain and pain in the hips and sciatic region was early made. Thus Paracelsus enumerates among the symptoms of diabetes, "dolor spinæ quæ plerumque in ischiâ incipit." These sciatic pains have been considered to be of a rheumatic character, and the salicylates have been employed with benefit, in some cases, for their relief. But admitting the value of the salicylates in some forms of glycosuria and even in some cases of established diabetes, and also the benefit derived by their use in the sciatica sometimes accompanying these forms, yet I am not disposed to believe that this painful complication is dependent on rheumatism. Indeed the fact that the pain comes on most severely shortly after food and decreases in

severity as the influence of the meal passes off, points rather to an increase of the saccharine matter in the blood.

5. **Ophthalmoscopic changes.**—The special changes which may be observed in the retina and its vessels in the chronic forms of Bright's disease, according to Gowers from whose work on *Medical Ophthalmoscopy* the following summary has been taken, are as follows:—

(1) A diffuse slight opacity and swelling of the retina, due to œdema. (2) White spots or patches of various size, for the most part the result of degeneration processes. (3) Hæmorrhages. (4) Inflammation of the intra-ocular end of the optic nerve. (5) Atrophy of the retina and nerve may sometimes result from and succeed the inflammatory changes. These changes may affect one eye only.

These conditions are not, however, equally prominent in every case, but vary according to the stage and form of the disease. According to the element that is most conspicuous four types may be distinguished. In the *degenerative form*, which is most common, small whitish spots rounded at first, but becoming irregular as they increase, form in the retina. These may be observed near the optic nerve entrance, or at a distance often very small white spots are arranged in a radiating manner round the macula lutea. Sometimes larger spots coalesce to form white areas, which surround the disc. These changes may occur without any alteration of the disc itself, but sometimes its edge becomes blurred, and the tint reddish-grey. Hæmorrhages are of less frequent occurrence than in the other forms, when they occur they are usually adjacent to the white spots. When small they have a striated arrangement, the blood lying between the nerve-fibres; they are often parallel to vessels. When larger they are often flame-shaped or irregular. Irregular and rounded hæmorrhages are in the deeper layers of the retina. In the *inflammatory form* there

is general swelling of the retina with obscuration of the disc. The arteries are concealed, whilst the veins if visible are tortuous and distended. Hæmorrhages are numerous, large and striated. White spots, more or less

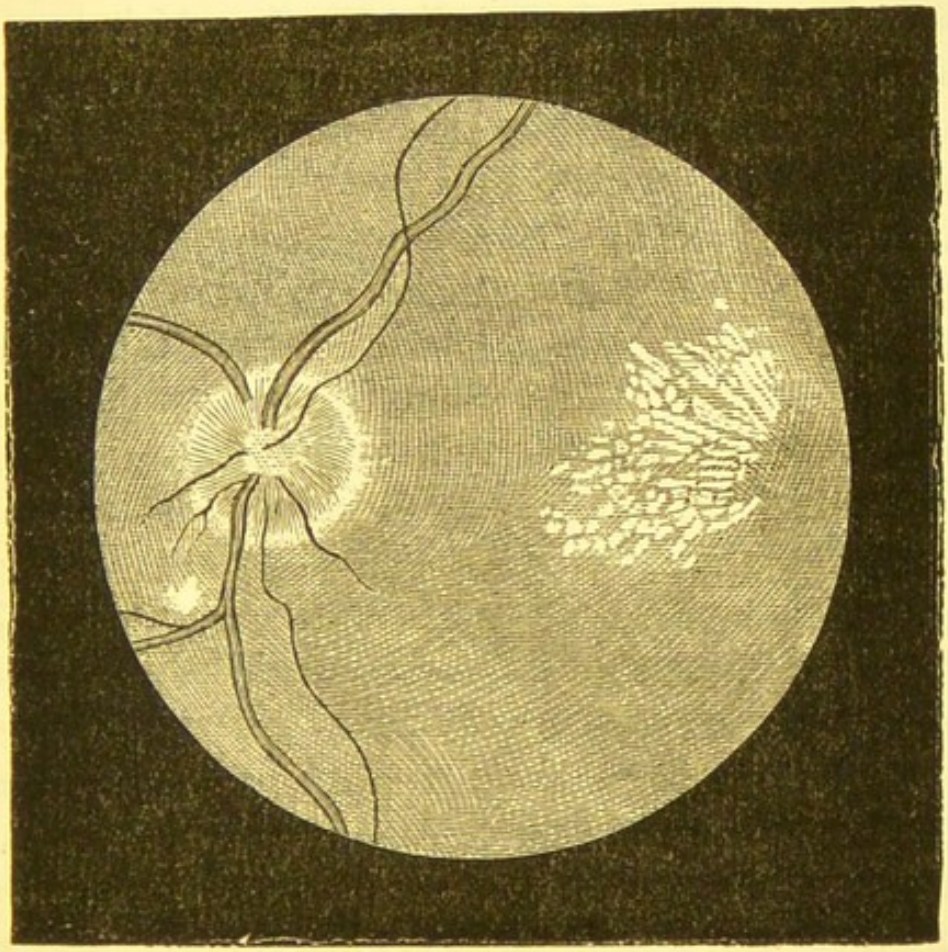


Fig. 3.—Albuminuric Retinitis.

uniform in character, especially in acute cases, are abundant, large, rounded, and soft edged. In the *neuritic form*, the edges of the optic disc are veiled by a greyish-red swelling of moderate degree. The arteries are narrow and the veins curve over the side of the swelling. On oblique illumination, a white reflection may frequently be observed at certain spots on the surface of the swelling. Slight degenerative changes usually accompany this form, and careful examination will detect one or more white spots near the neuritic swelling. Hæmorrhages are

of rare occurrence. This form when it subsides, may be followed by atrophy. The *hæmorrhagic form* is characterised by the size, number, and predominance of the hæmorrhages, accompanied with but slight degenerative change or inflammation of the disc or retina. In the earlier stages vision is usually unaffected, but as the changes progress, it becomes more dull (amblyopia), though sight is rarely altogether lost, colour vision may, in rare cases, be affected.

With regard to the causes producing the degenerative, inflammatory, and neuritic forms, only hypothetical suggestions have been advanced. The hæmorrhage, no doubt, results from rupture of degenerated vessels, under the stress of increased pressure from an hypertrophied left ventricle. In addition to these well marked alterations, the arteries of the retina, especially in granular kidney, undergo diminution from one-half to one-third of their volume, and when slight swelling of the retina co-exists, the arteries may be invisible beyond the papilla. In these cases as Dr. Gowers has pointed out, the pulse is characteristically incompressible. The frequency of observation of these retinal changes, depends much on the stage of the disease, when it first comes under notice, and its character. Thus they are most commonly met with in the granular kidney, and rare in lardaceous disease, whilst in all forms the disease must have been in progress some time before they occur. Dr. Gowers agrees with the statistics collected by Eales who in one hundred cases of chronic disease, found retinal changes in twenty-eight per cent, or one in every three and a half cases. Besides these characteristic changes, other conditions may from time to time be noted, as hæmorrhage and degeneration of the choroid, detachment of the retina from serous effusion between it and the choroid; hæmorrhage

into the vitreous; and aneurismal dilation of the small vessels of the retina.

Temporary amaurosis may occur during the progress of chronic Bright's disease, without there being any ophthalmoscopic indication whatever to account for it, it is probably only a manifestation of the state of general uræmic intoxication, which accompanies granular degeneration of the kidneys.

In saccharine diabetes the patient is liable to impairment or loss of sight; the conditions producing this are:— (1) Cataract. (2) Impaired condition of the blood. (3) Changes in the fundus oculi.

Diabetic cataract is usually large and soft, and occurs in an advanced stage of the disease. That sugar has a direct action in producing this opacity of the lens, seems to be proved by the fact that frogs placed in sweetened water, speedily become cataractous. Amblyopia, with the absence of ophthalmoscopic appearances, is not of infrequent occurrence; it is attributed to the circulation of some toxic element in the blood, but of what nature is not determined. It can hardly be the amount of sugar, since no proportion seems to exist between the excretion of sugar and the degree of amblyopia. Although frequent in confirmed and severe cases, it is as far as my experience goes, quite as often complained of in mild cases. It may be interesting in future enquiries to ascertain if this symptom bears any relation to the amount of acetone found in the urine. The changes observed in the fundus oculi, may be thus enumerated. Simple atrophy of the optic nerve has been observed in some cases. In a few there has been a central defect in the field of vision, for colour or white, as in tobacco amblyopia, and this when the influence of tobacco could be excluded. Rarely retinal

changes are observed, these Dr. Gowers describes as bearing a resemblance to those of albuminuria, and still more so to those of pernicious anæmia. The retinal changes, when present, are hæmorrhages chiefly found in the nerve fibre layers, these may lead to secondary retinitis, or by their infiltration into the vitreous may cause opacities in it, or even hæmorrhagic glaucoma. White spots of degeneration are also frequently found scattered over the fundus of the eye, and atrophy of the optic nerve has been observed. The presence of considerable optic neuritis in cases of diabetes, mellitus and insipidus, would lead one to suspect the existence of organic brain disease.

6. **Derangements of the Respiratory System.** – Pulmonary complications form the most frequent termination of chronic renal disease. *Renal asthma* occurs in its most marked form in patients suffering from primary contracted kidney, and apparently depends upon a uræmic condition of the blood, since in many cases we are unable to attribute it to any other cause except nervous spasm. In some cases the frequency and intensity of the attacks, apparently correspond to an increased tension of the radial pulse, with a strong heaving, but somewhat irregular, action of the heart. But severe paroxysms may occur quite independently of any changes in the pulmonary or circulatory systems, and indeed in persons in every respect apparently healthy. In two patients, one a country gentleman, who were able to take strong and even fast exercise without distress to their breathing, attacks of renal asthma first called attention to the condition of their kidneys. Both had thought themselves strong hearty men, and attributed the seizures to attacks of indigestion. The paroxysms of renal asthma almost invariably occur in the night time, and during the earlier hours of the night. When they come on in the day time it is generally in con-

sequence of some nervous agitation, or as a prelude to more severe uræmic manifestations. The paroxysms, however, never attain the severe grade, nor come on so suddenly as in pure nervous asthma, or as in the dyspnœa associated with acetonæmia. The course is usually as follows, soon after the patient has gone to bed he experiences a sense of oppression at the chest, often accompanied with pains, which radiate from the cardiac regions, into the epigastric and hypochondriac regions. Soon this feeling of weight and oppression is succeeded by increased difficulty of breathing, and inspiration becomes short and laboured, whilst rhonchus is heard over the whole chest. The lips and face, however, rarely become livid, and the paroxysm after lasting about two hours, gradually subsides. The attacks are often followed by an increased flow of pale urine of low specific gravity; even in cases were it is already abundant, the increase is sufficient to attract the patient's attention. The paroxysms come on usually for several nights in succession, and then may leave the patient free, perhaps for a considerable interval. Neither their going, or their coming, can be accounted for by any alteration in the general condition of the patient. They will attack the same individual on one occasion when he seems to be in fair average health, and fail to recur when he falls back, and *vice versa*. Equally associated with a toxic condition of the blood is the peculiar panting dyspnœa that preceeds or accompanies acute diabetic coma, and which is supposed to be due to the presence of an acetone yielding substance in the blood. This dyspnœa has been likened to panting, caused in an animal, whose vagi have been cut, and has been well described as "air hunger," as characterising the nature of the dyspnœa, which is caused not by the difficulty of obtaining air by obstruction of the air-passages, or by spasm

as in the case of renal asthma, but by an increased demand for air. This form of dyspnœa sometimes preceeds diabetic coma by some hours, and may be the sole premonitory symptom. Thus, in a case Dr. J. Duncan asked me to see with him, a patient who for some weeks had been only slightly ailing, but whose urine contained traces of sugar, was seized early one morning with dyspnœa, which continued about six hours, when coma suddenly set in which speedily proved fatal. In this case the dyspnœa was the only indication for some hours, that the disease which was apparently a mild form of diabetes, was assuming a rapidly fatal character. *Bronchitis, pneumonia, pleuritic effusions and œdema of the lungs* occur as complications in both forms of chronic Bright's disease, though clinically, with the exception of pneumonia, they are essentially associated with the pale granular form. When met with in the interstitial form it is towards the end of the disease, when owing to the failure of the hypertrophied heart and vessels, the secretion of urine is diminished, and a tendency to dropsy is established, whilst morbid elements accumulate in the blood. The bronchitis of the pale granular kidney is always more or less associated with œdema of the lungs. The pneumonia of this form of Bright's disease is of the ordinary croupous form, whilst when it occurs in the interstitial form, it generally assumes the character of "pulmonary apoplexy" and is usually attended with profuse hæmoptysis. Effusions into the pleura, pericardium and peritonæum are nearly always associated with the pale granular kidney, when they occur in the progress of the other form, it is towards the end, and even then they are never so formidable as in this variety. They usually come on insidiously and rapidly, and the amount of fluid effused is always considerable. They are rarely attended with severe pain or fever. In many cases there is no pain at all and

only a moderate rise of temperature, and our attention may be only called to the existence of this complication by the increased difficulty of breathing and decubitus of the patient. Phthisis though frequently associated with chronic Bright's disease, is rarely developed during its course, and is nearly always an antecedent condition. Nephritis, moreover, when it occurs in a phthisical subject is almost invariably preceded, or is accompanied by waxy degeneration of the kidney. Phthisis, however, frequently occurs in diabetes as a secondary complication, especially in those cases that run a chronic course. Indeed in referring to the older writers, we find that phthisis is mentioned as of such frequent occurrence, as to be considered almost "universal." Though this universality cannot be maintained in the present day, the general dependance of phthisis in many cases of diabetes is abundantly proved. At the recent debate at the Pathological Society, (*Transactions*, 1883), Dr. Stephen Mackenzie brought forward statistics from the London Hospital to show that out of thirty-seven cases, pneumonic or phthisical mischief was present in twenty. Dr. Windle (*Dublin Medical Journal*, September 1883), has recorded the result of 333 post-mortems on diabetic subjects, and found the lungs normal in seventy-five instances only; in the remaining 258 cases, phthisis was present in 109 cases, whilst the other cases showed recent pneumonia, congestion, broncho-pneumonia, etc. Dr. Douglas Powell, however, at the same debate questioned whether phthisis and diabetes had anything in common, and brought forward statistics from the Brompton Hospital, which showed that out of 136 cases, in which the urine of phthisical patients was examined, in not one case was sugar found. Dr. Powell's statistics, however, only prove that diabetes has no dependance on phthisis, whilst Dr. Mackenzie's and Dr. Windle's show the converse, viz.,

that phthisis, or some pneumonic changes likely to produce that disease, do not infrequently develope in diabetic subjects.

7. **Derangements of Digestion.**—Acute renal affections are almost invariably accompanied with more or less disturbance of the digestive organs. In acute nephritis, especially in the catarrhal form, in which the kidney is usually much swollen, vomiting is often a prominent symptom; in the less severe varieties, scarlet fever nephritis for instance, the disturbance is usually less marked, though there is always loss of appetite, if not a certain degree of nausea. Nausea, with or without vomiting, is also a very constant symptom when there is irritation in the neighbourhood of the capsule or pelvis of the kidney. Thus, it is frequently found attendant on perinephritis, when the capsule is pressed upon from without; in renal abcess, pyo-nephrosis, hydro-nephrosis and in a rapidly growing carcinoma, which distend the capsule from within; and in renal calculus, when the irritation is applied to the pelvis of the kidney. In all the above mentioned instances, including the vomiting of acute Bright's disease, the act is purely reflex, and is thus to be distinguished from the vomiting that occurs in the chronic forms of nephritis, and which is clearly due to a toxic condition of the blood (uræmia). This reflex gastric disturbance sometimes affords us timely notice of the invasion of kidney mischief. Thus, in scarlet fever if a patient, who has previously been convalescing favourably, complains of a feeling of nausea, the urine should be at once examined. But the most serviceable indication is in the warning it often gives in cases of obstruction of the lower urinary passages of the implication of the kidneys. And particular enquiries ought to be made into the condition of the urinary organs, in all cases of chronic "biliousness" especially in elderly persons.

The *vomiting* that occurs in the chronic forms of Bright's disease is, as already stated, due to the toxic condition of the blood and system generally and is often one of the earliest symptoms of chronic uræmia. The following characters may help us to distinguish the two forms. Reflex vomiting is usually attended with marked gastric disturbance, and though it may come on when the stomach is empty, food either nauseates or is at once ejected. The vomit consists at first of a glairy highly acid fluid, often containing undigested food, and is not very profuse; when long continued it becomes yellowish and subsequently green from the bile, which the action of vomiting provokes to flow from the gall-bladder into the duodenum and thence into the stomach. Uræmic vomiting on the other hand, at first is generally confined to the morning hours, usually on first rising in the morning, though later in the disease it may occur at any time of the day. The vomit is usually very profuse, of low specific gravity, and at first of slightly acid reaction though in the later stages of the disease it is often alkaline and sometimes contains urea. The gastric disturbance is very variable, many patients with chronic Bright's disease, especially with pale granular kidneys, have not only good appetites but are even ravenous at times, and digest their food with comfort. In others there is simply loss of appetite, especially as regards meat, but no indigestion. *Dyspepsia* when it occurs in these cases is usually the result of fermentative changes taking place in the stomach, especially with regard to the albuminous constituents of the food, with the formation of lactic acid, butyric acid and hydrogen in form of marsh gas, hence the sour rancid odour sometimes perceived in the breath and in the vomit of these patients. With granular kidneys, however, associated with cardio-vascular changes, there is generally considerable loss of appetite, and the ingestion of

food is often attended with severe epigastric pains, apparently of a neuralgic character. *Diarrhœa* is also a very frequent complication of chronic kidney disease, especially when there is dropsy. In the early stages it affords relief to the water logged body, but towards the end it is apt to become intractable and adds to the existing debility. It is therefore necessary to use caution in the employment of purgatives for the relief of dropsy when the disease is drawing to a close. Diarrhœa sets in suddenly when a peri-nephritic or renal abscess bursts into the intestines, the nature of the diarrhœa will be explained by the subsidence of the tumour and the appearance of pus in the motions. A *constipated* condition of the bowels is generally observed when there is any considerable enlargement of the kidney, owing to the compression of the large intestine which crosses both kidneys on their anterior surface. This constipation which is often overcome with difficulty, is often, especially in the case of malignant tumours, followed by severe diarrhœa, most difficult to arrest, if the means resorted to for its relief have been too active. Constipation too is the prevailing condition of the bowels in diabetes, the motions when the bowels are relieved being hard, dry and scybalous. In some cases it alternates with diarrhœa, the loose motions being often frothy and yeasty in appearance. The *tongue* presents no characteristic feature in renal disease, except in some cases of diabetes. In acute affections it is usually coated as in pyrexia generally. In chronic Bright's disease it varies according to the condition of the digestive organs being sometimes broad, flabby, coated and somewhat œdematous, whilst in other cases it is glazed, beefy looking and cracked. In diabetes too, the appearance of the tongue varies, but in some cases, and those I have noticed to be invariably severe, the whole of the tongue assumes a peculiar bright

red appearance, suggesting the idea that the blood is flowing through the organ without being properly deprived of its arterial character, and which Dr. Pavy believes is caused by vaso-motor paralysis of the vessels of the chylopoietic vascular system and which he considers to be very similar to the hyperæmic condition of the ear which is brought about by the division of the sympathetic in the neck.

8. **Derangements of the Cutaneous System.**—In acute inflammatory affections of the kidneys, the skin presents the usual character noticeable in pyrexial affections generally. In acute nephritis, however, a remarkable ivory whiteness and pallor (anæmia) is observed at a very early period, whilst the subcutaneous areolar tissue may become infiltrated and swollen with dropsical exudation. In chronic nephritis associated with long standing dropsy, the skin apparently loses its function, at all events it is extremely difficult to get it to act, and in this state the use of powerful diaphoretics administered with the view of inducing perspiration is often followed by severe headache, and sometimes by more alarming cerebral symptoms (*see* Chapter iii., § Treatment). In the granular kidney unattended with dropsy, the skin becomes harsh and dry, having sometimes a powdery or even "frosted" appearance; this powdery matter is said to consist of urea, excreted vicariously by the skin. This statement, however, is not altogether correct. The powdery matter it is true contains urea, but the greater part of it is made up of broken down cuticular cells; this detritus is more abundant and evident in this disease than perhaps in others, owing to the extreme harshness and dryness of the skin which renders the cells more brittle, and also to the wrinkled condition of the skin which allows it to collect in the furrows. Patients suffering from waxy degeneration of the kidney have, in addition to the peculiar pallor of

chronic kidney disease, a muddy complexion especially noticeable by the brownish rings round the eyelids, which Dr. Grainger Stewart, who first drew attention to this fact, thinks due to the deposition of pigment in the tissue-element of the skin. All patients suffering from chronic renal disease are liable to erysipelatous and phlegmanous inflammations of the skin. A fact that should be borne in mind, in the treatment of pleurisy or other serous effusions, since a small blister or even a mustard plaster will sometimes give rise to the most formidable sloughing, whilst for the relief of dropsy only the finest punctures should be made. In diabetes the skin is harsh and dry, and it often exhibits the same powdery or frosted appearance noticeable in granular kidney, and sugar has been obtained from the deposit. Although this harsh condition of skin is generally maintained throughout the disease, attacks of profuse sweating will sometimes set in in the most unaccountable manner; frequently this sweating is unilateral. In some cases the skin remains moist throughout.

Patients suffering from diabetes are very frequently troubled with boils and carbuncles. They are also liable to other skin diseases, though not in the same degree of frequency, among them may be mentioned eczema, psoriasis and impetigo. Mild forms of diabetes, or rather glycosuria, are often associated with eczema, both being probably due to the same cause, viz., a gouty, rheumatic or strumous taint. The irritation of the sugar moreover, causes, unless means be taken to prevent it, a considerable degree of irritation of the external genitals which if neglected gives rise to an eczematous condition most difficult to deal with. Diabetic patients are also sometimes troubled with patches of psoriasis, whilst on the other hand persons who are the victims of extensive and inveterate psoriasis, are often found to be glycosuric as well. Impetiginous erup-

tions also are by no means infrequent. At the Seamen's Hospital, 1878, I saw a very severe form of this eruption attack a patient suffering from diabetes. It came out abundantly upon his legs and thighs, the pustules which were distinct were, however, thickly clustered together and resembled very closely the fully developed stage of concrete small-pox, only they were not umbilicated. After remaining out about a month or six weeks they slowly subsided and shortly after the patient died of acute diabetic coma.

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CHAPTER II.

Clinical Examination of the Urine.

9. **Method of Procedure.**—The following rules should be attended to:—

(1) When the patient first comes under observation, he should be directed to empty his bladder. The quantity of urine thus furnished should be measured, the specific gravity and reaction taken, the tests for abnormal products, sugar, albumin, etc., applied, and the deposit if any examined by the microscope and by chemical reagents. This procedure gives us an insight into the nature of the morbid conditions, but in order to judge of their extent and permanence, it is necessary to extend our consideration to the qualities exhibited by the whole of the urine passed during the twenty-four hours.

(2) After the preliminary investigation above described, has been concluded, the patient should be directed to collect his urine for the period of twenty-four hours. In order to insure accuracy the following particulars should be attended to. The bladder must be thoroughly emptied at a stated hour, say 8 a.m., which is to be recorded and that sample rejected. The next sample, however, must be kept and placed in a convenient receptacle, (a special form of urine jar, capable of holding five pints or three litres, and graduated, sold by Messrs. Griffin, Garrick Street, Covent Garden, is most serviceable for this purpose). Every succeeding sample must be placed in the jar, the last being passed exactly at 8 a.m., the next day. The

mixed urine thus collected, represents the urine of twenty-four hours, and is to be accurately measured. In hospital practice, or with intelligent patients in private, much useful information is gained, if before placing each sample in the jar, the quantity, the specific gravity, and reaction is also noted. By an examination of the twenty-four hours urine we learn the amount of water and the quantity of solids eliminated by the kidneys in that period, the prevailing character of the reaction, and then by submitting portions of it to volumetric analysis, we learn if it be desired, what variations from the normal occur among the usual constituents, and also the absolute amount of any morbid product, albumin, sugar, etc., that may be present.

(3) Having determined qualitatively the nature of the changes of the urine in disease from an examination of an individual sample, and quantitatively from a consideration of that passed in the twenty-four hours, we have still one investigation to make, to render our clinical enquiry complete, and that is to determine the influence of food and rest on the character of the secretion.

For this purpose it is best to collect the night urine as distinct from that passed in the day. Thus, the patient on going to bed empties his bladder, and all urine passed during the night including that voided on rising in the morning, is the night urine; whilst all urine passed subsequently, up to the time of going to bed is considered the day urine. In many cases, as we shall presently learn, it is an advantage to collect the day urine in separate lots, as the forenoon and evening portions.

(4) Should any difficulty arise preventing the collection of the twenty-four hours' urine, or that of the day and night period; then the patient must be directed to bring with him two samples, the one passed fasting, the other about two hours after the principle meal of the day. That passed

the first thing on rising, and the after dinner urine is the best for this purpose.

(5) When we are unable to obtain the twenty-four hours' urine, and a quantitative estimation is made of the constitutents, we are of course unable to ascertain the absolute amount of the substance passed into the urine in the twenty-four hours, but only the percentage amount. This, if we have taken the specific gravity of the urine, often affords us a valuable indication, though of course it is not so satisfactory as when the absolute amount can be calculated. But unless that precaution is taken a mere percentage estimation is valueless, indeed it is worse than valueless it is misleading, for instance, to say that a sample of urine contains 1·9 per cent. of urea means nothing, but if we say that a sample of urine with a specific gravity 1·020 contains 1·9 per cent., we imply that the proportion of urea in relation to the other solids is low; whilst a urine with a specific gravity 1·012, which has a percentage of 1·9 of urea, indicates that this substance is relatively in excess of the other solids.

(6) No definite conclusion should ever be drawn from the examination of a single sample of urine passed within twenty-four hours. Owing to the neglect of this rule many mortifying errors in diagnosis have occurred, and positive statements have been made which have subsequently required modification.

10. **Variations in the Quantity of Urine.** *Relation of the Urinary Water to the Solids.*—The mean average quantity of urine passed by a healthy adult in the twenty-four hours may be stated at fifty fluid ounces, of which close on 950 grains, about two ounces, is solid matter. If French measures are used, as they generally are now for the calculations of urinary analysis,

then the amount may be roundly expressed as 1450 cubic centimeters, of which 58 grms. are solid matter. Thus it will be seen that solids constitute very nearly four per cent. of the urinary secretion. A knowledge of this fact enables us to employ a very simple formula to express the relationship of the solids to the water of the urine in any given case. This formula consists in doubling the two last figures of the specific gravity of the fluid. For since we know that specific gravity bears a constant relationship to the amount of solids present in a fluid, any variation in their amount will cause a variation in the specific gravity. And frequent determinations have shown that whilst four per cent. of solids is the approximate yield on evaporation, 1·020 is the mean average specific gravity of the normal twenty-four hours' urine taken at a temperature of 60° F. So that if we have ascertained the quantity of urine passed in the twenty-four hours and its specific gravity, we have no difficulty in determining whether the solids on any given day are increased or decreased. Thus, in the case of normal urine, the individual has passed 1450 c.c. in the twenty-four hours and the specific gravity is 1·020, then by multiplying the two last figures of the specific gravity by two, we have forty grms., the amount of solid matter in 1000 c.c. in other words exactly four per cent., and to find the amount for the whole period is simply a matter of proportion, thus $\frac{1450 \times 20 \times 2}{1000} = 58$ grms. of solid matter passed with the urine in twenty-four hours.

This co-efficient, which was originally suggested by Trapp, gives very close results, but care should be taken when employing it, to observe the temperature at which the specific gravity is taken, since every difference of 7° F. from the temperature at which the instrument was graduated, represents a difference of one degree in the

registration of the urinometer. It is necessary therefore either to record the temperature, or else make the correction for the variation at the time of observation. Again as urinometers often differ materially from each other, it is important when making a series of observations, for comparison, always to use the same instrument.

To illustrate the practical value of this method, the following instance may be taken. The collected urine of twenty-four hours of a patient suffering from chronic renal disease amounts to 1650 c.c., and has a specific gravity of 1·016, which according to Trapp's formula gives 52·8 grms. of solid matter passing out by the kidneys in the twenty-four hours. Thus $\frac{1650 \times 16 \times 2}{1000} = 52{\cdot}8$ grms. Now if we coagulate the albumin by boiling and filtering it off, and when cold again take the specific gravity of the filtered urine, we find that this is lower. Suppose it has lost two degrees, and instead of a specific gravity of 1·016 it is 1·014, then again applying Trapp's formula we find that the urinary solids, minus the albumin, amount to 46·2 grms., $\frac{1650 \times 14 \times 2}{1000} = 46{\cdot}2$ grms., or 11·8 grms. less than the amount of urinary solids usually passed in health; whilst the difference between the two specific gravities, 1·016 and 1·014, roughly represents the amount of albumin passed out of the system in the twenty-four hours. In cases where the specific gravity of the urine is above 1·025 it is advisable to use Hæser's co-efficient 2·33.

Under ordinary circumstances we rely entirely on the urinometer to give us an estimate of the amount of solids present in urine, but in some cases, however, the amount obtained is so small, that we are unable to float the instrument freely in the secretion. We may then either dilute the urine with distilled water, multiplying the last figure of the

specific gravity of the mixed fluids by their united volume. Thus if we add to half an ounce of urine, one and a half-ounce of distilled water, we have four volumes, one of urine and three of water, and the specific gravity of this mixture is 1·007, then 7×4 gives the specific gravity of the unmixed urine as 1·028. Or the specific gravity bottle may be used, which gives the weight of the urine as compared with that of an equal quantity of distilled water at a standard temperature. For this purpose a bottle, fitted with a glass-stopper, constructed to hold 25 or 50 grms. of distilled water, measured at 15° C. to a mark on its neck, is filled with urine. The bottle and its contents are then weighed, at a temperature of 15° C., which is obtained by plunging the bottle into hot water, if the temperature is lower than this, or into ice cold water if higher. The weight obtained, subtracted from the empty bottle, when multiplied by 4 if 25 c.c., or by 2 if 50 c.c., of urine have been used, gives the specific gravity in hundreds. When very accurate determinations are required, or only extremely small quantities of urine are available, it may be necessary to evaporate the urine to dryness in a small platinum capsule and weigh the residue. For clinical purposes however, this will hardly ever be necessary, and as the process can only be performed in the laboratory, and only with accuracy then by persons thoroughly trained to analytical operations, the details of the process need not be given here. For the examination of the urine of patients at their own homes, the practitioner will find the specific gravity beads, a very useful substitute for the urinometer which owing to its fragility is apt to get broken. One of these beads, which are numbered 5, 10, 15, 20, 25, 30 respectively, is placed in the urine, say one numbered 15, if this sinks then the next highest number is used, if this latter floats, then we read the specific gravity as ranging be-

tween 1·015 and 1·020. On the other hand if the first bead floats, we add the bead next lowest in number, if this sinks, then we read the specific gravity as between 1·010 and 1·015, and so on.

The clinical indications afforded by the observation of the relations subsisting between the urinary water and the solids, as obtained by measurement of the twenty-four hours' urine and the specific gravity, are numerous and important. For not only does the procedure yield a clue in many cases to the nature of the disease, but it gives us important information as to the extent of the tissue metabolism going on in the body. The following are some of the more important results to be obtained by such observations.

(1) *Urinary water increased, specific gravity greatly diminished.*—When the specific gravity is much reduced (1·002-1·005) we have the condition known as *hydruria*, such as occurs temporarily in hysteria or under great nervous excitement, or permanently in diabetes insipidus. When only moderately reduced (1·010) if tolerably constant, an early stage of granular kidney may be suspected, especially if the pulse exhibits signs of tension, even if albumin is not even yet detected. Some forms of glycosuria may also be attended with a profuse flow of urine of low specific gravity. These cases are often associated with temporary albuminuria, and the sugar, the quantity of which is not great, often intermits with uric acid deposits. Considerable excretion of urine of low specific gravity, frequently occurs in persons in a low state of health, in these cases the deficiency in the amount of solids passed, is due to deficiency of urea. This condition is termed *anazoturia*.

(2) *Urinary water increased, specific gravity normal or only slightly diminished.*—This condition is found whenever there

is increased tissue metabolism going on in the body unattended with pyrexia, it is appropriately termed *polyuria*, for though the specific gravity of the urine is not increased, still it is not greatly diminished in proportion to the quantity of water. Thus the patient passes, say 3200 c.c. of urine in the twenty-four hours of a specific gravity of 1·015, then by Trapp's formula $\frac{3200 \times 15 \times 2}{1000} = 96$ grms. of solid matter are excreted, as compared with 58 grms. which represents the normal excretion of that period. The whole of the urinary solids may be increased, sometimes only one or two constituents. When due to an increase of urea we have the conditions described by Prout as azoturia; when the phosphates are in excess, then the case may be considered to be one of those described by Tessier under the term "phosphatic diabetes."

(3) *Urinary water increased, with increase of specific gravity.*—Points of course to diabetes mellitus, or an exaggerated form of the preceding condition.

(4) *Urinary water normal, specific gravity lessened.*—Sir Andrew Clark has described a condition which he considered due to "renal inadequacy" in which the urea is very deficient. It seems however to differ little from Willis's class anazoturia, except that there is no marked increase of the urinary water.

(5) *Urinary water lessened, with increased specific gravity.*—This is a condition which accompanies all pyrexial states, and is especially marked in those attended with profuse sweating as in rheumatic fever; or with diarrhœa. Associated with albuminuria it is the condition of urine met with in acute and in early stages of chronic tubal nephritis. In certain cases of irritative dyspepsia with increased tissue metabolism, the amount of solids passed by the urine is increased. Murchison observing how often

urates (lithates) were deposited from such urines, believed the condition was caused by the excessive formation of uric acid in the body, *lithæmia*, and that the urine being saturated with its salts they were deposited. (See Lithuria).

11. **Reaction.**—The reaction of normal urine is acid. The average degree of acidity of the twenty-four hours' urine is equivalent to about two grms. of oxalic acid, that is to say, the urine requires so much sodium hydrate to neutralize it as would be required to neutralize two grms. of oxalic acid. It is on this fact that the quantitative estimation of the acidity of the urine is based. A solution of sodium hydrate is made by dissolving 6·35 grms. of pure caustic soda in distilled water, filling up to one litre. One cubic centimetre of this solution represents ·01 grms. of oxalic acid. This solution is to be gradually added from a burette to 100 c.c. of urine placed for the purpose in a beaker or glass vessel, till the exact point of neutralisation is hit, which is shown by blue litmus paper ceasing to be reddened, and red litmus is not blued. Now if 4·5 c.c. of the solution is required for this neutralisation, then the acidity of 100 c.c. of urine corresponds to 0·045 grms. of oxalic acid, and from this the acidity of any amount of urine can be calculated by proportion. The acidity of the urine varies however greatly at different periods of the day, being influenced by various physiological circumstances. These variations are tolerably constant and regular, so that writers speak of the increase and decrease of the acidity as the *acid and alkaline tide*. The following table compiled from observations made by myself, will show the nature and extent of this ebb and flow.

Time.	Total acid as oxalic acid.	Acidity per hour as oxalic acid.
11 p.m. to 8 a.m.*	1·14 grms.	0·12 grms.
8 a.m. to 11 a.m.	0 21 ,,	0 07 ,,
11 a m. to 1 p.m.*	0·40 ,,	0·20 ,,
1 p m. to 4 p.m.	0·11 ,,	0·03 ,,
4 p.m. to 7 p.m.*	0·29 ,,	0·09 ,,
7 p.m. to 11 p.m.	0 07 ,,	0·02 ,,

* Breakfast, 8.30 a.m. Lunch, 1 p.m. Dinner, 7 p.m.

The causes producing these variations have been differently assigned. Dr. Bence Jones thought the depression in the acidity of the urine, corresponded to the withdrawal of acid from the circulation to supply the acid for the gastric secretion. Dr. Roberts on the other hand believes the depression is caused by the entrance of the newly digested food into the blood, and as he points out that the normal alkalescence of the blood is due to the preponderance of alkaline bases in articles of diet, a meal is therefore equivalent to a dose of alkali. I have also pointed out that the depression also occurs at a time when the elimination of carbonic acid is most active, viz., after rising, exercise, or after a meal. The acid reaction of the urine is due mainly to the presence of *acid sodium phosphate*, and to some extent to the acid salts of uric and hippuric acids. How an acid secretion like urine can be separated from an alkaline fluid, like the blood, for many years required an explanation. In 1874, however, I demonstrated the fact that if we take a weak alkaline solution (5 per cent.) of two salts known to exist in the blood, viz., neutral sodium phosphate and sodium bicarbonate, and place them in a U tube, fitted with a diaphragm at the bend, and an electrical current be passed through the fluid, the reaction at the positive end of the tube becomes acid, whilst that at

the negative end is rendered more alkaline. This results from the decomposition of the two salts, thus :—

Sodium Bicarbonate. Neutral Phosphate. Sodium Carbonate. Acid Phosphate.

$$NaHCO_3 + Na_2HPO_4 = Na_2CO_3 + NaH_2PO_4$$

The explanation of the paradox of the alkaline solution thus yielding an acid, is due to the fact that sodium bicarbonate is in reality an acid salt, although it has an alkaline reaction. This explanation also serves to explain another paradox, how after the administration of certain alkaline carbonates, the urine becomes more alkaline, which has been observed both by Bence Jones, Beneke, Parkes and myself.

The acidity of the urine increases gradually after it has been passed, owing partly to an acid fermentation of the mucus and pigmentary matters, and partly to the formation of acid urates. This increase of acidity is chiefly noted in some pathological conditions, especially in diabetes and in febrile urines. The maximum is reached in from three to four days, when it becomes ammoniacal from the decomposition of the urea. The increase in the acidity and its nature may be shown by employing Berthôlet's method of "partage," which is based on the fact that mineral acids are but slightly soluble in ether, whilst the organic acids are readily so. Thus if we estimate the acidity each day by means of the sodium hydrate solution, we find that it steadily increases; but if in addition, we agitate a portion of the urine with an equal bulk of ether, and then withdraw the etherial solution, we shall find that each day the etherial solution will become more charged with acid than on the previous day. The reason for this being, that the acidity of the urine was at first due almost entirely to acid sodium phosphate, which is but slightly soluble in ether, whilst as fermentation proceeds organic acids, lac-

tic and acetic acids are formed, which are readily "parted" by the ether from their solution. (*Clinical Chemistry*, pp. 181-189).

The pathological conditions under which changes in character of the reaction of the urine varies, may be considered under three heads, as causing :—

(a) Highly Acid Urines.
(b) Fixed Alkaline Urines.
(c) Volatile Alkaline Urines.

(a) Highly acid urine may be due either to absolute or relative increase of acid. Acids and acid salts are as is well known continuously entering the blood. (1) They may be introduced into the body from without in the food. The quantity, however, thus derived under ordinary conditions is comparatively small, since nearly the whole of the saline constituents of the food are alkaline, or become so by conversion in the system. Still, a small quantity of acid sodium phosphate is derived from the juice of flesh, and this passes no doubt unchanged into the blood. (2) Acid, too, is generated in the alimentary canal from fermentative decomposition of the saccharine matters taken with the food, or of the amylaceous principles that have been converted into sugar. In health this fermentative process is most active at the lower part of the small intestines, and in the first portion of the large intestine. (3) Lastly, acid is generated in the tissues of the body. Thus, in a condition of inactivity the lymph fluid of all tissues is alkaline or neutral; on activity being evoked the reaction becomes acid. This is well seen in what follows the contraction of muscles, in which the contraction wave gives rise to sarcolactic, carbonic, and other volatile fatty acids, and probably glycerin-phosphoric acid. Of these acids the carbonic passes directly into the blood in a free state. With regard to the other acids, their dis-

tribution and combination with the inorganic bases, likewise set free by the process of tissue oxidation, is so highly complicated that little is known about them.

The acid thus formed in the body is discharged from the system by three channels, (1) by the lungs, (2) the skin, (3) the urine. Acid is also removed from the stomach by the gastric juice, but as this is neutralised by the soda-salts of the bile and pancreatic juice, it need not be considered as a channel of discharge, except perhaps under very abnormal conditions, when it is poured out as acid vomit under circumstances of (reflex) irritability.

So long as the discharge of acid from the system passes off regularly, and is distributed in normal proportion among the secretions concerned in its removal, its presence on the mucous surfaces with which it comes in contact is unfelt. When, however, the production of acid is excessive, or the distribution of the acid among the various secretions is irregular, so that one becomes more highly charged with acids than the others, then the secondary effects due to "acidity" make themselves manifest. These, when the formation of acid is only slightly in excess, or is only temporarily induced by casual disturbances, may be limited to slight heartburn in the case of the stomach, some itching or nettle-rash of the skin, a little bronchial catarrh, or some degree of irritability of the urinary passages. When, however, the formation of acid is excessive or long-continued, the secondary diseases it gives rise to become formidable in their nature. Attacks of acute dyspepsia, accompanied with paroxysms of pain, cramp, vomiting, and diarrhœa, so severe and often so long-continued as to reduce the patient to the utmost stage of prostration. Intractable skin diseases, like lepra, psoriasis, and eczema, severe asthmatic paroxysms, and

chronic bronchitis, frequent attacks of gravel and other renal and urinary affections. Excessive formation of acid, determined probably by certain textural and neurotic conditions, is very likely the cause of the severe inflammation of the structures in and around joints, such as we witness in gout and in attacks of acute rheumatism. An over-acid state may also be considered a predisposing cause of diabetes, since glycosuria may be temporarily induced by the injection of dilute acid into the portal system; whilst the discharge of large quantities of highly acid urine, which takes place day after day, shows that the production of acid in the body is excessive.

These are the most palpable and direct manifestations of an outburst of an over-acid state, but there are many other ailments, such as palpitations and flutterings of the heart; exaggerated pulsations of large arteries; irregularities and intermissions of the pulse; aching pains in the limbs; burning patches; neuralgia; megrim; vertigo; noises in the ears; depression of spirits; sleeplessness, &c.; which many writers describe as arising from irregular manifestations of the gouty state, and which Dr. Murchison, with an equal show of reason, refers to functional disorder of the liver, but which, without committing ourselves to any definite theory, may be conveniently considered as arising quite as frequently from an accumulation of acid in the system.

The acidity of the urine may be increased relatively, owing to concentration of the urine, thus in hot weather owing to increased action of the skin, the amount of urinary water is lessened and consequently the degree of acidity rises; similarly in pyrexia, especially rheumatic fever, and in diarrhœa. This relative increase may not only be caused by a diminution of the water excreted, but from deficiency of the alkaline phosphates; this condition is

frequently met with in the urines of ill-nourished or strumous children.

(b) Fixed alkaline urine is due to the excessive elimination of the carbonates of potash and soda. The alkalescence is termed fixed, because the blue stain given to red litmus is permanent. Such urine is generally cloudy when passed, from precipitated phosphates, which are insoluble in alkaline solutions. These urines often contain an excess of calcium phosphate, which will form an abundant deposit (see Phosphates,) and uric acid, but frequently the excess of the alkaline carbonates is the only morbid conditions to be noted with regard to them. The conditions that lead to the passage of alkaline urine, containing an excess of alkaline carbonates, may be thus summarised. *(a)* General debility and the feebleness with which the respiratory act is performed, leading to the accumulation of carbonic acid in the system. With regard to this point, it is interesting to note that urine alkaline from the presence of carbonates of the fixed alkalies is frequently met with in patients convalescing from acute diseases. *(b)* Diminished secretion of bile, which is the frequent result of the duodenal catarrh produced by the irritation of the acid contents of the stomach being poured into the intestines, gives rise to an accumulation of alkaline carbonates in the blood, the bile being the chief secretion by which alkaline salts are removed from the body; for though a portion of them are undoubtedly reabsorbed into the blood from the intestines, a considerable proportion of them are discharged with the fæces. Obstruction, therefore, to the discharge of bile leads to their retention in the blood, and consequently being eliminated in greater quantity by the kidney. *(c)* The acids formed by fermentative changes being of the fatty acid series; these on entering the system are oxidised

into carbonic acid, and thus uniting with the bases of the alkaline oxides form carbonates of these bodies, and by increasing the alkalescence of the blood will diminish the natural acidity of the urine and even render it alkaline.

This form of alkaline urine is chiefly met with in debilitated persons, and those suffering from flatulent dyspepsia, especially that affecting the small intestines. It is associated with tolerably distinct features, such as loss of weight, weariness, irregularity of bowels, flatulence, frequent micturition, more or less sallowness of complexion, great despondency, urine alkaline or else neutral or faintly acid, depositing phosphates on boiling, and effervescing on the addition of dilute acid.

(c) Volatile alkaline urine is caused by the presence of ammonium carbonate, the result of the decomposition of urea. It is termed volatile because the blue stain given to red litmus disappears on drying. When the urine is alkaline from the presence of volatile alkali, we have in addition to the deposit of calcium phosphate of lime, crystals of ammonio-magnesium phosphate. The ammoniacal condition of the urine is due to a ferment *(micrococcus ureæ)* which can be isolated by filtration; it consists of spherical globules which settle at the bottom of the vessel and appear to increase by budding. The decomposition that occurs may be thus represented:—

Urea.		Water.		Ammonium Carbonate.
CH_4N_2O	+	$2H_2O$	=	$(NH_4)_2\,CO_3$

This ammoniacal fermentation of the urea takes place in the urine only after its secretion by the kidneys, and does not occur in normal urine unless it becomes mixed with the products of decomposition from the mucus of the genito-urinary tract, or the ferment introduced into the bladder

by dirty catheters, or the urine already alkaline from fixed alkali is received into dirty chamber vessels.

The iridescent film which is so often found on the surface of the urine, consists of a pellicle composed chiefly of calcium phosphate and crystals of ammonio-magnesium phosphate. It often has no clinical significance beyond the fact, that the urine has been received into a utensil which has not been properly cleaned. For if we take a sample of normal urine of acid reaction and divide it into two portions and place them both in beakers, each of which contains a drop of stale urine, and then render the portion in one of the beakers alkaline with liquor potassæ, ureal decomposition will set in very much earlier in the beaker containing the alkalised urine than in the one permitted to retain its normal acid reaction, and crystals of triple phosphate speedily form. Dr. Owen Rees has advanced a theory that it is by no means necessary for ammoniacal urine to depend on the decomposition of urea; he maintains it can be formed by the secretion of the mucous membrane, which owes its alkalinity to fixed alkali, and which, mixed with the urine, unites with the acids of the ammoniacal salts and sets free ammonia. In answer to this, it is sufficient to state that the existence of ammoniacal salts in urine, except as the result of the decomposition of urea has been denied by most chemists, and moreover if this view were correct, ammoniacal urine would be more frequent than it is, since whenever the mucous secretion of the urinary passages was increased, the urine would become ammoniacal. Clinical experience teaches us that this is not the case, though there can be but little doubt that the presence of alkali greatly favours ureal decomposition, and the process is induced more rapidly. The experiments of Feltz and Ritter have proved incontestably, that two factors are

required for the production of ammoniacal urine; viz., a previously diseased state of the genito-urinary organs and the introduction of the special ferment. In all catarrhal conditions of the urinary surfaces, ureal decomposition will readily occur on the introduction of the organism, but the most characteristic is that attendant on the catarrh following lesions of the spinal cord.

12. **Colour.**—Healthy human urine is best described as amber coloured, that is yellow with just a tinge of red. It is only recently that the nature of the pigments which impart this colour to urine, has been rendered at all definite though still there are many points in dispute. The following will express the views at present held on the subject, without entering into the questions under discussion. The pigmentary matters of the urine are derived from two sources: 1. From the colouring matter of the blood by the reduction of hæmatin in the liver, under the action of the bile acids, by which the bile pigments are formed, and these by absorption from the intestines are discharged by the urine as *urobilin* or *choletelin*. 2. From indol, which is probably derived from the decomposition of proteid substances by pancreatic digestion. Indol being absorbed by the intestines is converted into *indican* in the alkaline blood, in which form it appears in the urine. With regard to the relative quantities of the two pigments, urobilin is more abundant in healthy urine than indican, which sometimes may not be present at all. In morbid urines, however, the reverse generally obtains and indican is abundant and gives rise to several important reactions.

(1) *Urobilin* was first separated by Jaffé from normal urine, it corresponds to the pigment obtained by R. Maly, by dissolving bilirubin in dilute soda ley and adding sodium amalgam, air being excluded, and which he

termed hydro-bilirubin. MacMunn by passing nitrous vapours into an alcoholic solution of bilirubin, obtained a final oxidation product which he has named *choletelin*, and which he believes to be a further oxidation product of urobilin. For all practical purposes they may be assumed to be identical, at all events the term urobilin is the most aplicable to the pigment derived by the oxidation of the bile pigments and which appears in the urine. All authorities are agreed with regard to the derivation of these pigments. In the first place hæmatin is formed by the action of the bile acids on hæmoglobin, and bilirubin is formed; this is oxidized in the intestines into urobilin and this absorbed into the blood is discharged by the urine, (according to MacMunn, urobilin is further oxidised in the intestines and enters the blood as choletelin in which form it is eliminated).

Urobilin as obtained either directly from bilirubin, or from the urine, presents the following characters. It is a brownish red powder soluble in alcohol, ether, and chloroform. It gives no play of colour with nitric acid which distinguishes it from bilirubin. In acid solutions, when sufficiently dilute, it gives a broad band extending from *b* to a little beyond F; in alkaline solutions the band is less refrangible. Its presence in urine may be shown by adding ammonia till the urine is alkaline, filtering, and to the filtrate adding a few drops of zinc chloride when a green fluorescence will be observed, especially if the filtrate be rendered dilute. If the urine contains any bile pigments these must first be separated by milk of lime and carbonic acid. The composition of urobilin is given as $C_{32}H_{44}N_4O_7$, its relationship to bilirubin being shown by the following reaction:—

$$\underset{\text{Bilirubin.}}{2\,(C_{16}H_{18}N_2O_3)} + H_2O + H_6 = \underset{\text{Urobilin.}}{C_{32}H_{44}N_4O_7}$$

The urohæmatin of G. Harley, the urochrome of Thudichum, the urophain of Heller are probably all bodies allied to urobilin, modified perhaps by the different modes of preparation. Urobilin is the most prominent pigment in healthy urine, and according to some is the only normal pigment. Its quantity is increased in febrile conditions, in organic and functional derangements of the liver, in valvular disease of the heart, and in anæmia.

Stokvis (*N. Rep. Pharm.*, xxi., 123) has described another pigment derived from the oxidation of bile pigment; and which according to MacMunn only appears in urine when there is grave disturbance of the system and in disease of severe character. It differs from urobilin in being insoluble in ether and chloroform, and not forming insoluble compounds with lead acetate. It is soluble in dilute acids, water, and alcohol. Its solutions are light yellow, these when rendered alkaline and boiled with reducing agents, yield a beautiful rose colour which gives a spectrum of a broad band in green. In thick strata the band begins close to D and extends to *b*. In thin strata the band falls short of *b*.

(2) *Indican.* Although some have maintained that indican is not present as the normal colouring matter of urine, still there are few healthy urines, when treated with strong hydrochloric acid, that do not give the characteristic reddish violet reaction, though only faintly. The quantity, however, is greatly increased in many forms of disease. Indican, which corresponds with Heller's uroxanthin, is probably derived from indol, one of the products of pancreatic digestion, and is met with in the intestinal canal and in the fæces. A small portion of this indol (C_8H_9N) absorbed into the blood is probably converted into indican ($C_{52}H_{62}N_2O_{34}$) by the alkaline salts of that fluid, traces of which escape by the urine. Should the quantity of

indol formed, or absorbed, be increased, there is also a proportionate increase in the amount of indican observed in the urine.

To show its presence, place 4 c.c. of strong nitric or hydrochloric acid in a test tube and gently heat, then float an equal quantity of urine, freed from albumin, on the surface, when a ring will develop at the point of contact, which is violet if only little indican is present, and more distinctly blue if there be much. To separate this as a chloroform solution, mix the acid and urine together, add a few drops of chloride of lime solution till a greenish tinge is perceptible, then agitate with 10 c.c. of chloroform and set aside. The chloroform will separate out tinged of a bluish or violet hue, according to the amount of indican present.

The amount of indican is increased in hot weather, probably from the concentration of the urine. A meat diet has the same effect. It is increased in diabetes mellitus, Addison's disease, cancer of the stomach, typhoid fever, dysentery, and the reaction stage of cholera. In obstruction of the intestines the quantity is greatly increased, owing as Senator has observed, to this condition favouring the absorption of indol. Urines containing indican are generally acid and contain an excess of uric acid, they also frequently have a slight reducing action on Fehling's solution, either from the excess of uric acid or from the presence of indiglucin, though the presence of this substance is disputed. The blue, green, and red urines occasionally met with in disease are generally supposed to be indican in different stages of oxidation, forming pigments designated by the terms urrhodin and uroerythrine. Indigo has been met with as a constituent of urinary calculus or as a deposit. Dr. Ord (*Path. Soc. Trans.*, vol. xxix., p. 157) accounts for its presence by the

fact of the indican in the urine being converted into indigo by contact with highly acid urine.

In addition to the increase, or variation of, these normal pigments, the urine in disease may be coloured by the presence of blood, bile, melanotic deposit, or by many articles of food or medicine.

Blood is of course most readily detected by the presence of the red corpuscles, and the characteristic spectrum of oxyhæmoglobin of two bands, one near D, the other near E, changed to one broad band between D and E, by the action of reducing agents. However slight the hæmorrhage, even if not sufficient to give a decided colour to the urine, blood corpuscles will be observed unless decomposition has destroyed them. Their presence in fresh urine distinguishes between hæmaturia and hæmoglobinuria, in which latter case they are dissolved before they are passed. In this form of hæmorrhage, however, there is generally in addition a third band noticed in the spectrum, between C and D, known as methæmoglobin (see Hæmoglobinuria). Small quantities of blood, 1 in 1500, will give to urine a smoky tinge. When present in more considerable quantities the tint varies and is much affected by the reaction, acid urines, with an equal amount of blood, giving a darker tint than alkaline. The urine of hæmoglobinuria is characterized by a deep port wine or ruby colour.

Bile. The general tests for bile are given further on, where we consider bile among the abnormal products that may appear in the urine; here reference will only be made to the spectroscopic appearances of some of the modified bile pigments as they may appear in urine. The bile pigments are bilirubin, biliverdin, and bilifuscin; of these bilirubin is the chief, the other two being formed from it by the assumption of

water, thus—bilirubin $C_{16}H_{18}N_2O_3 + H_2O + O = C_{16}H_{20}N_2O_5$ biliverdin; and bilifuscin is bilirubin plus one atom of water. None of these pigments give any spectrum unless acted upon by reagents. We have already mentioned how bilirubin, converted into urobilin in the intestines, appears in the urine as its normal colouring matter, and have described its spectrum. A similar change occurs when bilirubin is abnormally present, as in icteric urine, by adding strong nitric acid containing a few drops of free nitrous acid (Gmelin's test for bile). At first when we examine this reaction by the spectroscope, we find the solution gives a broad shading in orange and yellow, and a broad band at F. As oxidation proceeds this shading clears up and the band alone is visible extending from *b* to a little beyond F, the spectrum of urobilin which has been formed by the action of acid on the bilirubin. Another bile spectrum of great interest in urinary pathology, is that yielded by the bile acids by Pettenkoffer's test. This according to MacMunn gives a band outside D and a broad band at E.

Melanin is sometimes met with in urine, occurring in persons suffering from melanotic cancer, and in the urine of persons after repeated attacks of ague. One of the best examples that have come under my notice was a deposit passed by an infant, a few weeks after birth and shortly before its death, and which was sent me for examination. I was unable to learn if there was any special clinical indication, and no post-mortem was made. Melanin deposits from urine in minute lumpy granules which are soluble in liquor potassæ, the alkaline solution being decolorised by passing a stream of chlorine through it. Melanin may be distinguished from carbon granules, coal dust, or soot, which may be mixed with urine for purposes of deception, by the fact that these latter are insoluble in liquor potassæ.

Extraneous colouring matters. Many substances taken as food or medicine may colour the urine temporarily. They are chiefly vegetable colouring matters such as derived from beet-root, carrots, whortle berries, logwood, senna, rhubarb, santonin, turmeric, etc., and can readily be distinguished by the alterations affected in the colour when treated with acids and alkalies. The salicylates when administered, impart a smoky tint to urine, so does carbolic acid when absorbed from wounds, the presence of these substances is detected by the blue colour given by their solutions with ferric chloride. With salicylic acid, it is sufficient to add a few drops of ferric chloride directly to the urine. To separate carbolic acid, the urine should be acidulated with hydrochloric acid and the mixture distilled, the distillate gives with ferric chloride a blue colour (p. 87). In carbolic acid poisoning the sulphates disappear from the urine, being converted into sulpho-carbolates. Dr. Maguire (*Brit. Med. Journal*, Oct. 25, 1884) has pointed out that certain brown urines which occur abnormally, are often due to the presence of pyrocatechin and protocatechuic acid formed in the body, probably from compounds of the aromatic group resulting from pancreatic digestion. If these do not undergo their proper transformation in the system, they are eliminated as the above named substances. They are probably identical with the substance called alkapton. The urines containing them may be at first light-coloured and become brown by exposure, in others the brown colour is observed from the first.

Although the colour of normal urine for twenty-four hours when mixed may be described as amber coloured, still individual samples passed during that period, vary considerably in shade. Thus the morning urine, *urina sanguinis*, is more red than yellow, whilst after the inges-

tion of large quantities of fluid it is more or less straw coloured. In disease the variation of the colour often affords a very valuable indication as to the nature of many diseases, the colour should therefore always be noted in clinical records.

Variation of Normal Constituents.

13. **Urea,** CH_4N_2O.—This substance can be obtained pure from the urine, by first precipitating the phosphates and sulphates with a saturated solution of barium nitrate (1 vol.) and barium hydrate (2 vols.) and filtering them off, and then evaporating the filtrate to a syrupy consistence, and treating this residue with nitric acid, sp. gr. 1·25. Crystals of urea nitrate are thus formed, these are decomposed by boiling with a solution of barium carbonate, and evaporating the mixture again to a syrupy consistence. This is then treated with boiling alcohol and the solution filtered whilst hot through animal charcoal. The filtered solution is then concentrated; on cooling crystals of pure urea will be formed. These crystals form four-sided prisms and are extremely soluble in cold water, their solution is neutral to test-paper. A drop of this solution placed on a glass slide and touched with a drop of nitric acid, gives rise to a white shining precipitate consisting of rhombic plates of *urea nitrate*; similarly with oxalic acid we get a white precipitate of *urea oxalate*. A solution of mercuric nitrate in alkaline solutions of urea forms an insoluble compound (CH_4N_2O, $4HgO$). Hypobromous acid and hypochlorous acid decompose urea into water, carbonic acid and nitrogen. It is upon these reactions that the methods for the quantitative estimation of urea are based.

The quantitative estimation of urea is described in the appendix, whilst here is given approximate methods of determining the amount of urea sufficiently accurate for clinical purposes.

A. *Hypochlorite Process.* A simple and reliable method of approximately estimating the amount of urea in urine has been devised by Dr. Squibb, New York, and has been introduced by Mr. Martindale to the notice of practitioners in this country (*Brit. Med. Jour.*, Nov. 1884). It is so simple that the apparatus can be constructed in a very

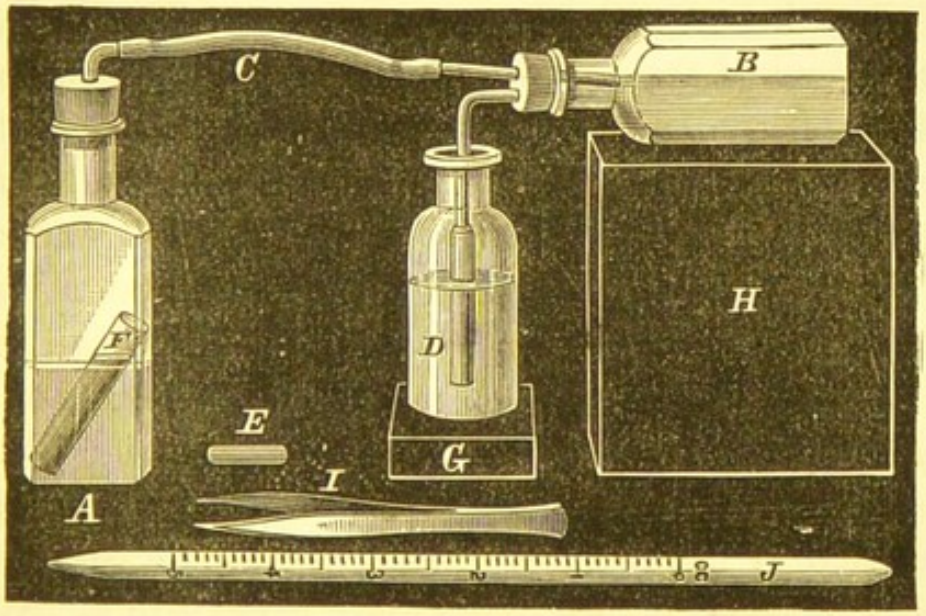


Fig 4.—Squibb's Apparatus.

short time, and so portable that it can be readily carried by the clinical clerks round the wards during the visit of the physician. It consists of two wide-necked vials, A and B (see fig. 4), joined together by a piece of india-rubber piping. In A, which is allowed to stand upright, is placed the urine, and the solution to effect the decomposition. The cork of B is fitted with two glass tubes, one communicating with A by means of the india-rubber tubing, C; the other, which acts as an overflow pipe, is turned down so that the overflow

may discharge into a graduated measuring glass, D; B is filled with water. Finally, B laid on its side is placed on a book or block of wood, so that laying flat its lowest side is on a straight line with the neck of A. All being ready 40 c.c. of solution of chlorinate of soda (*United States Pharmacopœia*) are introduced into A, and 4 c.c. of urine are placed in a small tot or beaker, F, which is carefully introduced into A by means of a pair of forceps so that the urine does not mix with the chlorinated solution. The measuring glass (D) to receive the displaced water, is then rinsed out with water so as to leave the inner surfaces as wet as they will be left when it is emptied for measurement. The stopper is now taken out of the overflow tube, and when the few drops of water which follow its withdrawal have ceased, the tube is placed in the receiving glass. The vial, A, is now inclined so that the chlorinated solution comes thoroughly in contact with the urine. Effervescence ensues and nitrogen gas passes over into B displacing the water which flows into the receiving jar. When no further discharge of gas occurs the process is over. The apparatus is then allowed to stand a short time for the temperature to adjust itself to that of the room, during which time a little water will pass up from the receiving glass back into B. When this movement ceases, the measurements can be made. Now each cubic centimeter of water displaced, is equal to a cubic centimeter of gas that displaced it—and as a c.c. of nitrogen equals ·0027 gramme of urea, therefore the number of c.c. of water represents the number of times ·0027 gramme of urea is contained in 4 c.c. of urine. But it is more simple to obtain the percentage from 1 c.c. of urine, and therefore the number of c.c. of displaced water is divided by 4. Then this number being multiplied by ·0027 gives the percentage of urea in the urine. For example, suppose the displaced water from 4 c.c. of

urine to be 36 c.c. This divided by 4 gives 9 c.c. for each 1 c.c. of urine. Then 9 times ·0027 is ·0243 or ·0243 grm. for 1 c.c. of urine, or 2·43 grms. per cent. Now if the patient has passed 1200 c.c. of urine in the twenty-four hours, it is easy with these data to find out the total diurnal excretion of urea, for 1200 c.c. × ·0243 grm. = 29·16 grms. the amount of urea in the twenty-four hours.

The merit of this method is its simplicity and handiness. That it is absolutely accurate is not contended for, but in that respect it does not compare unfavourably with other clinical methods, and is to all intents and purposes quite as accurate as the hypobromite, or the soda-lime processes. Its advantages over the former lie in the fact that the chlorinated solution is more stable than the hypobromite and also that the apparatus is more portable, whilst the simplicity of the procedure gives it an immense advantage over the latter. A simple and fairly reliable process for the clinical estimation of urea was greatly to be desired, and with such an apparatus estimations of the amount of urea in urines ought now to become as much a matter of routine as the testing for sugar and albumin.

B. *Hypobromite Process* is based on the fact that hypobromous acid decomposes urea into water, carbonic acid, and nitrogen. The latter gas is measured as follows :—A flask of about 300 c.c. capacity is fitted with tightly-fitting perforated cork, and attached by means of india-rubber tubing to a graduated tube filled with water. Place in the flask, *a*, 25 c.c. of hypobromite of soda (100 grms. of sodium hydrate dissolved in 250 c.c. of water, and the cold solution mixed with 25 c.c. of bromine), at the same time place in the flask a small test-tube containing 5 c.c. of urine, taking care that the contents of the test-tube do not as yet mix with the hypobromite solution. Now at-

tach the flask to the graduated cylinder, *b*. Then tilt the flask so that the urine in the test-tube may freely mix with the hypobromite. The reaction now begins, and the gas depresses the water in the graduated tube forcing it into reservoir, *c*; in about five minutes the process is complete, and the amount of gas standing in the graduated tube can be read off, having seen that the water in both tubes is level. If the tube is graduated so that each measure represents one gramme of urea in 100 c.c. of urine, then to calculate the quantity in the twenty-four hours is only a matter of proportion.

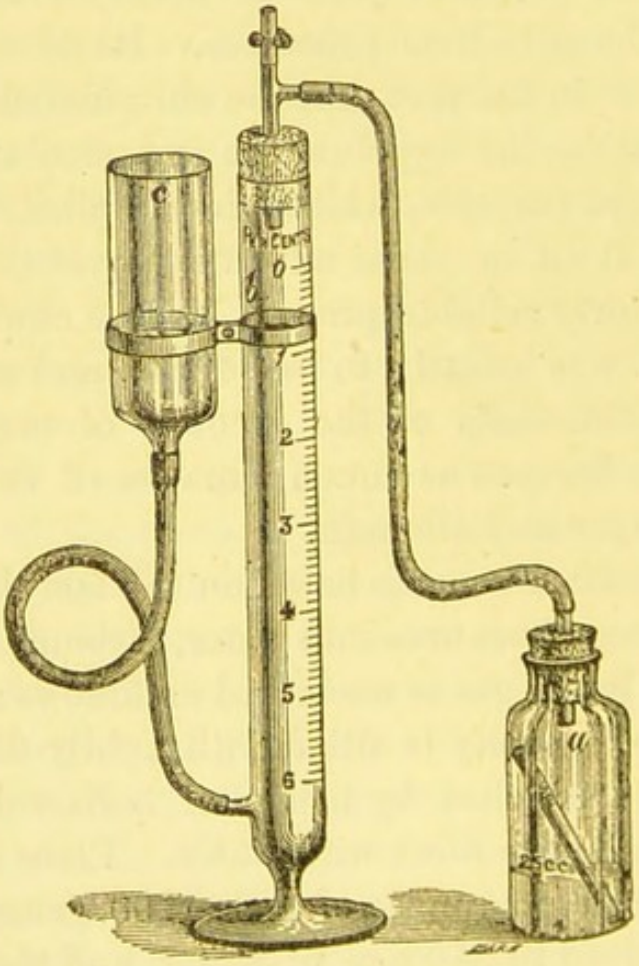


FIG. 5.—Gerrard's Apparatus.

In employing this test for the determination of urea in diabetic urine, it must be remembered that grape sugar increases the quantity of nitrogen evolved from urea by

sodium hypobromite, or the chlorinated solution by quite 7 per cent. The deficiency of nitrogen yielded with a pure solution of urea under the hypobromite or hypochlorite process, is about 8 per cent., the addition of glucose, therefore brings it up to the theoretic yield. This is of very little importance unless the analyses are made for the purpose of comparing a diabetic with a non-saccharine urine. It must also be remembered that the nitrogen evolved by the process does not come entirely from the urea, but also from the other nitrogenous constituents, uric acid, and kreatinin, it has therefore been proposed to deduct 4·5 per cent. from the total amount calculated to correct this error. But as the yield of nitrogen from urine is deficient by at least 7 per cent., the error is more than sufficiently covered.

In health, the daily average excretion of urea for an adult weighing 10½ stone may be taken as 33·5 grms, about 3 per cent., or if English measures be employed, 535 grains, or rather more than an ounce. For every additional pound in the weight of the body it is usual to add 3½ grains. This holds good up to a certain weight, but is certainly too high for very heavy persons who have ceased growing, and too low for young active individuals. I therefore adopt the following scale in calculating the normal excretion of different weights including childhood and youth; thus from 40 to 60 lbs., I consider 4½ grains of urea to each pound of the body-weight to represent the normal excretion; from 60 to 120 lbs., 4 grains; from 120 to 160 lbs., 3½ grains; 160 to 175 lbs., 3¼ grains; 175 to 196 lbs., 3 grains. Thus a child of five years of age weighing 40 lbs. would daily excrete 180 grains (11·7 grms. of urea). A lad of twelve weighing 80 lbs. would excrete 320 grains (20·7 grms.); a young adult weighing 117 lbs. would excrete 535 grains (33·2 grms.); whilst a

fully grown, middle-aged adult weighing 185 lbs. would excrete 555 grains (36 grms.) of urea.

In disease, the quantity of urea eliminated in the twenty-four hours may be steadily increased or diminished, whilst often sharp fluctuations are observable. These fluctuations are accounted for by the fact that in health the amount of urea excreted is proportionate to the metabolism of the nitrogenous elements of the food that have been converted into tissue, in disease no such relationship is maintained.

Urea is increased in all conditions of pyrexia, and this increase is closely connected with the rise of temperature. The connection between the increased urea and the rise of temperature can be readily understood if the recent explanation of the febrile process be accepted. Formerly it was held that tissue changes depended on the amount of oxygen taken in by the lungs, so that on increased respiration a more intense combustion took place, and metabolism was increased with the production of more carbonic acid and urea, whilst, when respiration was impeded, oxidation was imperfectly performed, and, as a consequence, many of the intermediary products, as oxalic acid, uric acid, etc., were not burnt off, but were eliminated in an imperfectly oxidised condition. It is upon this view that most of the chemico-pathological speculations at present held are based. But the view is now gaining ground that the cells are to a certain extent independent of the amount of oxygen supplied to them by respiration; that is to say though they originally obtain oxygen by the process of respiration, they are able, so to speak, to stow it away, and make use of it independently under certain vital conditions which bring about intramolecular changes in their composition, so that reduction is a prior, or at least a simultaneous, process with oxidation. According to this

view, instead of increased metabolism being the result of increased oxidation, it is the increase of the intra-molecular action in the cells themselves that occasions the demand for oxygen, and a more active condition of circulation and respiration. Accordingly, in fever, the earliest step is the increase of intra-molecular changes in the cells themselves, under the stimulus probably of the zymotic poison; for when the stored-up oxygen is exhausted, then a demand for a fresh supply causes an increased frequency of pulse and respiration, which continues so long as the stimulus (zymotic) acts on the cells and maintains this abnormal intra-molecular activity. The fact of the gradual and steady increase of the pulse, respiration and temperature, together with increased excretion of urea during the early stages of febrile action, gives support to this view.

Considerable increase in the amount of urea excreted, occurs, however, without pyrexia, as in Prout's cases of azoturia (see Polyuria). In these cases we must suppose the cells, under the influence of the nervous system, are undergoing intra-molecular changes with morbid activity, and so leading to increased tissue metabolism. In this condition the process stops short of pyrexia, and we have only reduction without increased oxidation. The excretion of urea is diminished in nearly all chronic affections also unaccompanied by pyrexia. In diseases of the liver accompanied by considerable destruction of liver substance, as in cancer, cirrhosis, or abscess of that organ, the amount of urea excreted is generally very considerably diminished. In acute yellow atrophy of the liver, an increase is noted in the early stages, but as the fatty degeneration advances it becomes considerably diminished, though as the amount of urine passed is very small, the percentage amount of urea may appear high. Rapidly growing can-

cer likewise causes a diminution. In Bright's disease the excretion is diminished, this is partly owing no doubt to diminished formation in the system generally, but chiefly to retention; since the amount of urea found in dropsical exudations, often nearly amounts to that found in the urine. As the dropsy disappears, so we find corresponding increase in the elimination of urea in the urine.

In diabetes mellitus the urea is considerably increased, partly owing to the animalized diet and partly from increased metabolism. A sudden fall in the excretion both in nephritis and diabetes is an unfavourable sign, and often precedes the onset of uræmia or diabetic coma. In women the excretion of urea is very variable, it is increased before and after, but diminished during, the menstrual periods.

14. **Uric Acid,** $C_5H_4N_4O_3$.—Uric acid is separated from urine in a free state by the addition to it of strong hydrochloric acid. The crystals are deposited as rhombic tablets of very variable form (fig. 6.) these are highly insoluble in

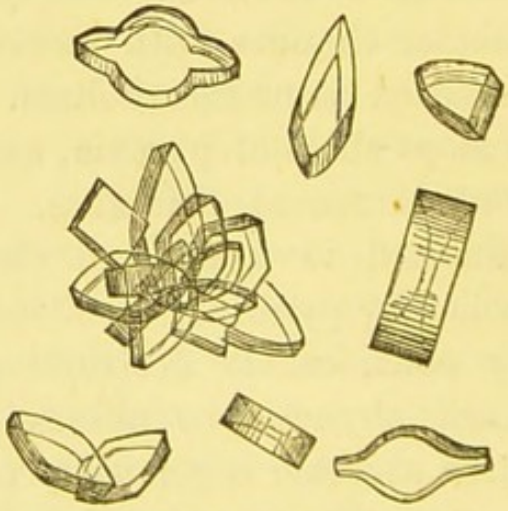


Fig. 6.—Uric acid crystals.

water (1 in 15,000 parts), freely soluble in alkaline solutions, from which they are re-precipitated by the addition of acid. A solution of uric acid, or its salts, evaporated to dryness,

and the residue touched with nitric acid and then with ammonia, developes a violet-red (*murexide*) coloration. Uric acid has a reducing action on alkaline cupric solutions, it can, however, be distinguished from glucose by the fact that uric acid is removable by precipitation with lead acetate, whilst glucose is not. If any doubt therefore exists as to whether the reduction is caused by uric acid or sugar in any given case, a few drops of lead acetate added to the urine, and the copper test applied to the filtered solution, then if the previous reduction was due to uric acid we shall now have no action on the copper whilst if it was due to sugar, the reduction will take place as before.

Uric acid is di-basic forming neutral and acid salts with the alkaline and earthy oxides. The most important being the acid urates of sodium and ammonium.

The following table gives some of the chief characteristics.

Urates.	Formula.	Solubility in Water.	Deposited as
Acid Ammonium	$C_5H_3N_4O_3(NH_4)$	1-1600	Amorphous or spiked globular masses.
Neutral Sodium	$C_5H_2N_4O_3Na_2$	1-77	Nodular masses.
Acid Sodium	$C_5H_3N_4O_3Na$	1-1200	Amorphous, rarely crystallized.
Neutral Potassium	$C_5H_2N_4O_3K_2$	1-44	Amorphous or in fine needles.
Acid Potassium	$C_5H_3N_4O_3K$	1-800	
Neutral Calcium	$C_5H_2N_4O_3Ca$	1-1500	Fine granules.
Acid Calcium	$(C_5H_3N_4O_3)_2Ca$	1-600	Amorphous or in fine needles.
Acid Lithium	$C_5H_3N_4O_3Li$	1-60	Amorphous and in fine needles.

The acid ammonium urate is found as a constituent of urinary calculi, and as a deposit in alkaline (volatile) urine. The neutral sodium urate is the chief salt of uric acid in normal urine, whilst the acid salt occurs pathologically as a constituent of urinary calculi and gouty tophi, in the latter it is often found beautifully crystallized.

The potassium urates are rarely found in urinary sediments or calculi, the acid calcium salt is, however, more frequent. Lithium urate is next to the neutral potassium urate the most soluble of all the salts of uric acid, hence the advantage of the administration of this base in gouty and calculous affections. When an acid is

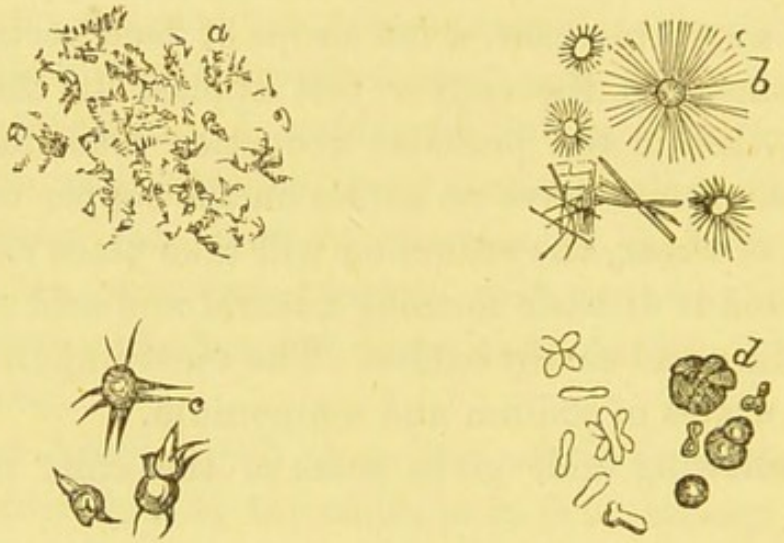


FIG. 7.—*a*. Amorphous urates. *b*. Crystals of urate of soda. *c*. Hedgehog crystals of urate of ammonium. *d*. Nodular masses of urate of soda.

added to a concentrated solution of urates a white gelatinous precipitate occurs. This in the case of a solution of neutral urates is caused by the separation of acid urates, and in the case of acid urates by the liberation of uric acid in an hydrated form. This point is deserving attention, because in testing concentrated urines for albumin with nitric acid, or picric acid, a ring either of acid urates or hydrated uric acid may be formed. It is distinguished, however, from coagulated albumin by disappearing when heated. It is also important because Prout believed that in many cases hydrated uric acid was set free in the tubuli uriniferi when the urine was secreted in a highly acid condition, and thus might become the possible nucleus of acalculus.

The amount of uric acid in the twenty-four hours' urine can be estimated as follows.

Collect the urine passed in the twenty-four hours and measure. Take 200 c.c. and add 20 c.c. of strong hydrochloric acid. Set aside in a tall urine-glass for twenty-four hours to allow the uric acid crystals to separate. Dry a small filter-paper in the air-bath at 100° C. and weigh. Collect the crystals on this filter and wash them well with water slightly acidulated with HCl. Dry them with the filter in the air-bath and weigh. For example, the weight of the dry filter is 0·27 gramme, with the crystals when dried it weighs ·42 gramme, therefore the weight of the crystals in 200 c.c. of urine will be 0·15 gramme, and if the quantity of urine passed in twenty-four hours be 1010 c.c.: then, $\frac{1010 \times \cdot 15}{200} = 0 \cdot 757$ grm.

If the specific gravity of the urine be below 1·015, it is necessary to concentrate it by evaporating the urine till the specific gravity stands at 1·020; since all the uric acid will not crystallize out, if the urine be very dilute.

The mean average quantity of uric acid daily excreted with the urine amounts to about 0·7 grms., or 0·5 grms. per cent.; in disease it may amount, in rare cases, to 2 grms. In healthy blood the amount is so unappreciable that many of the best observers deny its existence, and it is only in gout that traces of it can be obtained from blood serum. The fact that only such small quantities are obtained from the urine both in health and disease, has considerably modified the assumption that uric acid is one of those substances through which each particle of albumin passes before it is thrown out of the body as urea, and that whenever oxidation is imperfectly performed, intermediate substances are not all converted into urea, and so appear in the urine. Indeed, on the other

hand, the view is gaining ground, that in mammalian animals, who excrete urea instead of semi-solid urates, like birds, reptiles, insects, etc., that the amount of uric acid formed in the body is extremely small, and that urea is derived directly from conversion of the cyanogen compounds, and from the transformation of leucin and kreatin, without having passed through the form of uric acid. In health it is considered probable that the extremely small quantity found in the tissues is destroyed as soon as formed, since no appreciable traces can be found in the blood. The extremely small quantity found in human urine is probably not derived from the body generally, but is one of the products of the metabolism of the kidney, and which instead of being destroyed at the seat of formation, as is the fate of uric acid in other parts of the body, is got rid of more economically by being passed off directly with the secreted urine. In gout, the only disease in which uric acid is present in an appreciable amount in the blood, it is probable that uric acid escapes destruction, or may be formed in such excess that it is not all destroyed. From the organs therefore, where the blood current is active, it is probably swept away into the general circulation, whilst in tissues where the blood current is feeble as in the cartilages of the joints, of the ear, and in the straight portions of the tubuli uriniferi it remains as a deposit in the form of sodium urate. Dr. Latham *(op. cit.)* believes that uric acid is produced from glycocin formed in the liver from the glycocholic acid of the bile, which is converted, not into urea as hitherto supposed, but into a hypothetical amido body, this body passes into the circulation and when it reaches the kidney is conjugated with urea, and ammonium urate is formed.

Deposits of uric acid, or of the urates, or both mixed together, occur whenever the urine becomes concentrated,

or its acidity rises. Deposits of urates are chiefly due to the former cause, consequently we find them present in the urines of pyrexia; they are often persistently passed when there is any disturbance of tissue metabolism, accompanied by an increase in the quantity of urea, this condition is often a prelude to the onset of constitutional disease as phthisis, cancer, etc. Crystalline deposits of uric acid are on the other hand, generally noticed when the urine attains a high degree of acidity. It does not, however, follow that the urine passed from the bladder need exhibit a highly marked acid reaction, since as Prout pointed out, a small quantity of extremely acid urine, passed at one period of the day may set free the uric acid at that time, whilst the subsequent samples being less acid, may diminish the total acidity of the urine collected in the bladder. Excessive acidity of the urine may be caused by an over acid state, or irregular discharge of acid from the system generally, or by the withdrawal of the alkaline bases, or by the relative increase in the normal acidity of the urine by concentration. (See Lithuria).

15. **Hippuric Acid,** $C_9H_9NO_3$.—Hippuric acid crystals as obtained from urine are pointed rhombic prisms, and may be mistaken for crystals of uric acid, or even triple phosphate. They are, however, soluble in alcohol, which uric acid is not, whilst their not dissolving in acetic acid proves that they are not crystals of triple phosphate. The separation and estimation of hippuric acid is a long and tedious process, and little available for clinical purposes, the mode of procedure is therefore not given here, but is referred to in the appendix.

About 0·8 to 1 grm. of hippuric acid is passed with the urine in the twenty-four hours. The excretion is greatly increased in diabetes, with it is said a corresponding

diminution of uric acid, and in most febrile affections. It is also augmented by the use of certain vegetable substances, as cranberries, blackberries, plums, etc. As hippuric acid contains the radical of benzoic acid, it is not surprising that the administration of benzoic acid should lead to an increase of hippuric acid in urine. According to some observers, the increase of hippuric acid is accompanied with a corresponding decrease of the uric acid excreted, and therefore benzoic acid and benzoate of soda have been administered with the view of checking the tendency to the deposition of urates and uric acid, but it has been shown by Dr. Cook (*Brit. Med. Journal*, July, 1883) that the benzoates do not diminish the excretion of uric acid but only prevent its crystallization. Kühne has observed that benzoic acid given to patients suffering from disease of the liver, passed unchanged into the urine instead of being converted into hippuric acid, from this it has been assumed that the place of transformation of the vegetable aromatic constituents of our food is the liver.

16. **Other organic acids.**—In addition to uric acid and hippuric acid, traces of other organic acids, chiefly derived from the aromatic acid series, may be found in most urines, these are phenylic, damaluric, damolic, taurylic, and kryptophanic acids. Of these the *phenylic acid* is the only one of clinical importance, from the fact of its appearing in increased quantity in the urine after the administration of the salicylates, or in carbolic acid poisoning. Urines containing an abnormal quantity of this acid acquire a violet colour on the addition of ferric chloride, the solution becoming bluish on exposure, and finally acquiring a muddy cloudiness. A chip of fresh firwood moistened in dilute hydrochloric acid, will acquire on exposure to strong sun-light, a deep blue colour if a fair amount is present in solution. In cases of carbolic

acid poisoning, it may be necessary to obtain it from the urine for more definite examination. For this, about 100 c.c., of the urine must be boiled for some hours with an equal quantity of lime water. The precipitate filtered off and the filtrate evaporated to about 25 c.c. This is strongly acidulated with hydrochloric acid, and the mixture after standing twenty-four hours is again filtered. The filtrate is then distilled, when a turbid milky liquid is obtained, this by repeated rectification yields an oily yellow coloured liquid, which gradually sinks to the bottom of the vessel. To obtain phenylic acid quite pure, this oily fluid must be subjected to fractional distillation, but this for practical purposes is unnecessary, it being sufficient to prove the presence of phenylic acid, with its allied acids, as being in considerable excess. *Benzoic acid*, $C_7H_6O_2$, may be found occasionally in stale urines, but as it is somewhat volatile and passes off as the urine evaporates, it often escapes observation, it is formed from the decomposition of the hippuric acid.

Hippuric Acid. Glycocin. Benzoic Acid.

$$C_9H_9NO_3 + H_2O = C_2H_5N_2O + C_7H_6O_2$$

Kühne has shown that in cirrhosis of the liver benzoic acid administered as medicine, may pass unchanged into the urine.

Lactic acid, $C_3H_6O_3$, is formed in normal urine after emission as the result of acid fermentation. In certain forms of dyspepsia and in the early stage of rickets, lactic acid may be obtained from the freshly passed urine. It can be separated by evaporating the urine to one-fifth its bulk, at a temperature a little below 100° C., and then filtering. To the filtrate, baryta water is to be added, and the mixture filtered. Then acidulate the filtrate, with a few drops of strong sulphuric acid, and distil. The residue after distillation is to be shaken with alcohol and allowed

to digest. After standing some time the alcoholic solution is to be filtered off, and the filtrate mixed with milk of lime and evaporated to dryness. The residue is dissolved in water, and a stream of carbonic acid gas passed through the solution, which is to be heated to 100° c. When the solution is cold, the precipitate must be removed by filtration, the filtrate evaporated to dryness, and the residue dissolved in rectified alcohol. The alcoholic solution is concentrated and set aside, in a day or so crystals of calcium lactate will deposit.

Oxalic acid, $C_2H_2O_4$, is present in extremely minute quantities in combination with potash, soda, and lime. It is, however, often present in excess, and then a crystalline deposit of calcium oxalate, CaC_2O_4, is thrown down from the urine. The crystals of calcium oxalate assume various shapes, the most common being the square letter envelope shape or octohedral, and which are alone characteristic. When present in a discoid form, or as diamond points, or as dumb-bells, their character must be determined by their chemical reactions; they are insoluble in acetic and oxalic acids which distinguish them from deposits of the earthy phosphates, whilst they are soluble in mineral acids, which distinguishes them from anomalous forms of uric acid crystals. Under the blow-pipe the crystals are reduced to calcium carbonate, which effervesce on the addition of dilute acid.

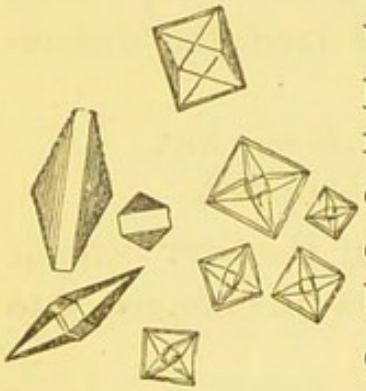


Fig. 8.—Oxalate of lime.

To estimate the amount of oxalic acid in urine the following method is the most accurate. The urine is rendered alkaline with ammonia, and then treated with calcium chloride to complete precipitation. The whole is

next evaporated to a small volume, strong alcohol added, and the mixture laid aside for twelve hours, it is then filtered, and the precipitate washed with alcohol and ether. The precipitate is subsequently washed with water and acetic acid in succession; the residue dissolved in hydrochloric acid, filtered, and the filtrate first made alkaline with ammonia and then strongly acid with acetic acid. The resulting oxalate of lime is collected on a filter, washed, and converted into caustic lime before weighing.

The conditions which lead to the formation and deposition of calcium oxalate from the urine, will be considered in the section which treats of the morbid conditions of the urine, dependent on derangements of digestion. (See Oxaluria).

Palmitic acid, $C_{16}H_{32}O_2$.—Minute traces of a saponifiable fatty acid, said to be palmitic, though it is probably a mixture of it with stearic and oleic acids, can be separated from normal urines. In fatty degeneration of the kidney, in all purulent affections of the urinary passages, in phosphaturia, when there is evidence of the breaking up of the phosphorised fatty elements of the nerve centres, this saponified fatty acid is formed in increased quantities. The mode of separating it from the urine is described under the head of fatty matters in urine.

17. **Kreatinin,** $C_4H_7N_3O$.—Kreatinin may be obtained by rendering the urine (200 c.c.) alkaline with milk of lime and then adding calcium chloride till a precipitate ceases to be formed. The precipitate is then removed by filtration, and the filtrate evaporated to near dryness. The residue is heated with alcohol (50 c.c.), and the alcoholic solution after standing some hours is evaporated to half its bulk. When cold, a small quantity of a solution of zinc chloride (specific gravity 1·2) is to be added. After standing some time crystals of kreatinin zinc chloride will

be deposited. These are to be boiled with an excess of hydrated lead oxide for some hours, the solution filtered through animal charcoal, and the filtrate evaporated. The residue is then treated with boiling alcohol (50 c.c.), and the solution concentrated to one-fourth its bulk. On standing, oblique rhombic prisms of kreatinin will be deposited. These are soluble in 100 parts of alcohol. It is an extremely powerful base, giving an alkaline reaction with test-paper. About 0·6 to 1·2 grm. is said to be passed into the urine in twenty-four hours. It is apparently derived from the decomposition of kreatin in the blood.

$$\overset{\text{Kreatin}}{C_4H_9N_3O_2} = \overset{\text{Kreatinin}}{C_4H_7N_3O} + H_2O$$

Nothing positive is known with regard to the clinical or pathological import of its variations in disease, though from the fact that it is derived from kreatin, one of the products of muscle decomposition, we might look for an increase in the early stages of muscular atrophy, or in pyrexial conditions accompanied with rapid wasting.

18. **Phosphates.**—Phosphoric acid in the body combines with the alkaline oxides of potassium and sodium to form *soluble* or *alkaline* phosphates, and with the earthy oxides of calcium and magnesium to form the *insoluble* or *earthy* phosphates. The former being extremely soluble are never separated from the urine in the form of a deposit, whilst the latter being insoluble in alkaline solutions are deposited whenever the urine becomes alkaline.

To determine separately the respective quantities of the alkaline and earthy phosphates, we have first to determine the whole amount of phosphoric acid combined with both kinds of bases, which is done by the process described in *Appendix* I., No. 3. Having determined the total amount of phosphoric acid, the earthy phosphates are removed from another sample of the urine by

precipitation with liquor ammonia, and the amount of phosphoric acid in the filtrate determined by the same process as before, the result gives the amount of alkaline phosphates which remained in the filtrate after the removal of the earthy phosphates by precipitation. Then by deducting the amount of phosphoric acid in combination with the alkaline bases from that of the total phosphoric acid, we learn the amount of the earthy phosphates present. Thus, for example, the total phosphoric acid in the twenty-four hours' urine amounts to 3·1 grms., and that in combination with the alkaline bases is 1·9 grms., then the phosphoric acid in combination with lime and magnesia amounts to 1·2 grms. These figures represent approximately the normal excretion of phosphoric acid in the twenty-four hours' urine, and its distribution among the alkaline and earthy bases.

a. The Alkaline Phosphates exist in the blood in the form of neutral sodium and potassium phosphates (hydrogen di-sodium phosphate, HNa_2PO_4), but appear in the urine as acid sodium and potassium phosphates (di-hydrogen sodium phosphate, H_2NaPO_4), and thus cause the acid reaction of that secretion. This change of the neutral into the acid salt is caused by a decomposition effected by the act of secretion in which the bicarbonates and neutral phosphates in the blood, are changed into carbonates and acid phosphates respectively. The acid salt in obedience to the law of diffusion passing out into the urine, whilst the carbonate remains in the circulation as follows :—

Bicarbonate		Neutral Phosphate		Carbonate		Acid Phosphate
$HNaCO_3$	+	HNa_2PO_4	=	Na_2CO_3	+	H_2NaPO_4

This explanation of the seeming paradox of how an acid secretion can be formed from the alkaline blood was

first suggested, and proved to be experimentally possible, in a communication addressed to the *Lancet*, July, 1874.

The presence of the alkaline phosphates can be detected by the following tests. (1) A yellow precipitate with silver nitrate soluble in excess of ammonia or nitric acid; (2) a yellow precipitate with nitric acid solution of ammonium molybdate.

The clinical significance of the alkaline phosphates has been little studied. Under normal conditions they appear as acid salts in the urine, and give that fluid its acid reaction. Should they not be converted into acid salts in their passage through the kidney they may appear as neutral phosphates, in which case the urine will be neutral or alkaline, though when this is the case the alkaline carbonates are also usually present in excess since these urines invariably effervesce on the addition of dilute acid. When excreted in excess, which is the case when much animal food is taken, when there is marked disintegration of the nervous system, especially as Zuelzer has pointed out, those cases attended with marked depression, and during fevers, the increase is *pari passu* with that of the earthy phosphates, so that there is really practically little to be gained by making a separate estimation of the two, the estimation of the total phosphoric acid being a sufficiently close indication. In scurvy I have observed a remarkable diminution of the alkaline phosphates as in the four cases given here:—

Cases.	Alkaline Phosphates 1 week after admission.	Alkaline Phosphates after 2 weeks of lemon-juice.
Case 1	0·76 grms.	1·6 grms.
,, 2	0·57 ,,	1·6 ,,
,, 3	1·25 ,,	1·7 ,,
,, 4	0 87 ,,	1·3 ,,

In these cases the diet was the same throughout, the only difference being the administration of 2ozs. of lemon-juice daily, which could not possibly account for the decided increase of the alkaline phosphates. It therefore seems to me probable, that the alkaline phosphates are retained in the system in scurvy, to supply the deficiency of the other alkaline salts, the carbonates and bicarbonates, which are withdrawn when fresh vegetables are withheld, (see *Clinical Chemistry*, p. 292).

Dr. Gee (*St. Bartholomew's Hospital Reports*, vol. viii.), has pointed out the remarkable diminution of phosphoric acid, even to complete absence, in cases of ague.

Schultze (*Zeit. f. Biologie*, xix., p. 301), has remarked a considerable diminution of phosphoric acid in the urine after the administration of bromide of potassium.

A deficiency of the alkaline phosphates is often noted in the urines of ill-nourished and strumous children, which deposit a considerable quantity of uric acid. The alkaline phosphates are also considerably diminished in chronic Bright's disease.

b. The Earthy Phosphates.—The phosphoric acid in combination with the earthy bases in the urine forms three salts, calcium phosphate ($Ca_3,2PO_4$), magnesium phosphate ($MgHPO_4,7H_2O$), and ammonium-magnesium phosphate ($NH_4MgPO_4,6H_2O$). The latter however only being formed as the result of disease of the genito-urinary passages.

Calcium Phosphate is deposited from the urine in two forms, most commonly as amorphous granules, occasionally as fine acicular or stellar crystals, (fig. 9). This deposit only occurs when the urine is alkaline or is rendered so artificially; on the addition of acid it is speedily dissolved. No special clinical distinction can be made between the amorphous and crystalline deposits, except that the former is by far the most common. The fine acicular crystals

may be mistaken for uric acid crystals, in all cases therefore it is well to add a drop of dilute acid to the deposit under the microscope, if the crystals are calcium phosphate they will dissolve, if uric acid they will not dissolve. Occasionally this deposit will come down in urines, which

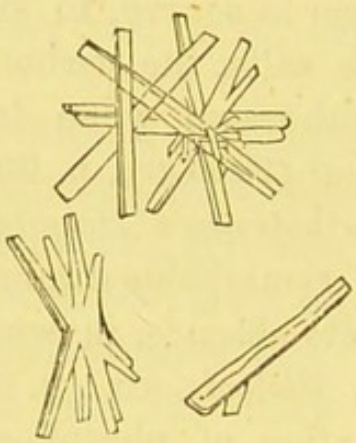


FIG. 9.—Stellar phosphates.

are slightly acid, on boiling, and this turbidity is likely to be mistaken for albumin, only the latter is not redissolved by the addition of acid. The cause of this deposition of calcium phosphate is generally assumed to be the driving off of free carbonic acid, which is supposed to keep the calcium phosphate in solution, by boiling. If this were so then the precipitate should be permanent, but it redissolves on cooling. Salowski (*Zeitschrift für Phys. Chimie*, 1883) believes the precipitation is caused by the decomposition of an existing combination of calcium phosphate and alkaline phosphate. Dr. Smith of Dublin (*Brit. Med. Jour.*, 1883, vol. ii., p. 68) from experiments made with Dr. Emerson Reynolds, believes the precipitate depends on a nice adjustment in the proportions and basisity of the phosphatic salts existing in urine, and gives the following equation to explain what happens when heat is applied:

$$2(Ca_2H_2P_2O_8) + CaH_4P_2O_8$$
$$= Ca_3P_2O_8(\text{insoluble}) + 2CaH_4P_2O_8(\text{soluble}).$$

On cooling, an inverse change takes place.

Magnesium Phosphate is deposited with the calcium phosphate, and for all practical purposes they may be considered together. To separate the two if necessary, ammonium oxalate is added to the urine which throws down the lime as calcium oxalate, this is removed by filtration, and ammonia is added to the filtrate which precipitates the magnesia as ammonium-magnesium phosphate.

The clinical significance of deposits of calcium and magnesium phosphate may be considered with reference to deposits occurring simply from an alkaline condition of the urine without any excessive elimination of the earthy phosphates, and those due to excessive elimination.

Deposit of earthy phosphates without excessive elimination. The urine is alkaline from fixed alkali, and is turbid or whey-like from the deposited phosphates; or if the urine is clear and slightly acid when passed, it becomes turbid when boiled. The alkalinity in these cases, since the alkaline phosphates are not generally increased, is mainly due to the bicarbonates of potash and soda being excreted in excess, these urines consequently effervesce on the addition of an acid (see Phosphaturia).

Excess of earthy phosphates, not however always deposited. In these cases the amount of earthy phosphates is immensely increased, as is also the alkaline. The urine is generally alkaline, and when this is the case the earthy phosphates are thrown down as a mealy dense precipitate. This deposition often occurs in the bladder, the urine first passed being clear, the last portion being thick and passed often with great straining and irritation. Frequently, however, the urine is not alkaline but acid, so that no deposit occurs, and till a quantitative estimation is made it is impossible to tell that phosphoric acid is being eliminated in excess. In other cases the two conditions alternate, an alkaline reaction with deposits of phosphate alternating

with highly acid urine depositing uric acid and urates (see Polyuria and Phosphaturia).

c. Ammonium Magnesium Phosphate, ($NH_4MgPO_4,6H_2O$), is formed only when the urine becomes alkaline from volatile alkali (ammonia). This occurs whenever fermentation takes place in the urinary passages (see page 64). This salt is also called triple phosphate, and is met

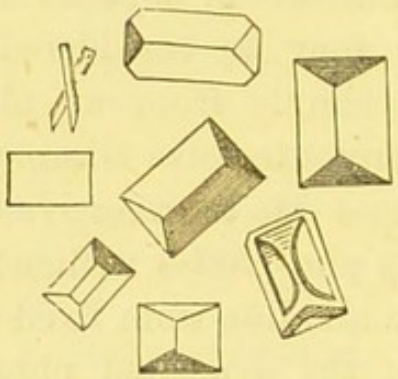


FIG. 10.—Triple phosphates.

with in different forms, the most characteristic being as triangular prisms (fig. 10), less frequently as feathery crystals. The crystals are soluble in dilute acids. Although usually found in alkaline, still they are sometimes met with in slightly acid, urine. In these cases it is probable that the urine contains a salt which reddens litmus paper, but which is not a free acid. A mixture of calcium phosphate and ammonium magnesium phosphate fuses under the blow-pipe into an enamel-like crust. The pathological conditions that lead to the formation of triple phosphate in urine will be found described in the section on stone and gravel (see Calculus).

19. **Unoxidised Phosphorus.**—Although the greater part of the phosphorus eliminated from the body passes out in the oxidised form as phosphoric acid in combination with bases, still a small portion, almost imperceptible under normal conditions, but increased in some pathological states, or by the influence of certain kinds of food, passes

off by the urine unoxidised in combination with organic substances, in the form of lecithin, protagon or glycerin-phosphoric acid. This can be indirectly estimated by boiling the urine for some time with strong nitric acid, which liberates the phosphorus from its organic combination, and oxidises it into this form of phosphoric acid, and the amount of phosphoric acid determined by the usual method (*Appendix* I., No. 3). Now if the amount of phosphoric acid has been previously determined in an equal sample of the same urine, before boiling with nitric acid, the difference between the two quantities will give the amount of phosphoric acid derived by the oxidation of organic phosphorus. Thus 100 c.c. of urine before boiling with nitric acid gives 0·172 grms., and after boiling, 0·183 grms., then the amount of phosphoric acid derived from the organic compounds weighs ·011 grms. Sotnischewsky (*Zeitschr. f. Phys. Chemie*, Bd. 4, § 215) gives a more exact process, as follows. The twenty-four hours' urine is rendered alkaline with milk of lime, and precipitated with calcium chloride. Filter, evaporate filtrate, and extract residue with alcohol. The residue not dissolved with alcohol is dissolved in water, to both solutions add a solution of ammonia and magnesia, and allow the mixture to stand twenty-four hours in order to remove traces of the inorganic phosphoric acid that may still be present. Filter, render the filtrate strongly acid with sulphuric acid, and boil for some time, in order to separate the glycerin-phosphoric acid. After cooling, solution of ammonia is to be added, when on standing crystals of ammonium-magnesium phosphate are deposited, these are to be collected and weighed, from whence the amount of phosphoric acid derived from the organic compounds can be deduced. Should it be required to estimate the organic compound as lecithin, the crystals of ammonium-magnesium phosphate

must be weighed in a platinum capsule, whose weight is known, and then brought to a white heat, till a glassy mass is left at the bottom of the capsule. This is magnesium pyrophosphate, which must be carefully weighed; now 100 parts of pyrophosphate are equivalent to 764·8 parts of lecithin. If therefore the pyrophosphate amounts to 0·026 grms., then the amount of lecithin in the twenty-four hours' urine will be 1·9764 grms.

Zuelzer (*op. cit.*, pp. 15-24), who has paid much attention to the clinical and pathological significance of the unoxidised phosphorus in urine, observes that the amount in normal urines is quite insignificant, it is increased however, whenever the animal is fed on such substances as brain, glycerine, butter, etc. Keeping the urine diminishes the amount, owing no doubt to the oxidation that occurs. The diseases in which it has been found in the largest amount, have been chyluria, pernicious anæmia, dementia, lesions of brain substance, diabetes mellitus, and after the administration of chloroform. L. Egmonnet (*J. Pharm.* § 7, p. 134), has found a notable amount of glycerin-phosphoric acid in the urine of phthisical patients, and that the livers of these patients contain often as much as 3·38 per cent. of lecithin. The same observer has also made an important observation on the excretion of the hypophosphites by the urine. Having injected sodium hypophosphite into the veins of a dog, it was found that the dose was eliminated in twenty-four hours; part as phosphate, and the remainder as hypophosphite. The amount of phosphate eliminated, however, appears to increase in greater ratio to that of the hypophosphite, in proportion to the increase of the dose. It need hardly be said that the subject is one of considerable clinical and pathological importance, and the estimation of the amount of lecithin daily passed out of the body by

the urine, ought to afford a useful indication of the extent as well as the intensity of nerve disintegration in certain morbid conditions of the nervous system.

20. **Sulphates.**—Sulphuric acid in the body combines chiefly with the alkaline oxides of potassium and sodium, and to a small extent with lime. They are extremely soluble, so that the sulphates never form a urinary deposit. Sulphuric acid is detected by means of barium chloride, to which a few drops of hydrochloric acid should be added to insure complete precipitation of the sulphate. This process is used for their quantitative estimation, (*Appendix* I., No. 4). The amount of sulphuric acid passing off from the body by the urine in the twenty-four hours, is about 2·5 grms. to 3 grms. The quantity is said to be increased by a meat diet, and decreased by a vegetable one, but this is misleading, since many vegetables in common daily use, as cabbages, beans, peas, etc., contain much sulphur, and onions allyl sulphide, and mustard allyl sulpho-cyanide. An habitually large excretion of sulphuric acid with excess of urea indicates, however, a preponderance of animal food. In disease, their excretion is increased in fevers, in acute rheumatism, meningitis and pneumonia. When carbolic acid has been taken in large quantities, the sulphates may entirely disappear from the urine, being converted into sulpho-carbolates.

21. **Unoxidised Sulphur.**—Only a small portion of the sulphur introduced into the body with the food appears in the urine. A considerable portion passes off by the bowels, a part of which consists of the sulphur of undigested food, a part of the sulphur of the altered bile acid (tauro-cholic), one-fifteenth of which Bidder and Schmidt have shown to be thus disposed of. The remaining portion of this acid is reabsorbed from the intestine, and the greater part undergoes further change in the economy, but

its ultimate fate is at present unknown. Whilst a very small portion passes off by the urine, and can be recognised even in health (Naunym and Dragendorff) by the ordinary tests for bile acids, and lastly a small portion of this acid is partially oxidised, and furnishes the sulphur product originally discovered by Ronalds, and which in minute quantities always exists in the urine. A portion of the sulphur introduced into the body is also eliminated by the skin, in the perspiration, hair, nails, and cuticle. The amount of unoxidised sulphur that passes off into the urine in health amounts to 0·4 grms. To estimate it we first ascertain the amount of sulphuric acid present as sulphate, by means of barium chloride, (*Appendix* I., process 4), and evaporate an equal portion of the same urine to dryness, and deflagrate it with potassium nitrate. By this means the unoxidised sulphur is converted into sulphuric acid. This is estimated by barium chloride, the amount of sulphuric acid obtained being of course greater than in the first instance, the difference between the two amounts, being the amount of unoxidised sulphur present. The clinical and pathological significance of an increase in the amount of this unoxidised sulphur in the urine has not been determined. It is observed in many instances of disturbed hepatic function, as well as in organic disease of the liver, and of course is always noted in cystinuria.

22. **Chlorides.**—Hydrochloric acid in the urine is chiefly found in combination with sodium, and to a less extent with potassium. The amount varies considerably from 5 to 8 grms. according to the amount of salt ingested. About one-fifth of the chloride of sodium ingested however appears in the urine as chloride of potassium, being decomposed by acid-potassium phosphate into potassium chloride and acid-sodium phosphate. The chlorides being soluble, they never appear in the urine as a deposit.

Evaporated to dryness, however, octohedral crystals and rhombic plates of urea and sodium chloride will be formed. Solution of silver nitrate throws down the chlorides as a white curdy precipitate insoluble in excess of nitric acid, but soluble in excess of ammonia. In applying this test to urine, it is necessary first to add a few drops of nitric acid to prevent the deposition of the phosphates. Two methods are employed for the quantitative determination (*Appendix* I., No. 5,) that of Liebig by means of a mercuric nitrate solution, or that of Mohr with silver nitrate.

The chlorides are diminished in all acute febrile diseases. In pneumonia the diminution commences at the stage of hepatization, they reappear gradually as resolution sets in. Parkes says that sometimes they may be retained some days, and that then they are poured out in such quantities as to raise the specific gravity of the urine, although the water is increasing and the other solids decreasing. In acute rheumatism with effusion into the joints, and in exudative pleurisy, a considerable decrease is likewise noted. The decrease in these diseases is mainly accounted for by the fact that the exudation material poured out is particularly rich in chlorides. In ague during the cold and hot stages, the excretion of chlorides is greatly increased.

Abnormal Constituents.

23. **Serum Albumin.**—Serum albumin coagulates at a temperature of 73° to 75° C., this is its chief distinguishing feature from all other forms or modifications of albumin, except serum globulin. The *heat test* therefore can be alone relied upon to prove the presence of serum albumin and serum globulin, the most important forms of albu-

min clinically. Other reagents precipitate it from urine, of which those most frequently in use are nitric acid, picric acid, potassio-mercuric iodide, acid solution of common salt, sodium tungstate, and potassium ferrocyanide with acetic acid, but as these also give reactions with other forms and modifications of proteid bodies, they are not to be relied on except as showing the presence of a proteid substance.

In testing for albumin, the following procedure should be adopted. The urine should be rendered perfectly clear. If alkaline and turbid from phosphates, a few drops of *dilute* acetic acid are to be added till the urine acquires a slight acid reaction when it becomes clear, but not otherwise. If thick from deposited urates, the urine must be warmed to a blood heat (40° C), when the deposit dissolves. If cloudy from mucus, it must be filtered.

(1) *Heat Test.*—A test-tube is then filled with the urine, and the upper-third heated over a spirit lamp, and the temperature gradually raised to the boiling point. Coagulation occurs just before ebullition, and varies from a mere haze to a dense white cloud, made up of masses of coagulated albumin, which does not redissolve on the addition of dilute acetic acid. By holding the test-tube up to the light against the coat sleeve, the slightest haze in the heated portion may be distinguished and contrasted with the perfectly clear fluid in the lower and cold portion of the test-tube. In employing this test we must guard against three fallacies. *a.* The cloud may be mistaken for phosphates, it can however be readily distinguished by the addition of dilute acid, the phosphates at once being redissolved, whilst albumin is not. *b.* If the urine is highly alkaline, the serum albumin may be converted into alkali albumin (casein), which is not coagulated by heat, this mistake however is not likely to arise if the precaution of

rendering the urine acid, as previously directed, is attended to. If however it has been neglected, the addition of a drop or so of dilute acid, or one of Dr. Oliver's citric acid papers will convert the alkali albumin into serum albumin, and the required coagulation will take place. *c.* If the urine be too highly acid, the albumin will be converted into acid albumin (syntonin) which also is not coagulated by heat, in this case a drop of liquor potassæ, or one of Dr. Oliver's sodium carbonate test papers, added to the urine, will convert the acid albumin into serum albumin, and coagulation will occur. It is rare, however, for urine to be passed so highly acid as to change the albumin into acid albumin, when it occurs, it is generally from using a test-tube which has been imperfectly cleaned, and contains a few drops of acid on its sides and bottom.

The heat test thus applied affords sufficient indications for clinical purposes, and though the more delicate reagents are useful in determining minute quantities of albumin, especially as regards the ultimate clearing up of an attack of albuminuria, they should never be entirely relied on, partly because they sometimes precipitate other bodies such as urates, alkaloids, peptone mucin, &c., and partly because in themselves they do not discriminate between the modifications and other forms of albumin. It matters little however which reagent is selected so long as heat is one of the tests employed. The other reagents besides heat commonly in use for clinical purposes are :—

(2) *Nitric Acid* (*Heller's Test*).—About thirty drops of strong nitric acid are placed in the bottom of a test-tube, and then an equal quantity of urine is floated gently over the surface of the acid, at the line of junction, a zone of coagulated albumin is developed, and which does not disappear when heated. Nitric acid gives this reaction as well with alkali and acid albumin as with serum albumin, but not

with true peptones. A fallacy may arise by the appearance of a zone of hydrated uric acid in highly acid urines, or amorphous urates in neutral urines, being developed at the line of junction, this however disappears when *heat* is applied. Crystals of urea nitrate may be formed on the addition of nitric acid to concentrated urines, but they too dissolve on the application of heat.

(3) *Potassio-Mercuric Iodide (Tauret's Test)* according to Dr. Oliver's researches is the most sensitive test known, and he considers that citric acid adds to its sensitiveness. It precipitates alkali and acid albumin, as well as serum albumin, also peptones, alkaloids and urates. The application of the *heat* test is therefore necessary to discriminate between these. *(a)* The precipitate redissolves when heated, which shows it to consist of either peptones, alkaloids, or urates. *(b)* A fresh sample coagulating by heat shows it to be serum albumin, and not acid or alkali albumin.

(4) *Picric Acid (Johnson's Test)* is also a very delicate reagent for proteid substances, and its use has been strongly advocated by Dr. George Johnson. It precipitates both serum, alkali and acid albumin, peptones, urates, alkaloids and oleo-resins, the four latter, however, are redissolved by heat. Dr. Oliver has shown that the addition of citric acid also renders its action more sensitive.

Other reagents are meta-phosphoric acid, sodium tungstate, potassium ferrocyanide with acetic or citric acid, and the brine solution of Dr. Roberts, consisting of a saturated solution of common salt with ten per cent. of hydrochloric acid. As they possess no advantages over the above, they need not be dwelt upon at length. The mercuric and picric acid and other tests are now conveniently applied by means of Dr. Oliver's prepared papers, an invention which has done much to facilitate the testing of urine at the bedside.

Serum albumin gives to its solutions a specific rotatory power for light of—56°, the polariscope has therefore been proposed for its detection, but there are many difficulties in the way of making a calculation in the case of urine, and it could only be available in the hands of an expert.

The procedure for making an exact quantitative estimation of albumin is described in *Appendix* I., No. 6. In no case ought the rough clinical method of judging the amount from the depth of the deposit at the bottom of a test-tube in relation to the amount of urine to be relied on; for independently of the fallacy arising from an individual sample being of a higher or lower specific gravity than another, it must be remembered that urates or phosphates, together with mucus, casts, granular debris, etc., are all liable to collect together at the bottom of the tube, and so swell the bulk of the deposited albumin.

The best ready method for determining approximately the amount of albumin present in urine is Dr. Oliver's, in which all the albumin in a measured portion of the urine is precipitated by a test-paper, and then the opacity is compared with a prepared standard of opacity, which is best furnished by a piece of ground-glass. The procedure is as follows:—The test-tube, which is flattened and graduated into twenty divisions of ten minims so as to hold 200 minims, has twenty minims of urine placed in it and then a test-paper (potassio-mercuric iodide is the most suitable), is dropped in. The contents of the tube are well shaken and the resulting opacity observed. This is done by placing a card, on which lines of various degrees of thickness are printed, behind the test-tube. If the opacity completely obscures the lines, we may dilute with water pretty freely from a graduated pipette, at first say up to six measures or 40 minims of water, shake gently, taking care not to froth the mixture. The opacity is again observed by means

of the printed card, if the opacity is still greater than that given by opaque glass, the standard of comparison, then water must be added one division (10 minims) at a time till the opacity of the urine in the test-tube exactly corresponds with the opacity of the standard of the ground-glass, and which is readily observed by means of the lines on the printed card. The calculation is made by multiplying together the known value of the precipitant, according to the test-paper used, and the number of times the volume of the urine has been increased by dilution; thus, in the case of the mercuric paper, *the standard of opacity is one-tenth per cent.*, if therefore it is necessary to dilute the 20 minims of urine to 180 minims then $\frac{180 \times \cdot 1}{20} = \cdot 9$ per cent. of albumin. If the albumin should be so abundant that the standard of opacity is not reached till over 200 minims of water have been added, the test should be again repeated, but this time only adding 10 minims of urine instead of twenty, then if the dilution is carried to 140 minims, $\frac{140 \times \cdot 1}{10} = 1 \cdot 4$ per cent. of albumin. When the lines on the card can be read at once without any dilution of water, the quantity of albumin is below one-tenth per cent. This method of Dr. Oliver's is one of the most valuable additions to practical urinary work that has been made for sometime past, for without going so far as to say that it gives absolutely correct results as to weight, it undoubtedly furnishes us with a very fair approximate idea as to the variations in the amount of albumin taking place from day to day in the progress of a case. No positive deduction ought to be made, however, from either the qualitative or quantitative determination of albumin in a single sample of urine, the qualitative examination should be extended to as many samples as possible, especially

those passed on first rising in the morning, after food, and after exercise has been taken, whilst a quantitative determination of the twenty-four hours' urine should be made at least once a week.

24. **Paraglobulin.**—Paraglobulin or serum globulin is generally found in urine, associated with serum albumin from which it may be separated by the addition of magnesium sulphate to complete saturation. The precipitate is filtered off, and carefully washed in hot water (75° C) till all traces of sulphate are removed; the filtrate contains the serum albumin. Paraglobulin can also be obtained by diluting the urine to twice its bulk with distilled water and passing a current of carbonic acid through the mixture; should the urine be neutral or alkaline it will be necessary to render it slightly acid, by means of a few drops of dilute acetic acid. Until the researches of Hammarsten it was supposed that paraglobulin was present in only small quantities as compared with serum albumin, and its presence in the urine was entirely overlooked. It is now shown that in blood the proportion of serum globulin to serum albumin is as 1 to 1·5, and in the urine it is sometimes met with in considerable excess of the serum albumin, this no doubt can be accounted for by the fact that it diffuses more readily through animal membranes than serum albumin. In rare cases, which however may become more numerous now we are taught to look for it, paraglobulin may appear without being associated with serum albumin. I have seen one such case whose "life" was declined for albuminuria and whose urine when first examined contained an abundance of both albumins, but on a subsequent examination only gave a trace of paraglobulin. As a rule, however, the two albumins are always associated; the paraglobulin has been found in excess in the following class of cases. *(a)* In

the intense hyperæmia following cantharides poisoning, etc. *(b)* In long standing cases of chronic nephritis complicated with lardaceous degeneration. *(c)* In the early stage of scarlet fever nephritis, especially in children. *(d)* In functional albuminuria associated with marked disturbance of the digestive organs.

25. **Modified Albumins.**—Acid albumin or syntonin, and alkali albumin or casein, are sometimes observed in the urine, when that fluid is either highly acid or alkaline. They are not separated from the blood in this form, but are produced by the action of the acid or alkali respectively of the urine, or in dirty test-tubes, on the ordinary albumin. As they give no reaction with heat, they may be overlooked unless they are reconverted into ordinary albumin, by adding an alkali or acid respectively. For this purpose in the case of acid albumin, the urine is neutralised with a few drops of sodium carbonate solution, carefully avoiding excess, and then heated, or better still by dropping one of Dr. Oliver's sodium carbonate test-papers into the hot urine, when a streak of albuminous opacity will follow the paper as it sinks to the bottom. In the same way with alkali albumin, we neutralise with dilute acetic acid and then heat, or drop a citric acid test-paper into the hot urine in the test-tube.

26. **Peptones.**—Peptones, or peptone like bodies are very frequently to be met with in the urine, both associated with albuminuria as well as independent of it. They give no precipitate with heat or nitric acid, but do so with picric acid, and with potassio-mercuric iodide, the precipitate being soluble when heated. Their special distinguishing tests are :—

(a) Rosy-red with alkaline solution of cupric sulphate. This is an extremely delicate reaction, and to obtain it satisfactorily, it must be performed in the manner described,

British Medical Journal, vol. i., p. 662, 1883; viz., a drachm of Fehling's solution is placed in the bottom of a test-tube, and then a drachm of the urine is to be gently floated on the surface, at the point of contact a zone of phosphates form, whilst just above this, if peptones are present, a delicate rose-coloured halo will float. Should the peptones be mixed with serum albumin the halo will be mauve, if only albumin is present, purple.

(b) Yellow precipitate with acid mercuric nitrate (Millon's reagent) and potassium iodide; this test has been devised by Dr. Archer Randolph of Philadelphia. It is based on the fact that if Millon's reagent be added to an aqueous solution of iodide of potassium, a red precipitate of mercuric iodide results, if however, peptones or bile acids are present the precipitate is yellow. To 5 c.c. of urine, which must be cold and only faintly acid, two drops of saturated solution of iodide of potassium are added, and then three or four drops of Millon's reagent, then if peptones or bile acids are present, a yellow precipitate falls, the question as to the presence of bile acids is settled by applying the special tests for them. The test is so delicate that it has been able to detect peptones in the proportion of 1 to 17,000 of water.

(c) A bulky flocculent precipitate with phospho-tungstate of soda, this test is much used in Germany.

The process for the separation of peptones from the urine is a long and difficult one, and as it would serve little practical purpose here, it is described in full in *Clinical Chemistry*, p. 148.

The occurrence of peptones in the urine, except as a rare event, has been doubted by Dr. G. Johnson, but the evidence both in this country and on the continent goes to show that their presence is far from being exceptional. Thus the observations of Hoffmeister, (*Zeit. f. Physiol.*

Chimie, bd. iv., § 260, and bd. v., § 73), Maixner (*Prager Vierteljahrsschf.*, bd. cxliv., § 75), and Jaksch (*Zeit. f. Klin. Medicin*, bd. vi., 413, 1883) have shown that the occurrence of peptones in urine is far from uncommon, for not only are they found in the urines of persons suffering from acute septic diseases, as typhus, diphtheria, tertiary syphilis, small-pox, cerebro-spinal meningitis, etc., but they appear also when pus or inflammatory exudations are absorbed in any part of the body. Thus Jaksch has found peptones in urine in croupous pneumonia, twenty-four times out of twenty-nine cases; in four cases out of five of pleuritic effusion; and twelve cases out of twelve cases of acute rheumatic effusion. But not only do peptones appear after the reabsorption of inflammatory exudations in the blood, but their characteristic reactions develope in urine whenever young cell forms are formed in excess along any portion of the genito-urinary tract, so that peptonuria occurs on very slight irritation of the urinary mucous surface.

Occasionally they are found associated with temporary or intermittent albuminuria, of these I have met with two instances in which the albumin would be present in one sample, and absent in another, and I am inclined to believe in these cases the albuminuria and peptonuria, were dependent on some functional derangement of digestion. In two other cases, peptones were present without any albumin being detected, there was no evidence of purulent reabsorption nor of pus in the urine, both cases presented a debilitated appearance, so that at first chronic Bright's disease was suspected; my friend Dr. Sansom has informed me he has met with a similar case. Again, peptonuria may result from decomposition of albumin taking place in the urinary passages, without the peptone being derived from the circulation, since any albuminous sub-

stance may be converted into peptone by prolonged contact with animal or even vegetable tissues. Peptone also is formed as an early product of the decomposition of proteid matter by bacteria. It will thus be seen that any given case of peptonuria requires extensive clinical investigation in order to determine the origin of these bodies.

27. **Hemi-albumose** *(Pro-peptone).*—Pro-peptone or para-peptone is one of the bye-products of gastric and pancreatic digestion. According to recent views, the initial stage of the digestion of albumin is the formation of anti-albumose and hemi-albumose, both are considered as para-peptones, the former resembling syntonin, the latter corresponding to what was formerly known as Meissner's peptone. It is this last product that is occasionally met with in urine, sometimes associated with true peptones, occasionally by itself. Dr. Bence Jones first drew attention to the presence of this proteid substance as an occasional constituent of urine, having found it in a case of osteo-malacia. Kühne (*Zeitsft. für Biologie*, xix., p. 209) has described a case of osteo-malacia, in which for nearly five weeks the patient passed urine rich in hemi-albumose. The urine deposited an abundant sediment consisting chiefly of urates and this proteid substance. He gives the following directions for its separation. The proteids were separated by precipitation with alcohol, and the precipitate washed and dried at a low temperature ; the dry residue was only partially soluble in water. The residue insoluble in water was again extracted with water, after treatment with a five per cent. solution of sodium chloride. The aqueous solution of pure hemi-albumose obtained by these means, coagulates when warmed, if the solution is free from every trace of acid or alkali, if these are present even in the smallest degree coagulation is prevented. Digested with pepsine, peptone alone is formed. Digested with trypsin and one

per cent. solution of sodium carbonate, after some days peptone, with leucin and tyrosin, are formed. Heated with potash, indol is produced. Boiled with sulphuric acid leucin and tyrosin are formed. The aqueous solution gives with excess of sodium chloride and acetic acid a precipitate which is soluble on the removal of the salt. Oertels (*vide* Ziemssen's *Handbuch der Therapie*, 1884) also found this body in the urines of two individuals, out of thirty-three, after the ascent of considerable heights. In one of the others serum albumin was found.

28. **Bile.**—Whenever the discharge of bile from the liver into the intestines is interrupted, a yellow tinging (jaundice) of the skin, as well as of the other tissues and fluids, takes place, owing to the biliary matters being carried into the circulation. The urine thus acquires a deeper colour varying from a darkish yellow to a colour like London Porter, and which gives a yellow stain to a linen rag when dipped into it. The tests for bile in solution are those that reveal the presence of the bile pigments, and the bile acids.

(1) *Bile-pigments (Gmelin's Test).* A few drops of the urine are placed on a white plate, and near them a few drops of nitric acid to which a drop or so of sulphuric acid has been added. The two fluids are then slowly intermixed by means of a stirring rod, when if bile-pigment be present a play of colours, of which green is characteristic, is observed. As a play of colours without the development of distinct green is given with other colouring matters, if there is the slightest doubt about the development of the green-tint the following test should be applied.

(Marechalts' Test). Float a few drops of urine upon the surface of some tincture of iodine placed in a test-tube; at the point of contact of the two fluids a delicate green colour will develope if bile-pigment is present.

(2) *Bile Acids.—Pettenkoffer's Test* is difficult of application, and often unsuccessful when applied after the manner described by most authors. I have found the method devised by my friend Mr. Francis, formerly Demonstrator of Chemistry at Charing Cross Hospital, however, most satisfactory for clinical purposes, and it has never failed to demonstrate the presence of bile acids, if present. The method is, floating the suspected urine on the surface of sulpho-saccharic acid. The latter he directs to be made as follows. Thirty grains of glucose dried over a water-bath, and when quite cold to be dropped into half an ounce of strong sulphuric acid. If the glucose is quite dry no carbonization occurs, and a delicate straw-coloured liquid is the result, and which will keep for several days in a closely stoppered bottle excluded from the light. A drachm of this placed in the bottom of a test-tube, and an equal quantity of urine floated on the surface, will give the characteristic purple reaction if bile acids are present. If there is no time to prepare the sulpho-saccharic acid, ordinary glucose or honey does as well. About five grains of this is added to a drachm of urine, and the mixture floated over the surface of strong sulphuric acid, in this case, however, more carbonization occurs, which obscures the development of colour reaction, than is the case with the first method.

In cases of doubt the bile acids should be separated from the urine for the purpose of testing. To do this, evaporate the urine to a thick syrup and treat with ordinary alcohol. Evaporate this alcoholic solution, and treat the residue with absolute alcohol. Evaporate this solution and dissolve residue in water. Precipitate with *neutral* lead acetate and filter. Dissolve the precipitate in alcohol and decompose with sulphydric acid. Filter on standing, the filtrate will deposit crystals of *glycocholic acid*. The filtrate

which was separated by filtration, after the precipitation with neutral lead acetate is now treated with *basic* lead acetate. The resulting precipitate is then treated in the same way as directed for glycoholic acid when *taurocholic* acid will separate out. This process it is said will detect the presence of bile acids when 0·001 per cent. are present in the urine.

For the spectroscopic examination of bile-pigment in urine, and the spectrum of Pettenkoffer's test, see *Colouring Matters of Urine.*

Jaundice was formerly regarded as being either *Hæmatogenous* or *Heptogenous* in character, and many pathologists were led to regard the presence or absence of bile acids as a diagnostic point, being present in the latter but not in the former. No such distinction can be made, since we have increasing evidence to show that all forms of jaundice are more or less heptogenous in character, and that in the so-called jaundice arising from blood poisoning (acute yellow atrophy, phosphorus poisoning, pyæmia, etc.,) there is always sufficient catarrh of the finer gall-ducts to account for the jaundice. So that though this form of jaundice is primarily caused by a morbid condition of the blood, which leads to catarrh of the finer hepatic ducts, it is absorption of bile already formed by the liver cells, which causes the jaundice, and not as was formerly supposed the conversion of hæmoglobin into bile-pigment in the circulation. Traces of bile acids are to be found according to Naunym and Dragendorff in normal urines. In the urines of dogs, as likewise bile-pigments, they are even more abundant, and very slight disturbances lead to their increase ; an important fact with regard to any deductions made from experiments on these animals. In cases of jaundice when there is no destruction of liver-tissue, the bile acids at first are

considerably increased, gradually declining as the case progresses, till they often cease to appear. In jaundice, associated with great destruction of liver tissue, as in acute yellow atrophy, rapidily growing cancer, etc., though they may be present at an early stage, they soon disappear, and as the process is usually rapid, may not be observed at all during the illness. The presence or absence from the urine of the bile acids, does not distinguish the nature of the jaundice but only the stage it has reached. As discoloration of the urine is one of the earliest indications of the general tinging of the tissues and fluids with bile, so is it the first to disappear when the obstruction to the flow of bile into the intestines is removed, and the urine becomes clear long before the deposited bile-pigment is removed from the skin and conjunctiva.

29. **Blood.**—Blood may pass into the urine from any portion of the genito-urinary tract, and the colour it imparts to that secretion depends on the amount. A very minute trace, one part in 1500, will give decided smokiness, and one part in 500 a bright cherry-red; urine containing blood is more or less albuminous, according to the amount of blood effused. Apart from the coloration, blood is recognised by the following tests.

a. Microscopic.—Blood corpuscles are recognised under the microscope by their peculiar bi-concave form and yellowish tint. They may, however, vary in shape. If the urine is moderately acid, they retain their natural form for a considerable time, but finally become jagged at the edges, lose colour, and do not adhere together. In dilute urines, the corpuscles become swollen and their concavity disappears. In alkaline urines, the colouring matter soon dissolves out.

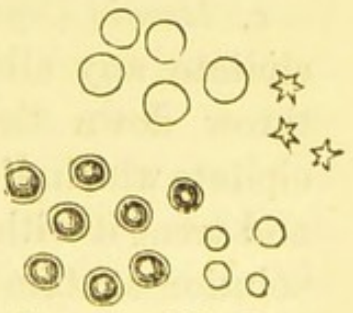


FIG. 11.—Blood-corpuscles in urine.

b. Spectroscopic.—A small quantity of urine containing blood is placed in a tube, and placed in the slit of the spectroscope, distilled water is then added till the spectrum becomes quite clear, except between D and E, where there is an intensely dark space. On further dilution this gradually clears up, leaving two bands, one near D, with well defined edges, and the other near E, broader, less shaded and defined at the edges. These bands are characteristic of oxy-hæmoglobin ; by the addition of reducing agents, these two bands are replaced by one broad band with diffuse edges, midway between D and E, this is reduced hæmoglobin. If the urine has undergone decomposition then we may have, if the urine is acid, the spectrum of acid hæmatin which gives one broad band between C and D, but nearer to C. If the urine is alkaline, then we may have the spectrum of alkaline hæmatin, this band instead of being nearer to C, approaches nearer to D, whilst the blue end of the spectrum becomes more obscure. In some instances especially in hæmoglobinuria, the spectrum of methæmoglobin will be observed, this closely resembles that of acid hæmatin, for which it has been often mistaken, it is however midway between C and D, whilst in acid hæmatin the band approximates closely to C.

c. Hæmin Crystals.—Boil the urine in a test-tube to precipitate any albumin present, adding liquor potassæ to throw down the earthy phosphates. Collect the precipitate which, if blood be present, will be tinged red, dry it and treat it with alcohol containing sulphuric acid. This solution contains hæmatin. Evaporate this solution, and then add a few grains of common salt, place the residue on a glass slide, add a drop or two of glacial acetic acid cover the mixture with a thin glass slip, and gently heat the whole. Examine when cold, when minute bluish-

red crystals of hæmin will be found dispersed through the residue.

d. Guaiacum Test.—Place a drachm of tincture of guaiacum in a test-tube, then add a drop of the suspected urine, and then float on the surface an etherial solution of hydrogen peroxide; if blood is present a blue ring will immediately form at the junction of the etherial solution and the guaiacum. This is an extremely delicate test for blood when present, but as other substances besides blood, that may be present in urine, give the reaction, it is not to be relied on as sole evidence as to the presence of blood.

Two forms of bloody urine are recognised clinically. (1) Hæmaturia in which the colouring matter is associated with the red corpuscles; (2) hæmoglobinuria, or hæminaturia, in which the blood corpuscles are absent.

(1) Hæmaturia.—*Nephritis.* Frequent in early stages of acute nephritis, urine smoky to reddish-brown, blood uniformly diffused through the urine which is generally acid. Excess of albumin, hyaline and epithelial casts, dropsy; less frequent in sub-acute nephritis, and only then attendant on fresh exacerbations of the disease; uncommon in chronic nephritis, and then only of incidental occurrence in common with hæmorrhages from other mucous surfaces.

Calculous pyelitis. Often considerable after exercise, diminishing when the patient is kept quiet in bed, when only a few blood corpuscles may be found by the microscope. Blood uniformly diffused through the urine which is generally acid. Pus cells always present in the urine, and the amount of albumin proportionate to the amount of blood. Generally accompanied with colic and retraction of testicle on the side affected. Hæmaturia may occur in other forms of pyelitis, besides that due to calculus in the kidney, but is rarely severe or persistent.

Cancer of Kidney. Hæmorrhage often very profuse with

large clots, and fibrinous moulds of ureters, etc. Generally accompanied with swelling in the loin, rapidly increasing in size. Large caudate cells of swollen columnar epithelium from pelvis of kidney often present, may be taken for cancer cells. Urine generally acid.

Disease of Bladder, Prostate and Urethra from cystitis, abcess, cancer, stone, gonorrhœa, etc. Blood often profuse, and the urine containing much mucus. In many cases the urine first passed is clear or at the most only smoky, but towards the end of micturition becomes more and more bloody. If due to stone or cancer, the mass can usually be detected by sounding. The urine is generally thick with muco-pus, and is often alkaline.

Morbid conditions of the Blood, as in scurvy, purpuric small-pox, measles, enteric fever, rheumatism. In rare cases hæmaturia has been known to precede an attack of frank gout, and in a markedly intermittent form as associated with a malarial taint. In these cases though the hæmorrhage may be profuse, clots rarely form in the urine.

Heart Disease. Hæmaturia sometimes, though rarely, occurs in valvular disease of the heart, consequent on the venous congestion.

Endemic Hæmaturia. The urine deposits dirtyish-white flocculent matter, containing short filaments of brownish colour and soft consistence, and larger reddish masses like blood clots, also highly refractive bodies, which may be identified as the ova of the Bilharzia hæmatobium.

(2) Hæmoglobinuria.—In these cases the urine contains the colouring matter of the blood, but not red corpuscles. It is probable that the colouring matter is dissolved out from them in the blood, very likely the change occurs in the liver (see Functional Albuminuria). The urine has a port wine colour, and is usually passed clear. It is always albuminous. On standing it deposits a brownish

sediment consisting of tube casts, epithelium, crystals of oxalate of lime, and crystals of hæmatin have been observed. The spectrum of this urine often exhibits the presence of methæmoglobin, in addition to that of oxyhæmoglobin. The attacks are paroxysmal, and preceded by chills, and are generally accompanied by a feeling of nausea, epigastric pain, and slight jaundice.

30. **Sugar,** $C_6H_{12}O_6$ *(Glucose).*—Normal urine contains minute traces of glucose, about ·05 grm. being passed in the twenty-four hours. This quantity may be enormously increased by circumstances which disturb the hepatic function, so that the amount passed out of the system daily can sometimes be measured by ounces. When the drain of sugar from the body is persistent or is only held in check by diet, the disease is termed "diabetes mellitus," when, however, the sugar is present in smaller quantities, and disappears on treatment, the derangement is spoken of as "glycosuria." The tests for sugar in urine are numerous, but it will only be necessary to consider three, those most generally in use, at length, merely enumerating the others which may be employed as confirmatory, or employed if by any chance the others are not obtainable.

(1) *Alkaline Copper Test.*—This test is based on the fact that alkaline solutions of glucose possess the property, when heated, of reducing salts of cupric oxide to cuprous oxide; the cuprous oxide being deposited as a red precipitate at the bottom of the tube or flask; thus :—

$$\underset{\text{Glucose.}}{2C_6H_{12}O_6} + \underset{\text{Potassium Hydrate.}}{2KHO} + \underset{\text{Cupric Sulphate.}}{2CuSO_4}$$

$$= \underset{\text{Glucose.}}{2C_6H_{12}O_6} + \underset{\text{Potassium Sulphate.}}{2KHSO_4} + \underset{\text{Cuprous Oxide.}}{Cu_2O}$$

This test is known as *Trommer's;* as, however, certain organic substances if present in excess in the urine may cause the precipitate to redissolve, it is necessary for urine

testing to employ a substance which will prevent this taking place, and this is done by adding tartaric acid in the form of Rochelle salt, sodio-potassium tartrate, to the alkaline copper solution (see *Appendix*, No. 7), the reagent thus prepared is known as "*Fehling's* test solution."

There are many modifications of Fehling's test solution, notably those of Pavy and Piffard, but they are all based on the same principle, and consist of cupric sulphate with a caustic alkali, and a tartrate of soda, potash or ammonia. These solutions are used both for the qualitative and quantitative determination of sugar. For the qualitative estimation of sugar, the procedure is as follows.

Place two cubic centimetres of Fehling's solution in a test-tube,* and carefully heat to the boiling point, then set it aside for a short time till nearly cool; if no deposit ensues on cooling, it shows the solution is in good order. The temperature is again raised to boiling point, and then one drop of urine is to be added, if sugar is present in any amount a yellow precipitate will form, which will become redder by exposure or prolonged heating. If only a very small quantity of sugar be present, the colour will be greenish rather than yellow, in this case a drop or so more urine must be added when the characteristic yellow colour will develop. In applying this test, the following precautions must be observed. *(a)* That the solution is in good order; by keeping the tartaric acid is converted into racemic acid, which has the power of reducing copper when heated, the test solution should therefore always be tried in the manner directed above before the urine is

* Since the test liquids keep better when the cupric solution is preserved distinct from the alkaline tartrate solution, it is advisable not to mix them till required, but store them in separate bottles and then for qualitative testing to add one cubic centimetre of cupric solution to one cubic centimetre of alkaline tartrate solution.

added. *(b)* To avoid adding an excess of urine, since excess of sugar dissolves the suboxide, and instead of a precipitate we get only a reddish yellow solution. *(c)* Uric acid and kreatinin when in excess have the power of reducing Fehling's solution, if any doubt exists as to whether the reduction is due to this cause or to sugar, lead acetate must be added to the urine before testing, this precipitates the uric acid, etc.; if therefore the reduction was due to these substances, no reaction will occur after their precipitation and removal by filtration. Besides, uric acid gives no reaction with either the indigo-carmine or the yeast test. *(d)* Although inosite does not reduce Fehling's solution, an olive-green cloudy precipitate is separated, which may be mistaken for that given with urine containing only a trace of sugar, it may be distinguished however by the fact that if the precipitate caused by inosite be removed by filtration, and the filtrate again boiled, the same greenish cloud will again form. Inosite, however, according to Dr. Oliver, (*Op. cit.*, p. 92) reduces indigo-carmine. The following medicinal agents give a reaction with Fehling; unoxidised phosphorus,* ammonium sulphide,* iron sulphate,* gallic* and tannic* acids, gelsemium, chloroform, resin. Those substances marked with an asterisk, according to Dr. Oliver's careful experiments, give reaction with indigo-carmine and picric acid as well. *(e)* Urine containing an excess of earthy phosphates when added to the alkaline copper solution, will throw down greyish flocks of precipitated phosphates, they are readily distinguished, however, from the precipitate of reduced copper by the absence of any tinge of red or yellow, and by their floating in the clear bluish-green solution. *(f)* In all cases the urine should be freed from albumin, if present, before applying the test.

For bedside purposes, the cupric test can be applied by

means of Dr. Oliver's prepared papers, or Dr. Pavy's pellets, or as I suggested in 1880, (*Lancet*, vol. ii., p. 192), in small glass capsules, each containing one cubic centimetre of Fehling's solution, supplied by Martindale, New Cavendish Street.

The quantitative determination of sugar by means of Fehling's solution is described in *Appendix* I., No. 7.

(2) *Indigo-Carmine Test.*—This has lately been re-introduced by Dr. Oliver, and he has made it readily available by means of his specially prepared test paper. It is based on the fact that glucose and certain carbo-hydrates when heated in the presence of an alkali, have the power of reducing indigo-blue to indigo-white, thus :—

$$\underset{\text{Indigotin.}}{2(C_8H_5NO)} + H_2 = \underset{\text{Indigo-White.}}{C_{16}H_{12}N_2O_2}$$

To apply this test, render the urine alkaline by means of a little sodium carbonate, and then add a few drops of sulpho-indigotate of sodium (indigo-carmine), and then heat in a test-tube, care being taking not to boil or shake the fluid, after a while the blue solution changes colour passing rapidly from blue to violet to red and finally to a pale yellow or white; on shaking the mixture the blue colour is restored, owing to the reconversion of the indigo-white to indigo-blue under the influence of oxygen. As the solutions required for this test undergo a gradual change on keeping, Dr. Oliver's prepared test-papers, which are very stable if kept dry, are the best for its application. A paper charged with indigo and sodium carbonate is placed in a test-tube and covered with distilled water (spring water will do but if very hard the solution is not clear though it does not interfere with the reaction), and then apply heat, till the fluid in the test-tube is deeply blue. Then add one drop of urine and boil for about ten or twenty seconds, then raise the test-tube above the

flame of the spirit lamp so that the mixture is kept hot, but does not boil, taking care also not to shake the fluid, and in a short time (about five seconds if the quantity of sugar is large, over twenty grains to the ounce, and thirty to sixty seconds if small), the change of colour will take place; now shake the tube and the blue colour will be restored. Should the urine be highly acid, or the water in which the indigo is dissolved be very hard, it is advisable to add a little more alkali, which can be done by dropping into the mixture an extra sodium carbonate paper. This precaution is necessary as in a case of diabetes in which there was an excess of sugar, and the urine highly acid, I failed to get the reaction till I had made this addition. In carrying out this test, as indeed in all analytical procedures, it is important to see that the test-tubes are perfectly clean, since a trace of nitric acid, liquor potassæ, Fehling's solution, or decomposing urine may modify considerably the reaction. The indigo test is not only useful in itself for determining the presence of sugar but is a valuable supplement to Fehling's, since the latter is reduced by uric acid and kreatinin whereas the indigo test is unaffected. It is also useful in determining a small amount of sugar in the presence of much albumin, pus, blood, etc., since these bodies do not interfere with the reaction, as is the case with Fehling's solution, before the application of which they have to be removed.

(3) *Fermentation Test.*—This requires time, but is an extremely valuable test especially as affording a rough clinical indication of the amount of sugar present. For this purpose the differential process recommended by Roberts is the one usually employed, and is as follows:— The urine is collected for twenty-four hours and carefully measured, and four ounces of this is taken and placed in an

eight-ounce bottle together with a small piece of yeast, and in another bottle of the same size a similar quantity of urine but no yeast. The two bottles are now to be put aside in a warm place for twenty-four hours, and after the lapse of that period, the contents of each having been poured into two urine glasses their respective specific gravities are to be taken. *The difference of each degree lost in the urine which has the yeast, indicates the presence of one grain of sugar in every fluid ounce of urine.* For example, if a patient passes 160 ounces of urine in the twenty-four hours; and the specific gravity of the urine in the bottle without the yeast is 1·042, and in the bottle with yeast 1·033 or nine degrees less (which represents the loss occasioned by the formation of carbonic acid), then as each degree lost represents one grain of sugar; the 160 ounces multiplied by 9 gives 1440 grains of sugar passed in the twenty-four hours. If French measures are employed, then each degree of specific gravity lost represents 0·2196 gramme of sugar in every 100 c.c. of urine.

In employing this test it is advisable to use a urinometer with a long index, so as easily to read off the variation in the number of degrees, and always to use the same instrument in recording the observations in any given case, since these instruments, especially those that have been in long use in hospital wards, rarely accord with one another. If these particulars are attended to, very close results will be obtained, quite sufficient to show the daily variations in the amount of sugar as influenced by diet, etc., although it is advisable from time to time, say once every fortnight to make a correct determination by means of Fehling's standard solution.

If definite results have been obtained by means of the alkaline cupric test, the indigo-carmine reaction, and by fermentation, our enquiry need not be carried further as

these tests are in themselves conclusive, and as these reagents are readily available they are the tests most likely to be resorted to. It will therefore be sufficient merely to enumerate the other reactions of glucose without entering into details. *(a) Moore's Test.* A brownish colour developed on boiling saccharine urine with liquor potassæ. *(b) Bötteker's Test.* Equal volumes of urine and liquor potassæ are mixed together in a test-tube, and two or three grains of bismuth subnitrate dropped into the mixture, which is then boiled, when sugar if present will reduce the bismuth to its metallic state and it will fall as a black precipitate. If the sugar is only in very small quantity the precipitate will be only greyish, in this case more urine and alkali must be added, and the mixture again boiled. Albumin and unoxidized sulphur are the only products likely to be met with in urine, besides sugar, that give a similar reaction with bismuth salts. *(c) Picric Acid Test.* The urine is rendered alkaline by liquor potassæ and a grain or so of picric acid added to the mixture, which is then heated, when if the smallest trace of sugar is present a deep mahogany-brown coloration will develop, caused by the conversion of picric into picramic acid. Normal urine when heated with liquor potassæ and picric acid acquires a distinctly brownish colour, but the coloration is never so deep as is the case if the most minute trace of sugar is present. Dr. G. Johnson has devised an exceedingly ingenious method of quantitatively estimating the amount of sugar by the depth of colour yielded by this reaction as compared with a standard colour prepared for comparison, an account of which is given in *Clinical Chemistry*, p. 157. *(d) Polarimetry.* Glucose possesses the property of rotating polarized light towards the right. This property has been made use of to determine the amount of sugar present in urine, by the amount of devia-

tion observed, which is done by means of an instrument called a saccharometer. The procedure requires a considerable amount of special skill and training, and as it is not generally available for clinical purposes, is not described here, the reader, however, will find an account in *Clinical Chemistry*, p. 158, and in other works more especially devoted to chemistry and physics. The specific dextro-rotatory power of glucose may be stated however, it is + 57·6°. *(e) Torula cerevisiæ* or yeast plant always developes in saccharine urine, and forms a characteristic white scum on its surface, and is associated with penicillium glaucum or mildew. It forms oval vesicles about the size of a blood corpuscle in which stage it cannot be distinguished from the other, the thallus, however, of the torula bears a brownish coloured spherical head of sporules.

The pathological significance of sugar in urine will be fully considered, when we come to consider the morbid conditions of urine dependent on functional derangements, (Diabetes).

31. **Inosite** (*Muscle sugar*).—Inosite is occasionally present in urine as a morbid product, to obtain it the urine is completely precipitated with sugar of lead, filtered, and the warm filtrate treated with basic acetate of lead as long as any precipitate is formed. It is better that the urine should be concentrated to one-fourth before it is precipitated. The lead-precipitate collected after twelve hours' standing is washed, suspended in water, and then decomposed by sulphuretted hydrogen. After the filtrate has been left at rest a short time, a small quantity of uric acid separates from it; this is removed by filtration, and the fluid so concentrated as to remain permanently turbid, when treated with an equal volume of alcohol. It is then heated until the turbidity disappears, and allowed to stand

one or two days. The crystalline mass thus obtained is purified by re-crystallisation. Inosite either separates in large rhombic tables, or in small tufted groups of oblique prisms. The crystals are soluble in six parts of water at 20° C. Their solutions do not undergo vinous fermentation, but readily take on lactic acid fermentation. They do not reduce Fehling's solution, but turn it an olive-green, and after a while a flocculent precipitate falls, and the supernatant fluid becomes blue, on filtering off the precipitate and again heating the solution, the olive-green colour is again developed. Another delicate test is to evaporate a pure solution of inosite to which a drop or two of nitric acid has been added, to near dryness, then touch the residue successively with ammonia and solution of calcium chloride, and then dry slowly, when a rosy-red colour will develop.

The pathological significance of the presence of inosite in urine has not been yet worked out. It has been found as an occasional constituent in certain diseases, diabetes, Bright's disease, phthisis, in syphilitic cachexia, and in typhus. Writing in 1880 *(Demonstrations Phys. and Path. Chem.)* I stated that the peculiar reaction with Fehling's solution as stated above, was often to be observed in examining urines, and Dr. Oliver (*op. cit.* p. 87), has since confirmed my observation, so that it is possible that inosite does appear in the urine more frequently than is generally supposed. In the cases I have met with, there has been usually some polyuria though not excessive, loss of flesh, general malaise, and always considerable aching of the limbs, in these instances no tangible disease was present. Again it is not at all uncommon to meet with this reaction in the intermittent forms of glycosuria, when for some days the copper has been fully reduced, and then only this olive-green coloration appears. The subject is deserving of more attention than has yet been paid to it.

32. **Lactose,** $C_{12}H_{22}O_{11}+H_2O$ (*Milk Sugar*).—Lactose is not infrequently met with in the urine of suckling women, sometimes in such quantities as to resemble true diabetes. A case of this kind has been under my observation at the London Hospital. A young married woman, aged twenty-nine, who was suckling her second child, applied as an out-patient in November 1881, suffering from debility with frequent and excessive micturition. The urine was examined and found to contain about three per cent. of sugar, she remained under treatment till January, and then ceased attendance. In April 1882, she applied again for some other complaint, and stated that she was again pregnant, and that since she had been so, the diabetic symptoms had disappeared, there was then no sugar in the urine. She was confined towards the end of the year, and again sugar was found in the urine, but not to the same extent as on the previous occasion. She became pregnant again about June, 1883, and was confined in March 1884, early in May she came again to the hospital, complaining that the symptoms had returned with great severity, but that she had been completely free from them during her term of pregnancy. On examining the urine it was found to contain an abundance of sugar, she is still under observation, and the amount of sugar has been diminished by the administration of opium. The child has been weaned. It has been shown that the sugar in these cases is not glucose, but lactose, as proved by the dextro-rotatory power being + 59·3°, instead of + 57·6°, and from characteristic crystals of lactose being obtained from the urine. Lactose gives the same reaction with Fehling's solution and indigo-carmine that glucose does, it is not, however, so readily fermentable with yeast.

33. **Lævulose,** $C_6H_{12}O_6$ (*Invert Sugar*) has been found by some observers in the urine of persons suffering

from symptoms analogous to those of diabetic patients, with or without glucose. It can be distinguished from glucose by the fact that it turns the plane of polarisation to the left instead of to the right. This rotatory power diminishes as the temperature rises, being —106° at 15° C; —79·5 at 52° C, and —53° at 90° C. Lævulose reduces alkaline copper solution like glucose. I have never met with a case similar to those that have been described, but I can readily imagine that the excessive ingestion of cane sugar, and the sugars of certain kinds of fruits might cause the appearance of invert sugar in the urine, especially in the case of disturbed digestion, or too rapid absorption, since we know that in the intestines cane sugar is converted into a mixture of glucose and lævulose.

34. **Alkapton.**—A yellowish resinous body is occasionally found in urine, which by exposure to air acquires a brownish tint, and so stains the linen. It was first discovered by Bödecker in the urine of a man convalescent from typhus fever. It does not ferment, and does not reduce bismuth like glucose, though it throws down a somewhat brownish mass. Dr. Maguire (*Brit. Med. Journal*, Oct. 25th, 1884), thinks that pyro-catechin which sometimes appears in human urine is the same as Bödecker's alkapton. With Fehling's solution, it gives peculiar reactions according to the amount of solution used. If only a small quantity of copper is added to the alkaline tartrate solution, on adding the urine containing alkapton the sub-oxide will not be deposited, but the solution acquires a yellow colour. If the copper be in excess, the sub-oxide is precipitated as with glucose, as a yellow precipitate which rapidly becomes a brilliant red. Basic lead acetate gives a white precipitate, which on exposure to air acquires a brownish-violet colour. It can be separated from urine by precipitating with basic lead acetate, the pre-

cipitate collected and suspended in water, and the mixture decomposed with hydrogen sulphide. The filtrate is then evaporated and triturated with barium sulphate, and then exhausted with ether. A brown mass is left on the evaporation of the ether, this must be dissolved in water and precipitated with neutral lead acetate, and the filtrate treated with basic lead acetate. This precipitate is then suspended in water and decomposed by hydrogen sulphide. The filtrate is then evaporated, when the alkapton will be deposited as a yellowish resinous substance highly soluble in water, but only sparingly in ether.

35. **Leucin and Tyrosin.**—Leucin and tyrosin when met with in the urine are invariably associated together, though their relative proportions vary greatly in different cases.

Leucin, $C_6H_{13}NO_2$, separates from urine in the form of circular oily discs (fig. 12, *a*) of a yellowish colour. To obtain it in a pure and crystalline state, evaporate the urine to dryness, and dissolve the residue in boiling alcohol, on cooling leucin will be deposited in white shining plates greasy to the touch, lighter than water, much resembling cholesterin in appearance, but distinguished from that body by being insoluble in ether.

Tyrosin, $C_9H_{11}NO_3$, is obtained from urine by precipitating the colouring and extractive matters with basic lead acetate, and decomposing the filtrate with sulphydric acid and filtering. The clear filtrate is then evaporated to a thin syrup, on cooling crystals of tyrosin will be deposited. The crystals (fig. 12, *b*, *c*), are long prismatic needles, which cluster together to form stellate masses or spherical balls. The crystals are sparingly soluble in cold water and alcohol, but soluble in alkaline and acid solutions. Warmed with a few drops of sulphuric acid, a solution of tyrosin gives after neutralization with barium

carbonate, a violet reaction with ferric chloride. Solutions of tyrosin heated with a mixture of mercuric and mercurous nitrate give a red colour.

When these bodies are in great excess, the mere evaporation of a drop of urine on a glass slide is sufficient for their detection; they then appear, the tyrosin as sheaf-like

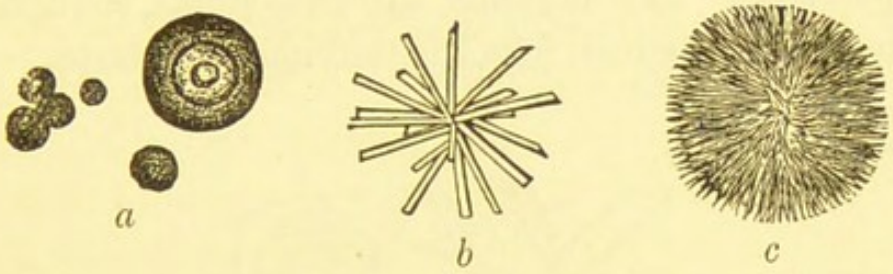


FIG. 12.—Leucin and Tyrosin.

bundles of fine acicular needles, and yellowish-green globules, the leucin in lumpy globular masses (fig. 12, *a*). The presence of these bodies denote rapid and extensive destruction of the liver cells. Hence they are met with in the urine in acute yellow atrophy of the liver and phosphorous poisoning, in malignant forms of typhus and small-pox. Recently Dr. Anderson (*Med. Chir. Trans.*, vol. xiii.), has stated that these bodies are to be found more frequently in urine, than has hitherto been allowed, and that they are to be met with under numerous pathological conditions, which affect the liver either intrinsically or from without. This statement, however, requires confirmation, but it is not improbable that if we looked more closely for these bodies, we might meet with them more frequently. With regard to the relative proportions of these bodies present in any given case, my experience leads me to the conclusion that tyrosin is more abundant in acute and rapid cases, whilst excess of leucin seems to denote a more chronic course.

36. **Cystin,** $C_3H_7NSO_2$.—Cystin forms a somewhat rare variety of urinary calculus, and is still more rare as a deposit. When present it may be separated from urine by adding excess of acetic acid, and allowing the mixture to stand some hours. The deposit is then collected, dried, and redissolved in ammonia. The ammoniacal solution is then slowly evaporated, when if present crystals of cystin will be deposited. The crystals are hexagonal, though a few may be rhombohedral, forming laminated groups. They

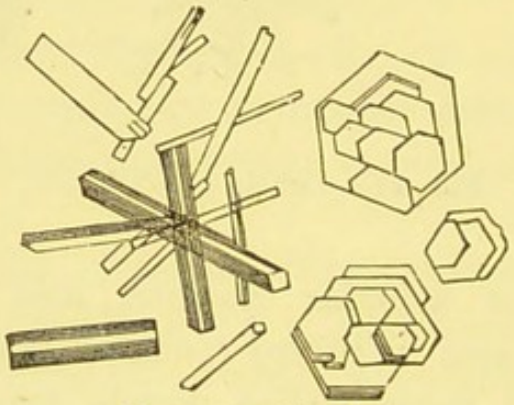


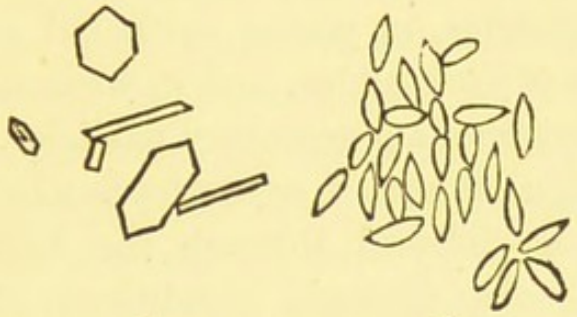
FIG. 13.—Cystin.

have a pale lemon colour turning greenish on exposure to light and air. The crystals dissolve in caustic alkalies, and in strong nitric acid, but the alkaline carbonates precipitate it from its acid, and acetic acid from its alkaline solutions. Owing to the presence of sulphur in its constitution, a black precipitate of lead sulphide is formed, if cystin is present, when the urine is boiled with caustic potash and lead acetate, this is a very delicate test for its presence. Deposits of cystin may be mistaken for urates, but cystin does not yield the murexide reaction, and does not readily dissolve when the urine is heated.

The clinical and pathological significance of cystinuria will be discussed in the section on Stone and Gravel.

37. **Xanthin,** $C_5H_4N_4O_2$.—Xanthin is the constituent of an extremely rare form of calculus, it has also been met as

gravel, the subjects have been always youths. To obtain it from a calculus, the powder is dissolved in dilute hydrochloric acid, and the solution evaporated when hexagonal and prismatic crystals of xanthin will deposit, (fig. 14, *a*).



a *b*

FIG. 14.—Xanthin.

When deposited from urine spontaneously as gravel, it occurs in white scales, or lemon shaped plates, (fig. 14, *b*), these dissolved in dilute hydrochloric acid will separate out in hexagonal crystals, on evaporation of the acid solution. Xanthin is insoluble in water, alcohol, or ether. Soluble in dilute hydrochloric and nitric acids. Dissolved in a little strong nitric acid, it leaves a yellow residue on evaporation, which when touched with liquor potassæ, and then warmed yields a dark purple colour. This reaction distinguishes it from uric acid, which gives a pink residue on evaporation with nitric acid, which on touching with ammonia gives a purple reaction, but not with liquor potassæ.

The clinical and pathological significance of xanthin will be discussed in the section on Stone and Gravel.

Hypo-xanthin or sarcine has been found in the urine of leucæmic patients associated with traces of xanthin, and excess of uric acid. The process for separating it is long and complicated, and as its separation is of little practical value, the account of it will not be given here. The student will find it given in *Clinical Chemistry*, p. 168.

Deposits derived from the Urinary Passages.

38. **Mucus.**—The mucus derived from the mucous membrane under the ordinary conditions of health consists of mucus corpuscles, or young epithelial cells, nucleated epithelial cells of the bladder, and in women of the vagina, with some amorphous pigmentary particles. This mucus when the urine is left at rest, separates as a light transparent cloud, which is diffused through the lower stratum of the secretion. In diseased conditions of the mucous membrane, the quantity of epithelium discharged may be enormous, and is often mixed with other morbid products such as pus, blood, etc.

Pure mucus forms a clear translucent mass, in which are observed mucus corpuscles, or young epithelial cells, and is derived from all parts of the genito-urinary tract. Mucus treated with acetic acid deposits mucin in stringy filaments. Mucin is not soluble in solutions of the alkaline salts, but dissolves in the caustic alkalies. It is freely soluble in lime or baryta water. It is not precipitated from its solutions by heat. Whilst only a slight turbidity is given with mercuric chloride. Its solutions are precipitated by acetic acid, citric acid, picric acid, alcohol, alum, basic lead acetate, and dilute mineral acids. In the case of these last, the precipitate is soluble in excess. It may be distinguished from albumin by its solutions not being coagulated when heated, and by being precipitated by acetic acid, and from pyin by giving no precipitate with mercuric chloride. Mucin when boiled for some time with dilute mineral acids, yields acid albumin and another body which closely resembles dextrose, by reducing alkaline solutions of cupric sulphate. Eichwald has also obtained from mucin a peptone body; by long

boiling with excess of lime water, passing a current of carbonic acid through the solution, removing the precipitate and evaporating the filtrate, and precipitating it with alcohol. These decompositions should be borne in mind since it is not impossible they may take place in the urinary passages under abnormal conditions, if this should prove to be the case, we should have an explanation that would account for some of the anomalous reactions we sometimes meet with in urines, in which traces of glucose and peptones are present, without our being able to assign any sufficient clinical reason for their appearance. In highly acid urines, if mucin is in excess, it will appear in fine threads or strings.

The amount of mucus is always increased in catarrhal and inflammatory conditions of the urinary passages, and the portion of the tract affected is generally indicated by the character of the epithelium, thus :—

Round Epithelium—rounded and spheroidal cells with well defined single nucleus, which does not require the action of acetic acid to render it visible, are derived from the urinary tubules chiefly from the convoluted portion. It is found in urine associated with renal casts, both attached to them (epithelial casts) or separate. In the early stages of acute nephritis many perfect cells will be observed, but as the disease advances the distinctive characters become obscured. Many undergo fatty degeneration and form fatty corpuscles, which adhering to the casts make the granular cast, some become withered and atrophied whilst others break up into amorphous granular debris. In some instances the nucleus divides so that the cell has the appearance of having multiple nuclei, and so be taken for a pus corpuscle, it may be distinguished from that, however, by the fact that it does not require the addition of acetic acid to render the multiple nuclei visible.

Columnar Epithelium is derived chiefly from the pelvis of the kidney, the ureters and the urethra. The cells are somewhat triangular but very irregularly shaped, being caudate, spindle and cylindrical, with well defined nuclei. They often adhere closely together. They greatly resemble cancer cells when swollen, especially in alkaline urine when they become much swollen, but they are by no means so large, perfect or numerous as cancer cells generally are. The part of the urinary tract they are derived from can only be determined by the clinical indications. If there is evidence of pyelitis they are derived from the pelvis of the kidney and ureter, if there is gonorrhœa from the urethra, if associated with small cylindrical plugs of mucus, and there is no gonorrhœa, they are derived from the lower part of the urethra and indicate irritation of the prostate.

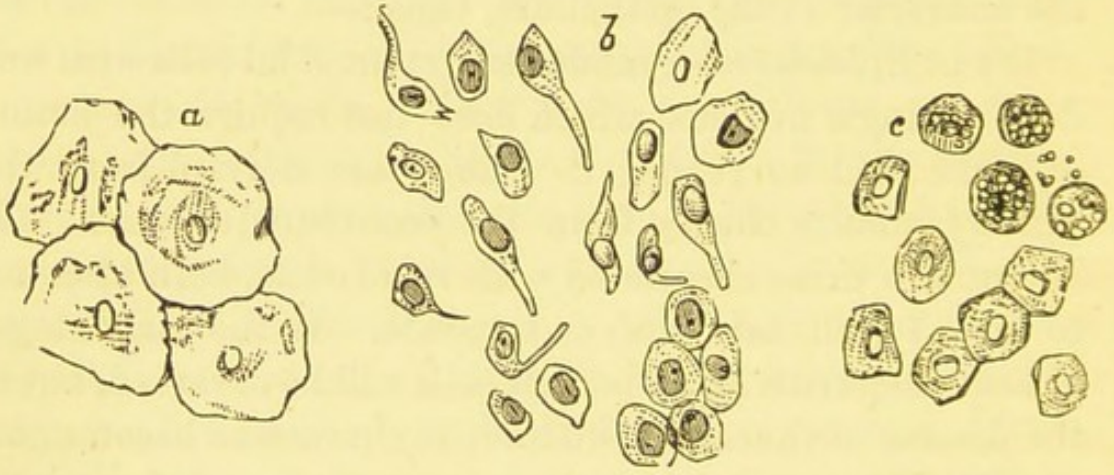


FIG. 15.—*a*. Vaginal epithelium. *c*. Renal Epithelium, healthy and fatty. *b*. Epithelium from the bladder, ureter and pelvis of the kidney.

Squamous Epithelium is derived from the bladder, and also in females from the vagina. The cells are large and rounded, considerably larger than renal cells, and generally have an irregular outline. It is always found in normal urine, and in females owing to the admixture of vaginal mucus is generally abundant. It is difficult to

distinguish between the epithelium derived from the bladder and that coming from the vagina, as a rule, however, vesical epithelium is smaller than vaginal.

Mucus Corpuscles, small oval cells of greyish colour rather larger than a blood corpuscle, generally surrounded by strings of mucus. On the addition of water or dilute acetic acid they swell up, become paler, and their nuclei are rendered more distinct. Caustic alkalies convert them into a gelatinous mass. Mucus corpuscles are young epithelial cells, which are discharged before the full period of development is reached, they cannot be distinguished from the pus corpuscle, except perhaps that a single nucleus is more generally observed than with the pus corpuscle. Tyson (*op. cit.*, p. 152), puts the relationship of the two very clearly when he says, "the pus corpuscle is a cell too rapidly produced to develop into normal tissue, whilst the mucus corpuscle is only accidentally arrested in its development.

Pigment Particles have been well described by Roberts. They are small celloids less than the size of a blood corpuscle, stained generally a reddish-orange. Sometimes the staining is complete, more usually dotted through the celloid. No pathological significance is attached to them. Dr. Richardson of Philadelphia has ingeniously suggested that they are produced by little scratches in the glass slide which have become filled with oxide of iron used in polishing the glass. This, however, does not account for the fact that they are undoubtedly more numerous in cases of Bright's disease, pyelitis, etc., than in normal urines. My own idea is that they are deposited particles of urobilin entangled in mucus, the greater the discharged mucus the more numerous will be the particles observed.

All forms of urinary epithelium are distinguished from mucus and pus corpuscles by the fact that dilute acetic acid is not required to render the nucleus visible.

39. **Pus.**—Pus consists of a liquid portion or liquor puris, and pus corpuscles. The liquor puris which is exuded liquor sanguinis contains a variable quantity of albuminous constituents, fatty matters and extractives. The proteid elements, amounting in laudable pus to 8·5 per cent., are serum albumin, para-globulin and traces of a peptone body. The fatty matters consist of neutral fats, cholesterin and lecithin. The extractives contain glucose, traces of urea and leucin. The pus corpuscles cannot be distinguished from the mucus corpuscles described above. These corpuscles are dissolved by caustic alkalies, and

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FIG. 16.—Pus-cells in urine, unaltered, and affected by acetic acid.

this furnishes a ready test for pus in solution, since by the addition of liquor potassæ to the deposit in urine, consisting of pus, it is converted into a viscid glairy mass like white of egg.

Irritation of any part of the genito-urinary tract will furnish pus, and it is extraordinary what a slight disturbance is sufficient to cause its formation, especially in middle aged and elderly persons. Exposure to cold, the passage of urine loaded with urates, oxalates or phosphates, will cause the presence of pus cells in the urine, even the use of highly seasoned dishes will often induce a catarrh of the mucous membrane, in feeble and delicate persons, of sufficient intensity to lead to the formation of pus corpuscles. In the recent discussion on the presence of traces of albumin in the urine under apparently normal condi-

tions, this possible source of albumin has been strangely overlooked, and Sir Andrew Clarke did good service at the last meeting of the British Medical Association, in drawing attention to the numerous extra-renal sources of albuminuria. It is, however, an undoubted fact, that a catarrh of the urinary passages so slight as to give rise to no symptoms, does frequently exist, sufficient to give rise to traces of albumin in the urine, and which can be only detected with delicate reagents. This liability of the mucous membrane to secrete pus on the excitation of a slight catarrh, is increased if any portion of the tract has been previously subject to acute inflammation, so that those who have suffered from gonorrhœa, gleet, or inflammation of the bladder are particularly sensitive to the action of any irritant applied to the surface. The urine of gouty persons is frequently purulent. Virchow has recently related how in his own case during an attack of gout his urine became albuminous and on examination was found to contain pus, with an abundant deposit of uric acid crystals. In these cases sometimes the whole urinary tract seems to be affected.

When the pus comes from the kidney it may be derived from an abscess of that organ, or from inflammation of the mucous membrane of the pelvis (pyelitis). In these cases, as a general rule, the urine does not contain much mucus and retains its acid reaction. It often comes in sudden discharges, this is caused no doubt by its passage down the ureter being obstructed by a coagulum, so that the purulent urine collects in the pelvis till by its pressure it overcomes the resistance to its discharge. When the pus is derived from the bladder it is generally mixed with a quantity of mucus (muco-pus), and the urine readily undergoing fermentation becomes ammoniacal. In consequence of this the reaction becomes alkaline, and the

pus is converted into stringy viscid masses, loaded with ammonio-magnesium phosphate in sufficient quantity as frequently to prevent or obstruct the flow of urine. Pus too may find its way into the urinary tract from without, as when abscess results from inflammation of the cellular tissue around the kidney (perinephritis), or at the base of the bladder, or from prostatic abscess.

Pus is deposited in neutral and acid urines as a dense creamy layer, in alkaline urines as a ropy stringy mass. To distinguish between pus and mucus when both are present is often difficult, the best plan is to add mercuric chloride, which precipitates the pyin, but not the mucin; this is filtered off, and the filtrate treated with acetic acid, which precipitates the mucin. To differentiate between albuminuria derived from the blood vessels, from the albumin of the liquor puris, is impossible, and we must rely on the general clinical character of the urine, and whether the amount of albumin observed corresponds to what one would expect from the number of corpuscles present, or is in excess of them.

40. **Casts.**—Various views have been expressed regarding the nature and mode of formation of the tube casts, that appear in the urine as the result of diffused inflammation of the kidneys. Some believe them to be formed from the epithelium, either by a secretion from these cells, or by their disintegration and fusion. Others, and this is the view generally held at present, regard them as the result of an albuminous exudate, poured out from the capillaries into the tubules. This exudate also saturates the epithelium, and loosens it, and thus ultimately leads to its disintegration and destruction. If the albuminous moulds formed by the exudate, come away before detachment of the epithelium takes place, then we have the small *hyaline cast* (fig. 17, *e*), if however, the epithelium is loosened, this

will adhere to the surface of the cast, and then we have the *epithelial cast* (fig. 17, *b*), if blood should be effused into the tubule, then blood corpuscles adhere, and we have the *blood cast* (fig. 17, *a*), if the epithelium has undergone degeneration, then the cast is covered with a granular debris, and we have the *granular cast* (fig. 17, *c*). As the disease advances and the tubes become bared of their epithelium and widened, the casts are increased in breadth, *broad*

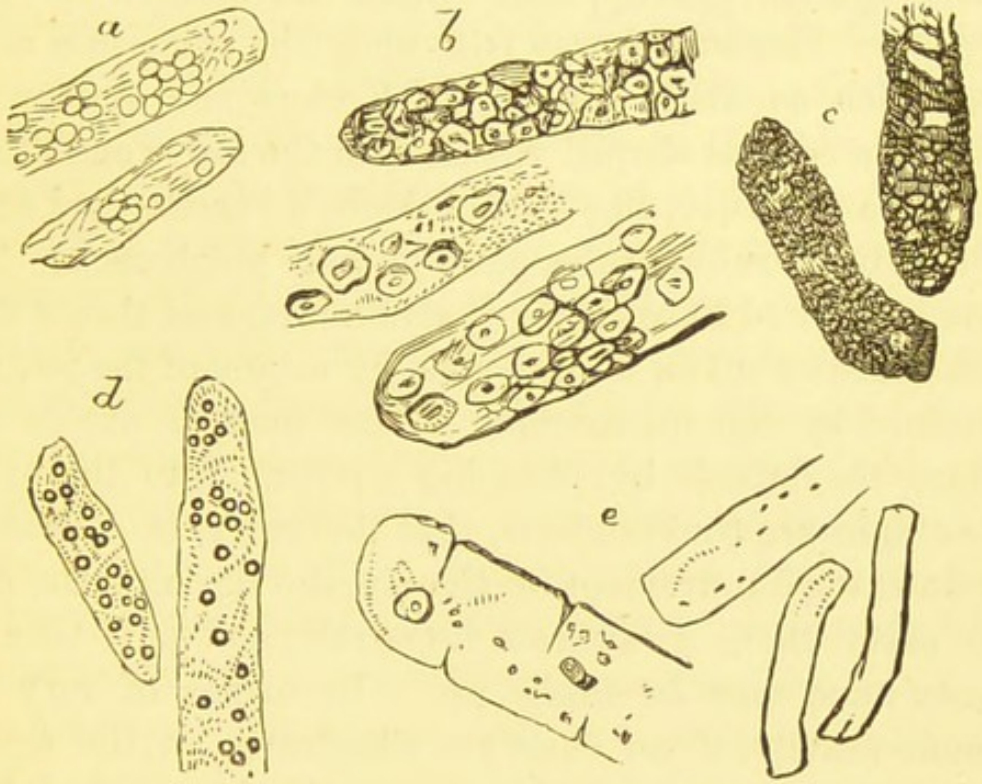


FIG. 17.—*a*. Blood casts. *b*. Epithelial casts. *c*. Granular casts. *d*. Fatty casts. *e*. Hyaline casts.

hyaline cast (fig. 17, *e*), these are often dotted with oil drops, the result of fatty degeneration of the renal cells, *fatty cast* (fig. 17, *d*). The hyaline casts often undergo a waxy degeneration, and stain deeply with iodine and methyl-violet. Casts therefore are either simply hyaline, or else hyaline material that has undergone degeneration, or to which epithelial elements have been added. Casts vary much in size, the small hyaline

rarely exceed ·025 μ, whilst the broad are often ·05 μ, in width, the epithelial and granular casts are usually of medium size and range from ·035 to ·04 μ. Crystals of triple phosphate, oxalate of lime, or uric acid often adhere to tube casts, according to the prevailing reaction of the urine.

The presence of casts in urine may be overlooked unless care is taken. As they subside slowly, especially in urines of low specific gravity, time should he allowed for that purpose. The surest way is to place the urine in a urine glass, such as made for me by Krohne and Sesemann, which is a conical shaped vessel, with the lower end drawn out into a fine tube, like that of Mohr's burette, and fitted with an india-rubber tube, glass jet and pinch-cock. The urine is allowed to settle for twelve hours, and then a drop or so is drawn off on a glass slide by means of the jet, and examined by the microscope. This method avoids disturbing the deposit by plunging a pipette into the urine, for so light are these objects, that the currents caused by the downward movement of the pipette through the fluid may carry them away from its nozzle, and so if they are scanty none may be taken up. In urines of very low specific gravity, if no casts are withdrawn at the end of twelve hours, it is advisable to sprinkle a very fine light powder on the surface of the urine. This by sinking slowly through the urine will carry any floating casts downwards with it.

Casts are never found in normal urine, nor is it probable that they ever occur except in association with nephritis. The instances in which they are found in jaundice, or when a renal calculus exists, or in dyspepsia associated with oxaluria, etc., is no evidence o the contrary, since the presence of these abnormal products in the urine may readily excite a degree of nephritis

sufficient to determine an exudate from the vessels surrounding the tubules. Tyson (*op. cit.*, p. 168) says, while it is not impossible for non-albuminous urine to contain casts, he has never met them, except in a few instances, and in these albumin had been already present, the albumin having disappeared before the last casts had been washed out. Casts are not met with in cases of purely functional albuminuria, whenever in such a case after albumin has been sometime observed, casts make their appearance, we may be sure that organic changes are also taking place. Although the presence of casts may be taken as confirmatory of acute or chronic nephritis, the fact of not finding them on one examination must not allow us to assume the contrary, since they are sometimes retained for a short while, or else passed in such scanty numbers as to be overlooked. Repeated examinations should therefore be made, when if any changes have occurred in the tubules they are sure to be discovered. Fine hyaline, epithelial and blood casts are met with in acute cases of recent origin. Broad hyaline, granular, waxy, and fatty casts indicate that the nephritis has passed from the acute to the chronic stage; in the later stages the granular cast disappears and the casts are altogether hyaline and fatty. It is doubtful whether casts are separated from the tubules in lardaceous degeneration of the kidneys, but as this process seldom, if ever, occurs without nephritis concurrently taking place, it is difficult to say in any given case whether the few hyaline casts generally observed in these cases are not due to this cause.

In addition to these casts simple aggregations of epithelial cells and fine plugs of mucus may be met with in the urine, forming fine cylinders. These mucus plugs form elongated fibrils often branched. In many cases they

seem to be formed by an highly acid condition of the urine precipitating the mucin, they are dissolved by liquor potassæ; they are more frequently met with in disease of the bladder than in renal disease. Pus casts are occasionally observed, they are generally found in the urinary tubules and in the urine in cases of disseminated suppuration of the kidney. As minute cylinders, mucous plugs in which are embedded amorphous granules and minute acicular crystals of phosphate of lime may be observed in most cases of vesical and prostatic disease. In the urine from a case of locomotor ataxy they constituted, with the exception of a mere trace of albumin, the only morbid phenomenon. The addition of liquor potassæ dissolved the purulent matrix leaving the phosphate of lime unaltered. Tubercular masses are found in the urine of persons suffering from scrofulous disease of kidneys or bladder.

41. **Fatty Matters.**—The urine normally contains a trace of fatty matter but so minute that over six pints yields but 1½ grain (Schunk). It is apparently a neutral fat composed of palmitin and stearin. When animals are fed upon excess of fatty articles, glycerin-phosphoric acid, according to Zuelzer (*op. cit.*, p. 18), is found in the urine, derived from some phosphorized fatty body, probably lecithin. It is also probable that the neutral fats are increased by a fatty diet, since oil globules have been detected in the urine of persons taking large amounts of cod-liver oil. In pathological conditions, fatty matters consisting of neutral fats, cholesterin and lecithin can be extracted from urine by means of ether. So also in chronic Bright's disease when the epithelium is undergoing fatty degeneration. In acute yellow atrophy of the liver, when the renal cells undergo acute fatty changes, the urine contains an excess of fatty matter. In the urine of a patient, who died of acute diabetic coma, I found an

abundance of oil globules. In chyluria, the urine contains a considerable amount of fatty matter which yields neutral fats, cholesterin and lecithin. As an urinary deposit, plates of cholesterin are sometimes met with, in these cases the cholesterin is not derived directly from the blood, but from old purulent collections of which the more soluble portions have undergone absorption. Leucin and cholesterin are sometimes mistaken for each other, the former, however, is insoluble, the latter freely soluble in ether. Fatty concretions (*urostealith*), consisting of a mixture of fatty and soapy matters mixed with mucus and withered cell forms, are sometimes formed in the urinary passages, these also point to some past purulent formation which has undergone concretion.

To separate the fatty matters from the urine and to obtain them in their separate forms, 100 c.c. of the twenty-four hours' urine must be evaporated to near dryness and the residue exhausted with ether. This is best done by boiling the etherial mixture in Drechsel's apparatus if at hand, or in a glass flask fitted with a long glass-tube twenty inches long, in this case the heat is best applied by keeping the flask in nearly boiling water and adding more ether to supply the loss by evaporation. After some hours the etherial solution is poured off and evaporated to dryness on a weighed platinum capsule, this gives the weight of the neutral fats, the cholesterin, and lecithin. To separate these, dissolve the residue in boiling alcohol and add baryta water, boil the mixture till the whole of the alcohol is expelled, filter whilst hot. The filtrate contains the neutral fats in the form of baryta soap; the precipitate consists of cholesterin and the products of the decomposition of lecithin, viz., neurin and glycerin-phosphoric acid. The precipitate is then mixed with water and treated with absolute ether, which removes the cholesterin; the etherial

solution is then poured off and evaporated; the residue dissolved in boiling alcohol evaporated and the crystallised cholesterin weighed. The watery mixture left after the removal of the ether is evaporated to dryness and the residue fused with sodium hydrate and nitre, the mass is then dissolved in water and nitric acid added. With this solution ammonium molybdate gives a yellow precipitate. Collect this precipitate, and dissolve it in ammonia. To this ammoniacal solution add a solution of magnesia, collect, wash, dry and ignite this precipitate, and then weigh. 100 parts of this magnesium pyrophosphate is equivalent to 764 5 parts of lecithin. To make the calculation, suppose we are examining the urine of a case of chyluria, and have found by the initial step, the weight of the total fatty matters, the neutral fats, the cholesterin and the lecithin, and for example sake we say they amount to 0·85 grm. in 100 c.c. of urine. The second step gives us the amount of cholesterin, which on weighing is found to be say ·09 grm. Whilst the third step, by calculation of the weight of the pyrophosphate, has told us the amount of lecithin, and which we will say amounts to 0·42 grm. Now if we deduct the ascertained weight of the cholesterin and lecithin from the total fatty matters the difference will represent the weight of the neutral or saponifiable fats. Thus, $0{\cdot}85-(\cdot09+\cdot42)=0{\cdot}34$ grm., so that the percentage composition of the fatty matters of this case of chyluria reads thus, neutral fats 0·34 grm., cholesterin 0·09 grm., lecithin 0·42 grm.

42. **Cholesterin,** $C_{26}H_{44}O$.—Cholesterin is a white crystalline substance, resembling spermaceti. It is deposited from its alcoholic solution in the form of glistening rhombic plates having notched edges; lighter than water, very soluble in ether, insoluble in water or cold alcohol. Touched with a drop of strong nitric acid and gently eva-

porated, cholesterin gives a yellow colour which turns red on the addition of a drop of ammonia. A mixture of two parts of strong hydrochloric acid, and one part of ferric chloride slightly diluted, evaporated with cholesterin gives a violet coloured residue. The conditions under which cholesterin is sometimes deposited in urine and the manner of separating it is described in the preceding paragraph.

43. **Fungi and Parasites.**—*Penicillium Glaucum.* Mildew developes in acid urine, and dies in alkaline urine. The sporules are oval, nucleated, vary greatly in size. According to recent experiments these sporules, removed, washed and dried at 55° C, on again being moistened will revive and then decompose dilute solutions of urea. The thallus is derived from sporules either by elongation or budding, and then forms an elongated, branched, cellular shoot, which rises to the surface of the urine and gives off branched tufts of sporules. It is always abundant in albuminous urine, and in urines containing much mucus. Kiesteine, a greasy looking pellicle, which forms on the surface of the urine of pregnant women, when kept a few days, consists of this fungus, mixed with fatty matter, and withered cell forms. The fatty matter is probably derived from the fatty degeneration of the epithelial cells, which are abundantly shed from the vagina and bladder in this condition.

Torula cerevisiæ. Sugar fungus resembles in its early growth that of the penicillium, but the thallus is distinct, having a round clustered head covered with a brownish powder. It is peculiar to saccharine urine. An excellent account of the development of these growths is given by Hassall (*Med. Chir. Trans.*, vol. xxxvi., p. 32).

Sarcinæ have been frequently found in urine, they have been met with in the pelvis of the kidney, but their chief seat is probably the bladder. They present the

characteristic wool-pack appearance, viz., cubical masses with transverse divisions, they are smaller, however, than those met with in the stomach or lung. They exist both in acid and alkaline urine. Their presence in urine is always associated with more or less lumbar pain, frequent micturition and abundant mucus deposit.

Bacteria. Dr. Roberts has described some interesting cases of bacteruria, occurring without decomposition of the urine. The organisms appear to be of one or more kinds. Some appear to resemble *bacillus subtilis*, and they mostly appear as short rods or filaments. They cause no decomposition in the urine, which keeps its acidity for some days. The patients complain of frequent and painful micturition and pains about neck of the bladder, there may be no manifest disease of the urinary organs. He has also met with micrococci chains in the freshly passed urine from a patient who had resided in South America, although he has repeatedly made examinations, he has failed to observe the same condition in any other case, he therefore thinks it probable that this latter is of exotic origin.

Stale decomposing urine speedily developes a number of small moving organisms, *bacteria termo*, and ammoniacal urine always contains the spherical bacterium, *micrococcus ureæ*, which causes ammoniacal decomposition.

Spermatozoa. Although spermatozoa can hardly be regarded as parasites it is convenient to consider them here. They consist of a club-shaped oval head and a fine whip-like tail. Their length is about $\frac{1}{600}$ inch. In urine they lose the vibratile movement observed in semen. The discussion of spermatorrhœa does not fall within the limits of this work except with regard to its occasional relationship with oxaluria where a few words will be said about it.

Entozoa. The following are the chief:—*Echinococcus hominis* or hydatid cyst, the hooklets of which may be found in the urine. *Strongylus gigas*, a nematoid worm, said to be occasionally found in the kidney. *Bilharzia hæmatobia*, a trematode worm, chiefly affecting the bladder and intestines, the ova of which are found in the urine. This parasite gives rise to the endemic hæmaturia of tropical climates, it has been especially observed in Egypt, the Cape and Mauritius. *Pentastoma denticulatum*, a minute parasite that has been found on one occasion in the kidney *Filaria sanguinis hominis* has been found in the urine of patients suffering from chyluria. A detailed account of these parasites will be found in the chapter on Parasites of the Kidney. In addition to these parasites, thread-worms, *ascarides*, round-worms, *lumbrici*, joints of tape-worms, *tænia*, may be discharged by the bowel into the urine. Moreover, the parasites of other animals may accidentally, or intentionally, find their way to the chamber vessel.

44. **Extraneous matters.**—Hair, fœtal bones, fæces, etc., may find their way into the urine from communication with cysts, or intestines, with the urinary passages. Fibres of linen from the cloths used in cleaning the chamber utensils, fragments of human or animal hairs, dust and debris of every kind and description, and which are only to be recognised by their microscopic appearance, a full description of which will be found in works especially devoted to the representation of microscopic objects. The student, however, who has made himself thoroughly acquainted with the chemical reactions and microscopic appearance of true urinary deposits, can never be misled by the presence of these extraneous and accidental matters. When, however, substances are introduced intentionally for the purpose of

deception, the fraud is sometimes difficult of detection. Thus, a short while since, I received a fragment of grit said to have come from the urinary passages. It charred under the blow-pipe flame, decrepitating with great violence, and the ash effervesced on the addition of dilute acid; it therefore closely resembled oxalate of lime. There was however, an insoluble residue, that resisted all chemical reagents, and was not reduced by the blow-pipe; the quantity at my command being small, I could not decide its nature. I then wrote to ask if more of the deposit could be obtained, and then I found that the insoluble residue consisted of sand. I therefore concluded that the deposit consisted of mortar, the organic matters which charred, being probably the hairy substances, which are mixed with good mortar to render it more binding, and perhaps some of the mucus from the urine in which it had been immersed. Cane sugar is not infrequently added to urine by hysterical patients, but this fraud is easily detected, more difficult is the diagnosis in the case of the addition of egg albumin, honey or blood. In these cases however, there is generally some important link wanting in the clinical evidence, which leads to detection, as soon as suspicion is aroused as to the patient's *bona fides*.

Organic Deposits separated from the Urine.

45. **Organized Deposits.**—In addition to the deposits derived from the urinary passages which we have just considered, it happens that substances derived from the blood, and ordinarily held in suspension in the urine, are often deposited. The causes of this deposition may generally be referred to either of the following conditions, or a combination of them. (*a*) To changes in the reaction of the urine,

as in the case of deposit of triple phosphate in ammoniacal urine, and uric acid in highly acid urines. (*b*) To absolute excess, as in certain conditions of the system when uric acid, oxalate of lime, or phosphate of lime is eliminated in excess. (*c*) To relative excess, when the proportion of water in the urine is diminished, as when urates are deposited in pyrexial conditions, or after profuse sweating. (*d*) To the absolute insolubility of the substance, as with cystin, xanthin, or leucin. As the chemical nature, and the clinical significance of the substances forming these deposits are discussed elsewhere, it is only necessary to enumerate them here, with a brief reference to their chief characteristics, by which they may be distinguished, and which are given in the following table. For fuller details the reader is referred to their respective headings.

Table of the chief Organized deposits separated from urine.

Deposit.	Form.	Heat.	Reaction of urine.	Liquor Potassæ.	Acetic Acid.	Special Character.
Uric Acid, p. 80	Rhombic crystals. Variable forms.	Very insoluble at all temperatures.	Acid	Soluble	Insoluble	Murexide reaction.
Urates, p. 81	Amorphous or spiked globules.	Soluble at 40° C.	Acid	Soluble	Insoluble	Murexide reaction.
Cystin, p. 132	Hexagonal plates.	Insoluble	Acid	Soluble	Insoluble	Soluble in liquor ammoniæ but not its carbonate. Blk. precip. when heated with liq. potassæ and acetic acid.
Xanthin, p. 133	Lemon-shaped crystals.	Insoluble	Acid	Soluble	Insoluble	Evaporated with nitric acid and residue touched with liq. potassæ deep purple reaction.

Table of the chief Organized deposits, etc. (Continued)

Deposit.	Form.	Heat.	Reaction of urine.	Liquor Potassæ.	Acetic Acid.	Special Character.
Calcium Oxalate, p. 88	Small octohedral crystals. Variable forms.	Insoluble	Acid or Alkaline	Insoluble	Insoluble	Soluble in acid sodium phosphate. Ash effervesces with hydrochloric acid.
Calcium Phosphate, p. 94	Amorphous or fine stellar crystals.	Insoluble	Alkaline (fixed)	Insoluble	Soluble	Neutral or faintly acid, urine becomes turbid on boiling, and clears up on addition of acid.
Ammonio-Magnesium Phosphate, p. 96	Triangular prisms or feathery crystals.	Insoluble	Alkaline (volatile)	Insoluble	Soluble	Mixed with phosphate of lime, the ash fuses under blow-pipe into an enamel-like crust.
Leucin	Oily discs.	Soluble	Acid or Alkaline	Soluble	Insoluble	Insoluble in ether.
and Tyrosin, p. 131	Acicular needles.	Soluble		Soluble	Insoluble	Solutions boiled with mercuric nitrate give red precipitate. Violet reaction with ferric chloride.

CHAPTER III.

Diffuse Inflammation of the Kidneys.

46. **Classification.**—Cotugno was the first physician who discovered that the urine of dropsical patients sometimes contained albumin, which he supposed resulted from an altered condition of the blood serum. Dr. Blackall, of Exeter, however, was the earliest observer who connected albuminuria with actual disease of the kidney, a fact which Bright a few years later worked out with such a degree of completeness that his name has ever since been associated with the disease. Dr. Bright distinguished one form, but three varieties, of diseased kidney as associated with albuminuria, and considered that each variety was only a stage towards the development of the complete form, which he believed was reached in the granular kidney. He held that the whole process was due to the presence of a morbid deposit in the kidney, leading to a granular condition of the kidney, and consequently applied the term "*granular degeneration*" to the disease in all its stages. The idea, however, of a morbid deposit soon gave place to more correct views, which attributed the changes in the kidney to the process of inflammation. Virchow, in Germany, and George Johnson, in England, were the chief exponents of this doctrine. Virchow insisted on the importance of distinguishing whether the changes proceeded from the epithelium (croupous or parenchymatous nephritis), or from the interstitial tissue (cirrhosis), or from the vessels (waxy degeneration). He clearly taught that though these three different forms were distinct from

each other, still that one form having lasted a long while might yet end in being complicated by one of the others, or by both of them together. Thus an old parenchymatous, or a long standing interstitial nephritis, might have grafted on it, in the stage of marasmus, waxy degeneration; or kidneys, the subject of parenchymatous inflammation, might undergo changes of an interstitial character. Dr. George Johnson further extended the idea of the multiplicity of the forms of Bright's disease, and classified them with regard to the changes that took place in the renal epithelium. Thus he divided the disease into an acute desquamative nephritis, a chronic non-desquamative nephritis, and a chronic desquamative nephritis. He also included waxy degeneration as a form of Bright's disease. He was the first, moreover, to point out the hypertrophied condition of the small arteries that occurs in contracted granular kidneys. In 1860, or eight years after the appearance of Johnson's work, Traube distinguished four forms of Bright's disease :—1. Circum-capsular, which was characterised by the growth of connective tissue round the glomeruli, and which pursued a chronic course from the first, and which corresponds to the chronic form of interstitial nephritis; 2. Inter-tubular which was attended by a new growth between the tubes, and which began acutely with more or less tendency to hæmorrhage; 3. Cirrhosis produced by venous congestion, as in long-standing heart disease; and, 4. Waxy degeneration of the kidney. According to Traube, the changes that took place in the renal epithelium in both the circum-capsular and inter-tubular varieties were secondary to those occurring in the connective tissue.

Though this view was not generally accepted, still Traube's investigations drew attention in a more marked degree to the importance of studying the nature of the

changes occurring in the connective tissue around the glomeruli and between the tubules, than had been previously done. The subject was closely followed up in England by Dr. Dickinson, and in Scotland by Dr. Grainger Stewart, and by them our knowledge was still further advanced, and the nature of the processes made more definite. According to Dickinson, whose classification has been generally adopted by the London schools, Bright's disease may be divided into three forms:—1. *Tubal nephritis*, acute or chronic, in which the renal epithelium and tubes are primarily affected by the inflammatory process, and which corresponds with acute and chronic parenchymatous nephritis; 2. *Granular degeneration* in which the inter-tubular matrix undergoes contraction; this may be the result of the chronic tubal nephritis, but generally arises as a primary condition; and, 3. *Depurative disease*, or in other words, waxy or lardaceous degeneration of the kidneys.

Dr. Grainger Stewart also recognizes three forms:—1. The inflammatory, which passes through three stages, viz., inflammation, fatty degeneration, and atrophy; 2. The cirrhotic or contracting form; and, 3. The waxy or lardaceous.

According, however, to more recent views, the classification of Bright's disease has been further simplified. Waxy or lardaceous degeneration has been excluded as a distinct form, and is associated with Bright's disease only when grafted on long continued inflammation of the kidneys. Similarly the false cirrhosis (cyanotic induration) of the kidneys, the result of venous congestion dependent on long standing disease of the heart is now generally considered as distinct from the diffuse inflammation, leading to granular contracted kidney. Moreover, the doctrine of the unity of Bright's disease has been revived, and histological

investigations have shown the important part played by the changes in the glomeruli in the evolution of chronic Bright's disease.

With regard to the unity of Bright's disease, Rosenstein (*op. cit.*) has stated concisely the view, which leads us to regard the alterations occurring in the kidney, as not due to two distinct inflammatory processes, the one parenchymatous and the other interstitial, but to refer them only to a diffused nephritis. Diffused inflammation, he says, is the basis of Morbus Brightii, an inflammation which like that of other organs begins with changes in the circulation. It is characterized by the exudation of lymph corpuscles, whilst at the same time the epithelial elements of the glomeruli and urinary tubules are affected by the inflammatory irritation. The kidneys, therefore, that come under observation in Bright's disease always show changes of all the tissue-elements, and though one element may be more prominent in its alteration than another, we are not therefore to speak of a parenchymatous or interstitial nephritis, but only of a diffused inflammation. "Only more or less the preponderance of one or more tissue-element determines the outwardly different form of the red swollen, large white, the pale granular or mottled, the white shrunken, and the red granular, kidney." Dr. Saundby (*Path. Soc. Trans.*, vol. xxxi., p. 150) has been from the first a consistent and strong supporter of this view. He considers the small red and large white kidney with all the intermediate varieties to be the result of an inflammation, which affects all the tissues, but varies in intensity. The parenchyma of the kidney, being the most highly organised, necessarily suffers most in proportion to the intensity of the inflammation. The large white kidney is the result therefore of repeated severe inflammation, whilst the small red kidney indicates

an inflammatory process of prolonged duration but of minimum intensity, and the intermediate varieties correspond to all different degrees of intensity possible between these extremes.

The more careful study of the changes occurring in the glomeruli, have shown that these changes are common to the several forms of Bright's disease, and have also given us an insight into the different relations they hold in the evolution of the several varieties. Klebs was the first to point out the changes that occurred in the interior of the Malpighian corpuscles in the early stage of scarlet fever nephritis, which consist of an increase of nuclear masses so great as to fill the capsule, and compress the capillaries. Klein (*Path. Soc. Trans.*, vol. xxviii., p. 431) confirmed and extended Klebs views, and further observations have shown that these changes in the glomeruli are not limited to cases of scarlet fever nephritis, but they are also observed in cases that have resulted from exposure to wet and cold, and other well known exciting causes of acute nephritis; so that although in these cases the parenchymatous changes are well marked and are apparently primary in their origin, still we are never without evidence of some degree of concurrent glomerular change. And though these are not so evident, as in those typical cases associated with scarlet fever nephritis, in which the changes in the glomeruli are apparently primary, still we cannot dissociate the two processes as two distinct inflammations, but must consider them as the result of a diffuse inflammation, in which the alteration of one element is at one time more prominent than another, according to the intensity or duration of the inflammatory process. The same holds good with regard to the development of the granular kidney in chronic nephritis. This has been illustrated by Professor Greenfield (*Path. Soc. Trans.*,

vol. xxxi., p. 157), who considers that the changes seen in the most typical forms of chronic Bright's disease, may be regarded as due to primary changes in the vessels and glomeruli, or more accurately in the glomeruli first, then concurrently in the arteries and the excretory tract. He shows that these glomerular changes are of almost constant occurrence in chronic Bright's disease, whilst also present in most acute cases. The relation, according to him, of the large white kidney and the granular contracted kidney, lies in the fact, that whilst the former is essentially a diffuse interstitial and parenchymatous inflammation, in which changes in the glomeruli are associated with general interstitial inflammation; the granular contracted kidney in its most typical form is not necessarily attended by interstitial inflammation, but may be dependent on primary glomerular change for its complete evolution, and that the subsequent changes are mainly atrophic.

The classification, therefore, that seems most in accordance with the views at present held, may be thus briefly expressed.

Acute Nephritis.—(*a*) *Tubal Nephritis.* (Syn., parenchymatous, catarrhal, or desquamative nephritis). A very acute form, primarily and mainly affecting the epithelium, and passing by gradual steps into a chronic stage. (*b*) *Acute Interstitial Nephritis.* (Syn., glomerular nephritis). A less acute form in which the glomeruli are mainly and primarily attacked, often characterised by considerable interstitial exudation. The renal tubules and epithelium become secondarily affected, dependent on the degree and duration of the inflammatory process.

Chronic Nephritis.—(*a*) *Chronic Tubal Nephritis.* (Syn., sub-acute interstitial, chronic parenchymatous, non-desquamative nephritis) A transitional sub-acute form, may result from either of the preceding, or originate independently. It may pass through three stages. 1. Enlargement, by epithelial proliferation and intertubal growth (large white kidney). 2. Regression and fatty degeneration (pale granular kidney). 3. Contraction caused by atrophic changes in the preceding form (small fatty granular kidney). (*b*) *Chronic Interstitial Nephritis.* (Syn., renal cirrhosis, chronic desquamative nephritis). Essentially a chronic form, commencing with changes in the glomeruli and vessels, atrophy subse-

quently taking place in the parts supplied with these vessels, together with some degree of interstitial overgrowth, and which is represented typically by the small red granular kidney.

47. **Causes of Albuminuria.**—After having discussed the nature of the inflammatory process that produces the variety of changes noticed in different stages of Bright's disease, it remains to say something relative to the clinical and pathological significance of ALBUMINURIA, a symptom which at one time was considered as being solely associated with this form of disease. Recent research, however, has shown that albuminuria has a far wider clinical significance than its relationship to diffused inflammation, and that it is associated with many other morbid conditions, such as disturbances of digestion, innervation, the introduction of toxic matters into the blood, &c. We have therefore now, in any given case of albuminuria, to consider whether it arises from organic lesion or from derangement of function, whilst again these two classes may be again differentiated into other groups, thus:

1. ORGANIC ALBUMINURIA.—(*a*) *Renal.* 1. Diffused nephritis or Bright's disease. 2. Cyanotic induration of kidneys in heart disease. 3. Degenerative changes in kidneys, as in parenchymatous degenerations, which is the cause of febrile albuminuria, and in lardaceous degeneration. 4. New growths, infiltrations, and parasites of the kidney may give rise to albuminuria, by causing inflammation or irritation. (*b*) *Extra-Renal* in which the albumin is mainly derived from the pus formed in the genito-urinary tract, as in pyelitis, suppurative nephritis, cystitis, urethritis, &c.

2. FUNCTIONAL ALBUMINURIA. 1. In derangements of the nervous system. 2. Derangements of digestion. 3. Altered conditions of the blood. 4. And in the so-called physiological albuminuria.

With regard to the causes that lead to the transudation of albumin into the urine in disease, or perhaps to speak more accurately, the condition that prevents its passage from the renal capillaries into the urine in health, is still the subject of considerable difference of opinions.

In the first place with respect to the question, how it is that the renal capillaries do not constantly transude a small quantity of albumin, since the systemic capillaries throughout the body generally transmit a fluid containing serum albumin ?

The reply usually given to this question is :—

(*a*) That the epithelium covering the glomeruli, or lining the urinary tubules, has the power of re-absorbing the albumin transuded by the vessels of the glomeruli, or of the tubules, whilst it permits the passage of the water, the urea, and saline constituents. When albumin appears in the urine, according to this view, it is owing either to the destruction of the renal epithelium, such as occurs in organic diseases; or to an arrest of its function which for a time is impaired or lost, and this it is urged is what happens in the so-called functional albuminuria.

(*b*) Others have urged the view, that as the rapidity of the circulation of the blood in the normal Malpighian vessels is probably greater than in any other capillaries in the body, that this is the cause why under ordinary circumstances, albumin does not transude; and it is urged that whilst under normal pressure, water and salts only pass out, an increase of pressure is required to ensure the passage of the blood serum. This augmented pressure may be induced by changes in the kidney itself; or by a disturbance of the general arterial pressure due to disorders of other excretory organs, especially of the skin and bowels; or from derangement of the nervous system, local, general, or reflex; or from obstruction of the return of venous blood, as in heart disease. In addition to these two distinct views, all parties agree that the passage of albumin into the urine is facilitated by an altered condition of the blood, especially as regards its specific gravity, and also that albuminuria is occasionally the result of the presence, in excess, of abnormal forms of albumin.

As to which of the two views is correct, the following considerations will perhaps enable us to form an opinion :

(1) The view that the layer of epithelium covering the glomeruli or lining the tubules, has the power of retaining albumin in health, and preventing its transudation into the urine, requires perhaps further experimental enjuiry before it can be accepted as a complete explanation.

Still as Professor Hamilton (*op. cit.*) has pointed out, there are several membranes which are possessed of very remarkable properties of a similar kind. Thus the shell membrane of the fowl's egg will allow a solution of sugar to pass through it in one direction but not in another; the skin of the grape has the same action; the gall bladder retains bile during life, and Descemet's membrane exerts a similar retentive action on the aqueous humour. Thus by analogy it is not unreasonable to claim a similar protective influence for the epithelial covering of the glomerular loops, or lining of the tubules, with regard to the passage of albumin.

Clinical evidence also gives considerable support to this view. Dr. Finlayson (*op. cit.*) has satisfied himself that the epithelium of the urinary bladder has the power of absorbing albumin, and therefore argues that the renal possesses the same function. Dr. M'Gregor Robertson (*op. cit.*) arguing from the analogy exhibited by other glands under the action of atropine, holds that if this substance influenced the secretion from the kidney it would do so through the renal cells. If they were paralysed, they would be unable to absorb the albumin which would then appear in the urine. He therefore put this view to the test of an experiment, and injected atropine under the skin of a cat whose urine was quite free from albumin; on the first and second day, the urine became albuminous, and disappeared on the third day, when the animal seemed quite recovered from

the toxic effects of the drug. This experiment certainly affords strong evidence as to the part played by the renal epithelium in the causation of albuminuria. Again the diseases of the kidney in which albumin is most abundant are always those in which the epithelium is mainly and primarily affected, as in acute nephritis, and chronic tubal nephritis; whilst in chronic interstitial nephritis, or the the indurated kidney of chronic heart disease, the albumin is never abundant during the early stages or progress of the disease, though an increase is observed towards the end, when the tubules become bared of their epithelium, and the same may be said with regard to lardaceous degeneration of the kidney. Again in diabetes mellitus, the albuminuria which so often sets in in long protracted cases towards the end, is always associated with some desquamation and fatty change in the renal epithelium. The question now arises if the renal epithelium retains the albumin transuded in health, what becomes of the albumin? The answer generally has been, that it is re-absorbed and removed by the lymphatic spaces and channels of the kidney. Nor is this supposition so improbable as the opponents of this view maintain, who urge that such an event is impossible owing to the scanty provision of lymphatic channels in the organ, since recent observations seem to show that the kidney is more abundantly supplied with lymphatics than has been hitherto supposed, whilst the arrangement of the tubules gives ample time for the absorption of the albumin, and its removal from the kidney. Thus as Dr. M'Gregor Robertson (*op. cit.*) has very clearly pointed out, the urine filtered into the tubule at first is comparatively rich in albumin, but when the urine reaches the loop of Henle, the amount of albumin it contains is greatly diminished. The contracted diameter of the loop of Henle, by delaying the

passage of urine, gives time for the absorption of a portion of the albumin.

There are some, however, who while admitting that the renal epithelium plays an important part in preventing the transudation of albumin, do not believe in its reabsorption by the renal cells. They consider rather that the cells act mechanically in offering a physical resistance to the transudation, and maintain that so long as the epithelium is not detached, even though it may have undergone considerable change, albuminuria does not occur. They illustrate this view by what occurs in phosphorus poisoning. Here there is extensive destruction of epithelium, but little or no desquamation of the cells, which have undergone acute fatty changes, in these cases the albuminuria is only slight, or may be absent. In petroleum or poisoning by chrome salts, on the other hand, there is acute necrosis and detachment of renal cells, with the appearance of a considerable amount of albumin in the urine. The same, they point out, occurs in tubal nephritis, where the changes in the epithelium and the desquamation are considerable, and which is characterized by highly albuminous urine; whilst with chronic interstitial nephritis, before the epithelium becomes extensively affected, the albumin is scanty, or may be absent, and does not appear in any considerable amount till the later stages of the disease when the tubules are denuded of epithelium. Finally some would limit the albumin retaining function to the epithelium of the glomeruli. (Heidenhain, *op. cit.*) According to this view, the epithelium of the tubules are concerned only in the removal of urea, uric acid, &c., whilst the flat epithelium which covers the glomerular tuft separates the water and salts, and restrains the albumin from passing through; injury or disturbance of function of this layer being at once followed by albuminuria. This

view which is rapidly gaining ground, is supported by the experiments of Posner (*op. cit.*) and others who by suddenly coagulating the albumin in the kidneys, found albumin always between the glomerular tuft and its capsule.

(2) The view, that regards albuminuria as the result of increased pressure in the renal vessels, naturally commends itself on account of its simplicity. And at first sight the explanation that the normal pressure in the renal vessels is only sufficient for the transudation of the water, and that increase of pressure is required to force the albumin through the glomeruli and cause its presence in the urine, seems sufficient. It also receives support from experimental evidence. Thus albuminuria can be produced by ligature of the renal veins, and also follows section of the renal nerves, or irritation of the spinal cord after section of these nerves. But experiments of this kind can hardly be appealed to as decisive on this point, since the effect of ligature of the renal vessels or nerves must affect the general nutrition of the kidney, and in some measure disturb the function of the epithelium. But the most considerable objection to the adoption of this view is, that it is not borne out by clinical experience. For instance, if we take the albuminuria, the result of long standing heart disease, we do not meet with highly albuminous urine, on the contrary it is scanty, and it is not till towards the end of the disease when the tubules become implicated in secondary changes, and pressure is diminished owing to cardiac failure, that the albuminuria attains anything like prominence.

Again, in chronic interstitial nephritis, the polyuria points to excess of pressure in the existing glomeruli, yet the amount of albumin is extremely small, and it is only towards the end of the disease when the vascular pressure fails, and the quantity of urine becomes diminished, and

the epithelium is destroyed, that the amount of albumin present in the urine is at all significant. Indeed, the fact that with the great destruction of the epithelium, which occurs in advanced stages of this disease, the albumin is present in such small quantities, has been advanced against the view that albuminuria is caused by the loss of epithelium. But in answer to this objection it may be urged that the vascular supply in the granular and contracted kidney has been already much diminished by the preceding process of contraction, so that the amount of albumin filtered through the surviving glomeruli and tubules, is considerably lessened, just as in cirrhosis of the liver, the jaundice is slight, owing to the previous destruction of the vessels supplying the lobules, and the consequent atrophy of their cells. On the other hand, in acute and chronic tubal nephritis, where changes in the epithelium are mainly primary, we have an excessive amount of albumin, which continues till this form of kidney disease enters on the stage of atrophy and contraction, when the amount of albumin declines as cardio-vascular changes develop; and this diminution continues so long as the increased pressure is maintained, but when the heart begins to flag, and the pressure in the renal vessels falls, and the water is diminished, the albuminuria once more is increased, though never to the extent as in the early period of the disease. Again, in those cases where pressure is increased in the capillary vessels, in disease of distinctly nervous origin, as in diabetes insipidus, one would expect that albumin would be transuded *parri passu* with the increase of hydruria, if the increased pressure theory was the correct explanation.

Lastly, if increase of pressure in the renal vessels were the cause of albuminuria, we should find albumin more frequently in the urine of healthy subjects after severe

exertion than we do. Undoubtedly powerful muscular exercise does induce in some persons, apparently healthy, the temporary appearance of albumin. But my experience accords with that of Oertels (*vide* Ziemssen, *Handbuch des Allgemeinen Therapie*), that such an occurrence is exceptional. Oertels experimented on thirty-three individuals, some of whom were in delicate health and some women and children, these he made to ascend considerable heights and afterwards tested the urine, in only one individual was it found albuminous after this severe exertion. It is true that Leube found albumin in the urine in 16 per cent. of the cases examined by him, of soldiers after long marches, but when we reflect that among adult males, especially of the class on whom the observation was made, the conditions likely to produce extra renal albuminuria would be numerous we need not be surprised at his results. Again, in making experiments of this kind it is necessary to particularise the test employed; thus, Chateaubourg (*op. cit.*) found albumin in 75 per cent. of the urines of soldiers examined after a meal, when potassio-mercuric iodide was employed as a test, whilst it was only found once when heat was used. The mercuric iodide test, as it is well known, having the property of precipitating other proteid substances, likely to be found in urine, besides serum albumin.

In conclusion taking all circumstances into consideration, I believe with the exception of those cases, where the albumin is plainly derived from the liquor puris secreted from the mucus surface of the genito-urinary passages, or from the blood poured out into the urinary tract from rupture of the vessels, or in those cases where the albumin is not serum albumin, but some other proteids, as paraglobulin, propeptone, peptone, which being more diffusible than serum albumin, pass through simply in merit of their

diffusibility, that in all cases of albuminuria the chief and primary cause is to be attributed to either the glomerular or tubular epithelium losing its function of retaining the albuminous portions of the blood plasma within the renal vessels. Undoubtedly increase of tension in the renal vessels plays a part in the causation of albuminuria, though not to the extent claimed for it. It acts probably by bringing a larger quantity of blood to the glomeruli, so that a larger quantity of albumin is transuded than the epithelium is able to take up, and also perhaps by disturbing the function of the epithelium as well; slowing of the blood has also the same effect. It is probable, however, that mere increase of pressure is never sufficient of itself to cause albuminuria unless some other condition is present, otherwise it would be impossible to account for the absence of albuminuria in many disorders in which increased pressure in the renal vessels is undoubtedly present. In fact as some observers have stated albuminuria does not result in those experiments made to increase the tension in the kidney by section of the nerves unless the renal vessels are injured.

Among the concomitant causes of albuminuria, variation of the specific gravity of the blood must be regarded as playing an important part. Thus, Professor Hamilton (*op. cit.*) has pointed out that any alteration in the specific gravity, either increase or deficiency, will probably give rise to serious obstructive effects, and thus indirectly lead to the appearance of albumin in the urine. Thus in chronic tubal nephritis, the specific gravity of the blood is always reduced, sinking as low as 1·020 to 1·018, and in these cases, caused no doubt by the hydræmia, the result of the diminished elimination of water by the kidneys, the transudation of serum in the form of dropsy is always more or less observable, and what occurs in the

systemic capillaries no doubt occurs in the renal vessels. The same probably explains the occurrence of albuminuria as the result of the anæmia and the hydræmia attendant on the process of certain chronic diseases. On the other hand, increase of the specific gravity of the blood may explain the albuminuria of an interesting character, occasionally met with in urines of high specific gravity, and loaded with urea

Again, toxic agents in the blood may cause albuminuria, either by inducing nephritis, or by their arresting the function of the renal epithelium, as is shown by the experiment of Dr. McGregor Robertson already quoted with regard to the action of atropine. In considering the causation of albuminuria in any given case, we must bear in mind the circumstances likely to modify the amount of albumin passed into the urine. Thus, in chronic interstitial nephritis as already stated, although the tension of the blood in the existing glomeruli is raised to its highest pitch, whilst the epithelium in the late stage is never normal, and the specific gravity of the blood much reduced, circumstances all extremely favourable for the transudation of albumin, still the amount passed throughout the disease is always insignificant. This is owing, as already explained, to the fact that in the early stage, the epithelium is so little affected, that it is able to reabsorb the albumin forced through by the increased pressure, whilst in the later stage when the epithelium is destroyed, so little blood is brought to the organ, owing to the compression of the vessels by the development of cicatricial tissue, that the amount of albumin capable of transudation is very much diminished. A very similar explanation may be offered to account for the small amount of albumin transuded in the indurated kidney, or chronic heart disease, and in lardaceous degeneration of the kidneys.

Acute Nephritis.

48. **Varieties.**—Acute nephritis, as has been already remarked (p. 158), occurs either in a very acute form in which the epithelium is mainly affected, or in a less acute form in which the glomeruli are primarily attacked, the renal tubules, and epithelium becoming affected at a later stage. No distinction up to quite recently was made between the two conditions, and acute inflammations of the kidney were spoken of as catarrhal, croupous, parenchymatous or desquamative nephritis. Now, however, the more acute form is generally spoken of as *tubal* nephritis, showing that the earlier stress of the disease has fallen on the tubules and renal epithelium, whilst the less acute form is spoken of as interstitial nephritis, or glomerulo nephritis, as pointing to the increased interstitial exudation and alterations in the glomeruli, which occur as primary changes. No very rigid line, however, can be drawn between the two conditions. Glomerular changes being often observed in quite an early stage of tubal and diffuse nephritis ; whilst it is rare to find a kidney the seat of a pure glomerulo nephritis, in which the renal epithelium has not already undergone some marked change.

49. **Symptoms.**—In the *hyperæmia* induced by certain irritants such as cantharides, oil of turpentine, nitrate of potash, mustard, cubebs, and copaiba, the symptoms are those of intense urinary irritation. There is an urgent and frequent desire to micturate, but little urine is passed; what little there is, is highly albuminous, and contains more or less blood, from a distinct hæmorrhage to only a few blood corpuscles. There is, however, no great shedding of renal epithelium, in some cases it has been stated to be quite absent, but there is an abundance

of fibrin which comes away as fibrinous moulds or may even form large coagula. These moulds and clots are often sufficiently large to block the urinary passages. Pain may be referred to the kidneys, but most frequently it is felt extending from the neck of the bladder to the glans penis. In hyperæmia of a less intense form the symptoms are increased frequency in passing small quantities of urine, accompanied with perhaps a little strangury. The secretion is albuminous and may contain a few blood corpuscles but no renal epithelium or fibrinous casts, there may be a feeling of weight across the loin but no pain reflected to the end of the penis. General dropsy is never the result of mere hyperæmia. No clinical line, however, can be rigidly drawn between hyperæmia, and inflammation of the kidney, nor can we definitely say when the one passes into the other.

The onset of acute nephritis is generally announced by a distinct sense of chilliness followed by heat and dryness of skin. There is headache, the pulse is full and hard, nausea is complained of, often actual vomiting, and there may be dull dragging pain across the loins and tenderness on pressure over the kidney. All these symptoms, however, in some cases may be absent. The patient is frequently called upon to void urine, which is highly albuminous, of dark colour, from smoky, blood-red, to a deep chocolate-brown or black, according to the amount present, and the reaction of the urine. The specific gravity is high, ranging from 1·020 to 1·040, the quantity passed in the twenty-four hours rarely exceeding 500 c.c., often falling as low as 250 c.c., and even may be completely suppressed. Uræmic convulsions often accompany this condition. The reaction is generally acid. The amount of solid constituents especially the urea is diminished. On standing the urine deposits an abundant chocolate coloured sediment

of blood corpuscles, urates, casts, epithelium, and the granular debris of these. In many instances it is difficult to find the casts, especially if there is much blood and granular debris present, but ordinarily they can be made out. They are found during the early stage, as small and hyaline, with epithelial cells (epithelial casts) attached, also blood corpuscles (blood casts). A little later on, dark granular casts make their appearance. The epithelium is much altered in its shape, and often difficult to recognise with certainty, but the round celled renal epithelium and the cylindrical epithelium from the pelvis of the kidney should be looked for. The nuclei of these cells when free may be mistaken for blood corpuscles, the latter bodies are recognised by their swelling up when the fluid on the slide is freely diluted with water.

Within twenty four hours, if the inflammation is severe and the secretion of urine much diminished, but generally within two or three days, *dropsy* makes its appearance. This may range from slight puffiness, to an intense anarsarca, involving the serous cavities, pleura, pericardium and peritoneum, or even causing death by suffocation, from œdema of the glottis.

Such are the general symptoms attendent on a severe attack of acute nephritis, we must now proceed to consider the variability of the individual symptoms, and the import of such variations. In severe cases, there is usually a definite onset attended with marked *pyrexia*. The initial elevation of temperature, however, is rarely extreme, seldom, if ever, in the absence of any other inflammation, exceeding 102° to 103°F, during the progress of the disease it may rise to 104°, but usually it fluctuates between 102° and 103°, to fall often very suddenly, rising again only in the event of a relapse or secondary complications. In some of its features the temperature chart

resembles that of an acute pneumonia, only the acme is reached more slowly and the period of status more prolonged, the sudden declension about the ninth or tenth day, however, is very like pneumonia.

The gastric disturbance and vomiting in the early stage, is plainly of a reflex character, and is directly proportionate to the severity of the inflammation; should nausea and vomiting occur, however, during the progress of the disease, it is to be referred to uræmic intoxication. The degree of pain experienced depends on the severity of the attack. Dickinson (*op. cit.*) has recorded a case of intense congestive nephritis, in which the swelling of the kidney substance was so great that the capsules of both were ruptured. Such a degree of swelling is however quite exceptional, as a rule it is difficult to get physical evidence of any enlargement, though in thin persons with relaxed abdominal walls, the upper extremity of the kidney on either side, but more markedly on the right, may be felt swollen and distended.

The frequent and urgent desire to *pass small quantities of water* is most noticeable during the development of the attack but throughout micturition continues very frequent, though the urgency disappears. The *amount* of *urine* passed in the twenty-four hours is always reduced, and in severe cases this reduction is considerable, and may amount to complete suppression. As the disease subsides, it becomes more profuse, and if there has been much dropsy, the discharge of water may become very profuse indeed towards convalescence. Taking a series of cases the average amount of urine passed during acute nephritis may be stated as from 300 to 400 c.c. during the early stages, and may be as much as 2000 c.c. to 3500 c.c. towards convalescence. The *urea* may be extremely reduced, indeed almost entirely absent; cases in which it

has fallen to 1·4 grms., and even ·72 grms., in the twenty-hours, have been recorded. In ordinary cases, however, the reduction rarely falls below 16·7 grms., instead of the normal 33·4 grms. A sudden fall after the establishment of the disease has a grave import, and is generally a prelude to uræmic convulsions. In calculating the urea it must be remembered that owing to the deficiency of the water secreted, the percentage amount of that substance will appear high. In normal conditions the percentage of urea ranges from two to three per cent., with an excretion of urine amounting to 1450 c.c. in the twenty-four hours. In acute nephritis, however, the percentage of urea may rise to four or five per cent., the secretion of water being, however, only 300 to 400 c.c., so that although the percentage amount is higher, the absolute amount is decidedly less. Similarly we find the *specific gravity* increased, though the total of urinary solids is less. Next to the urea, the chlorides are the most constantly diminished, and this diminution is the most marked when there is any secondary complication such as pneumonia, or pleuritis, or peritoneal effusion. They may fall from a normal excretion of say 6·2 grms. to less than 1 grm., and some instances have been recorded in which they have temporarily disappeared entirely for a day or more. The *phosphoric acid* is always reduced, but not to the same extent as we find it in chronic nephritis, the reduction is chiefly with the phosphoric acid in combination with the earthy bases. *Uric acid* is frequently deposited in a free state, and the urine is generally turbid, with highly coloured acid urates. Their presence in such apparent abundance is due, however, to the highly concentrated urine, and to its acidity, and not to any real excess. The relative excess, however, of the highly coloured urates, which persist nearly throughout the whole course of the

disease, imparts to the urine a deep brown colour, which may be taken for blood. *Blood* is present in nearly every case of acute nephritis, and is often the first symptom that attracts the patient's attention. The hæmorrhage may be so slight that it can only be detected by the presence of blood corpuscles, or if it be exceedingly profuse. Nephritis arising in persons who have been exposed to malarial poison, is often attended with this excessive hæmaturia. According to the quantity of blood present, the urine varies in tint from a mere smokiness to chocolate black.

Dr. Mahomed (*Med. Chir. Trans.*, 1874) has endeavoured to prove that there is a pre-albuminuric stage of acute Bright's disease in which only the crystalloids of the blood make their appearance. The test Dr. Mahomed employs in proof of his assertion, is that of guaiacum and ozonic ether. This test, however, as is well known, reacts with many varieties of albumin, and as in hyperæmia the fibrin elements of the blood plasma are in excess, I venture to think the guaiacum reaction is due rather to these than to the crystalloids of the blood; since if those were present, we should be able, which we are not, to demonstrate them by means of the spectroscope. Dr. Mahomed believed this presence of the crystalloids of the blood in the urine of acute nephritis, to be due to an increase of arterial tension, which preceded the renal inflammation. This increase of tension occurs in the majority of cases, and may be generally recognized on the first day of the disease, though the pulse shortly afterwards becomes soft and compressible and often times exceedingly intermitting. With regard, however, to the contention that increased tension is the cause of the guaiacum reaction in the so-called pre-albuminuric state of acute nephritis, I do not think it can be admitted, since there are many morbid conditions in which increased arterial tension is

a marked feature, in which the urine never gives the slightest reaction with guaiacum.

The hæmaturia may continue for a considerable time, or may cease only to re-appear on an exacerbation of the disease. Sometimes bloody urine is only passed in the day, the night urine being free from blood. This generally is observed in mild cases, with whom there is often a difficulty in keeping them strictly to their bed during the day time, or who if they remain in bed keep constantly moving about, sitting up to take food, etc. The hæmaturia invariably ceases before the albuminuria, I have never met with an exception to this statement.

The most important symptom of acute nephritis is of course *albuminuria*. Although the amount varies considerably it is generally abundant, though in some exceptional cases of dropsy after scarlet fever, the urine has been found non-albuminous. Dickinson has recorded cases in which the amount of dried coagulated albumin passed into the urine in twenty-four hours amounted to 21·9 grms. and 32·5 grms. These figures impress us with an idea of the immense drain that takes place in the system, and accounts for the extreme debility and anæmia that so speedily set in. Thus a patient passing 32·5 grms. of dry coagulated albumin in the twenty-four hours is losing during that period 12½ oz. of blood serum, or very nearly one-tenth of the whole mass of the blood! Such cases, however, may be considered as exceptional the general range in my experience is from 6 grms. to 13·5 grms. The most intense albuminuria, I have met with, has been in cases of puerperal nephritis, and nephritis associated with ague, the most moderate in scarlatinal nephritis. The amount of albumin generally declines after the first day or so, even in cases that eventually terminate fatally, but a steady daily decrease must be

regarded as a favourable symptom. For the purpose of recording the amount daily passed, the method suggested (p. 105) will give fairly accurate results, without resorting to the tedious process of drying and weighing out the coagulated albumin. Long after convalescence, traces of albumin will be found to occur in the urine especially after food, or exposure to cold, so long as this condition lasts the patient must remain under observation. No relationship subsists between the hæmaturia and the albuminuria. A highly albuminous urine may contain but little blood, whilst profuse hæmaturia is not necessarily attended with a high degree of albuminuria. The character of the casts met with in acute nephritis have been already mentioned (p. 141), as the disease progresses they become broader, lose their epithelial character, and become distinctly granular. In addition to the hyaline casts found in the urinary deposit, we find the renal epithelia. Some of these may present almost a normal appearance being only swollen and more translucent than ordinary, but retaining their nuclei. Others are apparently undergoing transition, their nuclei being replaced by inflammatory corpuscles. Again much of the epithelium is reduced to mere granular debris, among which may be found the white and red corpuscles of the blood.

The *dropsy* is next to albuminuria a most constant symptom. Thus Dickinson found œdema in thirty-eight cases out of thirty-nine. The intensity of the dropsy is directly proportionate to the diminution of the urinary secretion. Although the œdema is general, still it often happens, if the case be not severe and the onset sudden, that the dropsy first makes its appearance in the most dependent part; thus if the patient be kept in bed, across the loin, if sitting up in the lower limbs, there is generally, however, some degree of puffiness of the eyelids

and some effusion into the loose connective tissue of the penis and scrotum. There is also more or less passive effusion into the serous cavities, which sometimes becomes excessive. Ascitic effusion is the most frequent and generally the most extensive. Hydrothorax occurs in about 30 per cent. of recorded cases, whilst effusion into the pericardium though generally observed *post-mortem*, is rarely clinically demonstrable during life. Œdema of the glottis is fortunately of rare occurrence. As the disease passes off and the urinary secretion becomes free, the dropsy disappears, sometimes this occurs with amazing rapidity.

The special complications that may arise during acute nephritis are:—(1) *Uræmia*, due in part to the retention in the blood of the urinary constituents, and also to an alteration in its percentage composition, from diminution of its proteid elements, and the relative or absolute increase of the extractive matters. Like dropsy the severity of its onset is in direct proportion to the diminution of the urinary secretion. Uræmic convulsions are most commonly associated with the acute nephritis arising in connection with previous morbid conditions, as in scarlet fever nephritis or in the puerperal state. I cannot, however, agree with Bartels (*op. cit.*), in saying that it does not occur in acute nephritis due to other causes, though I admit that it is of less frequent occurrence. (2) *Acute affection of the respiratory organs*, such as pleurisy, pneumonia, and bronchitis, are frequent, especially among children. Pleurisy followed by purulent effusion, or pneumonia, also going on to suppuration, is perhaps the most frequent fatal termination of acute nephritis. Pulmonary œdema on the other hand is not so common an event as it is in chronic nephritis. (3) *Erysipelas*, or even gangrene, may attack œdematous parts, especially

if they have been punctured, though this complication does not so frequently arise as in chronic renal affections. (4) *Hæmorrhages* rarely occur, unless there has been some previously existing morbid condition of the blood. Thus epistaxis sometimes, though rarely, occurs in the nephritis of scarlet fever, diphtheria, malarial poisoning, or after typhoid fever, or small pox, and in the nephritis of pregnancy. I have never seen retinal hæmorrhage in a case of acute nephritis, of recent origin, except in puerperal nephritis, but then there was reason, also, to suspect chronic renal mischief the result of preceding pregnancies.

50. **Etiology.**—Prominently, before all other exciting conditions, exposure to (1) *Cold and Wet* must be reckoned as the most fertile cause of acute nephritis. Dr. Wilks and Dr. Dickinson attribute half or fifty per cent. of their recorded cases of acute nephritis to this cause. At the Seamen's Hospital, all my cases of acute inflammatory dropsy could be referred to exposure to weather, especially to damp cold. At the London Hospital, among the male adult patients that have passed through my out-patient room into the wards, or in less severe cases, have been permitted to attend as out-patients, I find quite two-thirds attribute the disease to exposure to cold, especially exposure after having been heated. Thus the stevedores, the coal loaders, and shipwrights, who work arduously for some hours, perspiring profusely meantime, and afterwards stand about docks and yards waiting for fresh jobs, whilst still heated, and often exposed to the keen wind blowing from the river, are frequent victims of acute nephritis. Sugar bakers, iron founders, etc., who are exposed to the great heat of the furnaces, and go out into the cold yards without putting on additional clothing, also furnish a large contingent. With regard to women, the influence of cold in the production of acute nephritis is less marked, but the

flower girls, and the saleswomen of the open stalls, supply us with more than occasional examples of the disease. I have never yet succeeded in obtaining a history of exposure to cold and wet in a case of acute nephritis occurring in childhood, though the numerous waifs and strays of the East End must often suffer from this exposure, and children are as liable as adults to attacks of acute nephritis; but with them it is nearly invariably found as a sequel to scarlet fever, measles, etc. Perhaps the extreme susceptibility of their respiratory organs to the influence of cold and their liability to acute attacks of pneumonia and bronchitis divert the morbid influence of cold in this direction. Dr. Dickinson has also observed this immunity to acute nephritis arising from cold among children, for in fifty-four fatal cases recorded by him, the disease was traced to wet or cold in but four. It does not appear however that dry cold, however severe, is sufficient to excite nephritis. The experience of Arctic expeditions proves this, the men may be half starved, may suffer from scurvy, may pass suddenly from hot cabins to the intense cold of the outer air, in fact are placed in conditions one would think particularly favourable to provoke nephritis, and yet renal affections are almost unknown. The same may be said of the North American hunters. Dr. Dickinson attributes this immunity of the frigid zone from renal disorders, to the fact that the cold increases the action of oxygen, which gives rise to increased combustion of the solids and fluids of the body, cold he thinks exalts the respiratory function, and diminishes the formation of urea, the kidneys therefore are not liable to suffer by the irritation of excrementitious matter, since the stress of excretion falls on the lungs. This explanation, however, is not quite satisfactory, for if there is increased combustion taking place in the body, the nitrogenous constituents

will be reduced as well as the fatty, so that there will be no diminution in the formation of urea, true there may be a disproportion between the excretion of carbonic acid and the urea, because in Arctic regions more fatty food is consumed *relatively* to the nitrogenous, but there is no diminution in conversion of the latter. Besides this, the increased oxidation of the tissues must lead to increased formation of urea, and by no other channel can it escape from the body except by the kidneys. The reason I think why acute nephritis is common in temperate, but rare in frigid regions, lays in the fact that one is damp cold, the other dry cold. I hold that damp is a factor of greater importance than cold in the causation of nephritis. Damp chills the surface of the body more completely than mere cold, against which we can protect ourselves by warmer clothing. The two conditions, however, acting together are more surely productive of catarrhal affections, than any other combination.

(2) Next to cold and damp, *morbid conditions of the blood*, as induced by certain acute diseases, play an important part in the etiology of acute nephritis. Among these, scarlet fever holds undoubtedly the chief place, certainly two-thirds of all the cases of acute nephritis, occurring under sixteen years of age, are due to this cause. Pregnancy is not unfrequently attended with a greater or less degree of nephritis (see Nephritis, Etiological Varieties of). Acute nephritis also often supervenes during the progress of such diseases as diphtheria, measles, small-pox, varicella, acute rheumatism, less rarely in typhus, enteric fever and relapsing fever, but more frequently the albuminuria observed is the result only of the high temperature and the parenchymatous changes it causes. Other less pronounced blood diseases may also occasion it, thus acute nephritis sometimes, though rarely, may be observed on

the outbreak of secondary syphilis. The absorption of pus from closed or ill-drained abscesses may give rise to it. Thus Dr. Matthews Duncan (*Med. Chir. Trans.*, vol. lxvii.) speaks of the copious albuminuria met with in cases of parametritis. Albuminuria also is not infrequently observed in the urine in cases of empyema before tapping. I have noticed it in cases of chronic dysentery with extensive ulceration of the intestine, and albumin will frequently be found in the urine in cases of strangulated intestine. The albuminuria, however, that is attendant on the acute nephritis, consequent on morbid conditions of the blood, must not be confounded with the albuminuria that so frequently occurs in states of pyrexia which is generally variable and transitory. Thus, in scarlet fever it often happens during the early progress of the disease, and the full development of the rash, that the urine contains albumin, this however, as the temperature declines and the rash fades, passes off, and the urine remains free, till convalescence has fairly set in, when, as is not unlikely, albumin reappears, but this time with all the appearance of acute nephritis, to wit, general dropsy and bloody urine.

(3) *Extensive lesions of the cutaneous surface* often occasion nephritis, but what the *rationale* of the process is, it is difficult to decide. Indeed, the question of the relationship existing between the cutaneous activity and the renal functions, requires to be reviewed under the light of recent physiological and pathological data. Bartels has pointed out, that when renal inflammation follows a skin affection, like an extensive burn for instance, the nephritis occurs at the height of the malady, and not after the subsidence of the pathological process in the skin, as is the case after scarlet fever. Dr. Southey has endorsed this statement, by reference to a case of psoriasis under his

treatment at St. Bartholomew's Hospital, in which a severe recurrence of the skin malady was attended with a sharp attack of nephritis, which subsided as the skin affection improved under treatment. In a case of my own, at the London Hospital, of acute general dermatitis, in an unusually severe form, and which was also seen by my friend and colleague, Mr. Tay, during the development of the attack, the urine was scanty, dark-coloured and albuminous, but as soon as the inflammatory process was over, and the patient was covered with large patches of scurf skin, the nephritis completely subsided. Now had this been a case of scarlet fever, and as the patient had had three similar attacks within two years, that supposition must be dismissed, the nephritis would have certainly increased during the process of desquamation. We must, therefore, regard the nephritis of scarlet fever, and of all acute specific diseases, as occasioned by some special morbid condition, which excites renal inflammation during the process of elimination. Whilst the nephritis, provoked by direct influence on the cutaneous surface, either from exposure to cold and damp, or following extensive lesions of the skin as after burns, cutaneous eruptions, etc., is caused probably by the non-elimination and consequent retention in the blood of deleterious excretory products. With regard to the nature of the excrementitious matter thus possibly retained, Fischer proved years ago that sodium butyrate injected into the veins of animals gives rise to nephritis. Now butyric acid is not only a constituent of human sweat, but also a product of the acid fermentation of pus.

(4) *The action of specific irritants and powerful diuretics* may induce nephritis. Of these cantharides gives us the most frequent example, in the intense renal hyperæmia that frequently follows the application of a blister, or

when it has been administered internally for criminal purposes. Mustard has a similar but less powerful effect, and so has oil of turpentine. Some persons are more susceptible than others to the action of these substances, and a very small blister, or a very ordinary dose of oil of turpentine will give rise to very severe strangury. Nitrate of potash has also been known when given in large doses to occasion nephritis. Salicylic acid and carbolic acid are also powerful renal irritants. Cases of acute nephritis, arising during acute rheumatism, and scarlet fever, treated with the salicylates, have not been infrequently recorded. Carbonic oxide gas also induces nephritis, probably, as Bartels has suggested, by inducing general paralysis of the blood vessels, and preventing the oxidation of the blood. Other toxic agents have a special influence on the kidney, but though acute nephritis may be occasioned by them as an initial step, they generally assume some other structural form. Thus lead plays an important part in the causation of chronic interstitial nephritis. Phosphorus, arsenic, antimony, the mineral acids, bile acids, and some organic acids, as oxalic, tartaric acid, etc., in poisonous doses produce acute fatty degeneration. Alcoholic intoxication often gives rise to albuminuria, but I do not think that single large doses of alcohol are so provocative of acute nephritis as has been imagined. The albuminuria in these cases is, I believe, due to a transitory hyperæmia, which subsides rapidly, owing to the volatility of the toxic agent. When, however, alcohol has been taken constantly in excess, acute nephritis may at length be induced as is shown by the cases quoted by Dr. Dickinson. As a general statement, however, it may be said that alcoholism is rather a predisposing than an exciting cause, and has a more important bearing on the etiology of chronic renal

disease, than of the acute form. The causes predisposing to acute nephritis, are chiefly those which greatly depress the bodily powers. Dr. Dickinson has pointed out that the influence of cold is most mischievous during exhaustion or sleep. Chronic alcoholism has undoubtedly the same effect. Defective sanitary conditions must always be considered as an important predisposing cause, and in epidemics of scarlet fever their influence is especially to be marked in the numbers who fall victims to acute nephritis, in proportion of those attacked with the fever.

(5) *Family predisposition* may in some cases be traced, though the heredity of the disease is not nearly so plainly marked as with primary granular kidney. Thus, at Doncaster, I saw a lad of nineteen, two of whose brothers had died previously about the same age of acute inflammatory dropsy. Again, about two years ago, I saw a man, aged thirty-five, as an out-patient at the London Hospital, with acute nephritis who told me his father died of Bright's disease at the age of forty-seven, and also a brother.

(6) *Sex and Age.*—The disease, as might naturally be expected, is more common among the male sex, owing to their greater exposure to the influence of cold, exhausting employments, and more general indulgence in alcohol. But as Dr. Dickinson has pointed out, from statistics of Dr. Tripe, that in children were the habits of the sexes are the same, scarlatinal dropsy occurs in males, in the proportion of sixty males to thirty-nine females, hence it may be inferred that the "masculine gender is a predisposing cause" though the inequality between the sexes becomes more marked in adult life. Acute nephritis rarely occurs after fifty, putting aside the cases that arise after scarlet fever, and which are most frequent between

the fifth and the fifteenth year, we find the period at which the kidneys are most susceptible to attacks of acute inflammation to be from the 20th to the 35th year, the first half of the epoch of adult life.

51. **Differential diagnosis.**—We have to distinguish: (1) between those cases in which we have a discharge of bloody and albuminous urine, and acute nephritis; and (2) between the acute, sub-acute, and chronic varieties of nephritis. With reference to the first class of cases, it has been already stated that the albuminuria which so frequently occurs during fever of any kind is not always to be considered as evidence of nephritis. In small-pox, measles, typhus fever, acute rheumatism, and diphtheria, albuminuria is a frequent symptom, commencing early in the disease and passing away as it declines, and though true nephritis does occur in these diseases, it certainly, with the exception of the last, is a comparatively rare complication, and when present occurs towards the termination of the illness. Hæmaturia, when present, may lead one to form a wrong diagnosis, since in many hæmorrhagic forms of small-pox, acute rheumatism, scurvy, purpura, etc., and in certain intermittent fevers, bloody and albuminous urine is a special feature. In these cases, however, dropsy is never present, nor is the urinary secretion and urea diminished in so marked a manner as in acute nephritis. Temporary albuminuria may sometimes occur during acute rheumatism, as the result of embolism of the renal vessels, as distinct from purely pyrexial albuminuria, and of nephritis. The diagnosis in these cases is often difficult and our conclusions must be mainly based on the general circumstances of the case, such as the existence of endocarditis, sudden onset attended with rigors, and followed by fluctuating temperatures, the evidence of embolism in other organs,

etc. The distinction between the hæmaturia of nephritis and hæmorrhages proceeding from the mucous membrane of the lower urinary passages can be readily made, especially if the points mentioned in the section on hæmaturia (p. 118) are called to mind. Nor ought there to be a possibility of confounding acute nephritis with any stage of granular or waxy kidney, though the fact must not be overlooked that intercurrent attacks of acute inflammation not infrequently occur in either of these conditions. Hæmoglobinuria may be taken for acute nephritis, if only one sample of urine come under observation; but the absence of blood corpuscles, and the paroxysmal character of the hæmorrhage ought to put us right on this point at once. The difficulty of diagnosis is greatly increased in cases in which acute nephritis supervenes on some already existing lesion of the kidney, as in renal calculus, cancer, etc.

52. **Course.**—Primary idiopathic acute nephritis is not in itself a very fatal malady, a large proportion of cases either terminating favourably, or else drifting into the chronic form of the disease. Speaking generally, we may say that a larger proportion of fatal cases result during the early stage of the disease, when the nephritis comes on after some extensive lesion of the skin, this is especially the case after burns; or in connection with blood-poisoning from the extensive re-absorption of pus; or septic matter, as in erysipelas, carbuncle, etc. The mortality is probably next greatest with scarlet fever nephritis; whilst acute renal inflammation induced by exposure to cold is not often immediately attended by a fatal result. On the other hand the cases of nephritis that arise from the latter cause are more apt, I think, to drift into the chronic form of the disease than those that arise from any other condition. Thus for instance if we take scarlet fever nephritis,

we find that a large proportion of the cases so attacked make a good recovery, if they do not succumb to the disease at its onset. Whilst with the cases of acute inflammatory dropsy, the result of exposure to cold, we find that the disease is rarely thrown off completely, that relapses are frequent, and the disease often drifts into the chronic form. This difference is no doubt accounted for by the fact, that in scarlet fever nephritis, the disease in a large proportion of cases occurs in persons otherwise healthy, whereas in nephritis the result of cold there is nearly always some existing predisposition, which determines the inflammation to the renal organs. Death when it occurs directly from an acute attack is nearly always occasioned by the disturbance of the renal functions and the retention in the blood of the urinary constituents ; in some rare cases, however, the fatal issue is caused by sudden œdema of the glottis, or by serous effusion into the pericardium. Suppression of urine is therefore always an ominous symptom, though not necessarily a fatal one, since cases are on record of perfect recovery, even after a complete suppression for more than two days. Another omen for evil is the sudden fall in the amount of urea excreted. This often precedes complete suppression, and if duly noted enables us to take precautionary measures. For this reason I instruct the nurse to measure each sample of urine passed, and take its specific gravity, in every case of acute nephritis, as regularly as I would direct the temperature to be taken during the progress of a continued fever.

With regard to the duration of an attack of uncomplicated acute nephritis, such as may arise after exposure to cold, or after scarlet fever, we usually find, if things go well, the urine becoming less dark coloured, and less scanty before the end of the first week. By the end of a fortnight in the

ordinary run of cases, the amount of urine passed nearly approaches the normal, the specific gravity has increased, though it does not yet approach the healthy standard; and the amount of albumin reduced from ·6 or ·5 per cent. to ·2 or ·15 per cent. By the end of four weeks the urine is usually normal in character, except that it still contains a certain quantity of albumin. If there has been much dropsy during the acute stage of the disease the secretion of urine now becomes extremely profuse often amounting to double the normal amount (2500 to 3500 c.c.) for days together, the specific gravity being proportionately reduced, though in reality the amount of solids excreted continues daily to increase, as will be seen if the amount of urine passed, and its specific gravity be carefully contrasted. Convalescence is often extremely tedious, and albumin is often found in the urine long after it has apparently become normal. In one case that completely recovered, traces of albumin were found in the urine for two years after the acute attack, that was seven years ago, and the patient is now quite free from any evidence of renal disease. In nephritis associated with a malarial taint this persistence of albumin is often very remarkable. Owing to the tendency to relapse, the convalescence must be carefully watched, it is a great mistake to allow the patient to leave the house too soon, and especially to allow him to visit some distant health resort, with a view to the re-establishment of his health—long railway journeys are particularly to be avoided.

53. **Morbid Anatomy.** — The structural changes found in the kidney the result of acute nephritis vary with the intensity and duration of the inflammation, In the less acute form, the kidney appears more rounded, thicker and heavier than the normal organ, whilst on section the cortex seems more swollen than usual, there is, however,

no very marked hyperæmia, the chief apparent change being in the tubular epithelium which becomes swollen and granular. This swelling of the glandular epithelium (cloudy swelling) is greater in the convoluted portion of the tubule, and is the cause of the enlargement of the cortex. The swelling may be so great as to obstruct the lumen of the tubule, either from the simple swelling, or by the accumulation of detached masses. The enlargement of the cells is due apparently to increase of the reticular structure, and gives to them a granular appearance, and which is sometimes so great as to obscure the nucleus. This granular substance is soluble in acetic acid, which distinguishes it from molecular fatty deposit. In these mild cases, no, or only slight, vascular changes are observable, and there is no appreciable alteration in the interstitial tissue. In the more severe cases, however, the structural lesions are more profound. The kidney may be swollen to twice its natural size, its capsule so tightly stretched that it flies widely apart when cut; it strips off easily, however, leaving a smooth, but extremely vascular surface, soft and friable. The cut surface drips with blood, which obscures the appearance of the section, on washing this away with water we find that the cortex is thickened, and of a reddish-brown or pale-buff colour, whilst the pyramids are intensely congested. The thickening of the cortex and its colour depend on the degree of inflammation, and the amount of epithelial accumulation in the convoluted portion of the tubules. Thus in the more congestive forms, such as follow on exposure to cold, the cortex is swollen and of a reddish-brown or chocolate hue; whilst in those cases which are characterised by excessive epithelial formation, the cortex is considerably distended, but the reddish-brown colour, of increased vascularity, soon passes into a pale-buff colour, acquired from the

opaque white epithelium that distends the tubules. The Malpighian bodies stand out as red points in the cortical substance. The intense vascularity both of the Malpighian corpuscles, and of the pyramids, is due undoubtedly to the interruption of the blood currents in the inter-tubular vessels, caused by the intra-tubular accumulation, leading to congestion at those parts of the organ.

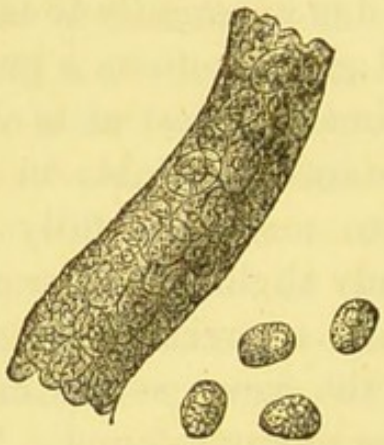


FIG. 18.—A tubule showing accumulation, etc., (Green's *Pathology*).

On examination under the microscope (1) *the tubules* especially in the cortex, are found distended with a brownish granular material, (fig. 18) which consists of renal epithelium, blood corpuscles, and a granular debris. The epithelia to a great extent, present a normal appearance, though more or less translucent, but with the nucleus retained; in others the nucleus is obscured by the granulation, which, as has been previously stated, is due to increase of reticular structure. In some instances the nuclei of the epithelia are being replaced by pus corpuscles, whilst much of the epithelium is reduced to a simple granular débris. Should the process be continued the epithelia lose their swollen granular appearance and contain instead molecular fat. Besides this accumulation of swollen epithelial elements, an albuminous exudate or

hyaline material, furnished from the vessels surrounding the tubule is poured out on its interior, forming a cylindrical mould, or cast, to which some of the epithelial elements and blood corpuscles adhere, and pass away together with the urine (see Casts, p. 141). In some cases the lumen of the tubule may be blocked with cylindrical fibrinous plugs, when many tubules are thus found affected, the condition must have played an important part in leading to the fatal result. (2) *The connective tissue, or inter-tubular substance*, in all severe cases, or in mild cases if the inflammation has been of any duration, rarely escapes change. The inter-tubular connective tissue usually has an albuminous appearance, and contains numerous small round cells among which may be seen inflammatory corpuscles and sometimes fatty granules. In some cases marked by con-

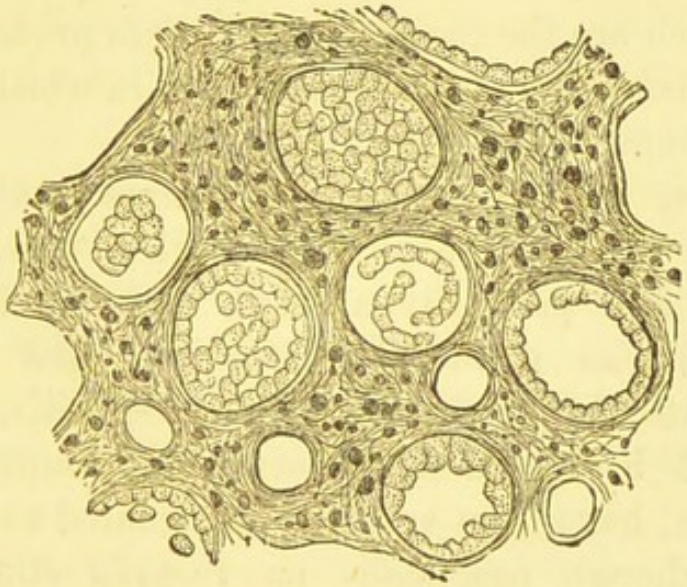


FIG. 19.—*Acute Nephritis*, showing, in addition to the intra-tubular changes, the cellular infiltration of the inter-tubular connective tissue × 200 (Green's *Pathology*).

siderable hæmorrhage (hæmorrhagic nephritis) the inter-tubular spaces will be found filled with blood. These changes are most marked in the cortex, and especially in the neighbourhood of the Malpighian bodies, and the cap-

sule. Should the case recover, these round cells are probably removed by the lymphatic vessels, and the interstitial tissue regains its normal condition. If, however, it should pass into the chronic form, the cellular infiltration will become more abundant and tend to form a fibrillated structure, such as we shall see occur when we come to consider the changes that occur in interstitial nephritis. (3) *The blood vessels* are in all acute cases greatly swollen and dilated, and sometimes covered with inflammatory corpuscles. Hæmorrhages into the urinary tubules, are of frequent occurrence giving rise to hæmaturia, and blood casts in the urine. They are also frequently found in the space between Bowman's capsule and the capillary coils of the glomeruli, and may be observed as fine brownish streaks on section of the kidney substance. The glomeruli are always greatly distended with blood. Such are the morbid appearances presented in the kidney, in those cases of acute nephritis in which the intra-tubular changes are predominant.

We must now consider the changes that occur in that form of acute nephritis in which the glomeruli are mainly and primarily affected, and which is spoken of by some as glomerulo nephritis, and by others as an acute form of interstitial nephritis, or from the fact of being chiefly observed in connection with scarlet fever, have been specially designated as scarlatinal nephritis, though practically as regards etiology there appears to be no material difference between this and the intra-tubular form of the disease. For though chiefly associated with scarlet fever, it has often been observed in cases that have resulted from exposure to cold and wet, and other well known exciting causes of acute nephritis. Klebs (*op. cit.*, p. 644), who first described the condition, showed that the chief change consists in the interior

of the Malpighian corpuscles being filled with a number of small angular nuclei, imbedded in a finely granular mass. These nuclei he considers result from the proliferation of the corpuscles of connective tissue, which binds together the capillaries of the Malpighian tufts. In glomerulo-nephritis the increase of these nuclear masses is so great as to completely fill the Malpighian capsules and compress the capillaries. At an early stage, the tubules are but slightly affected, there is a little cloudy swelling of the parenchyma, and little or no proliferation of the epithelium, or marked interstitial change. Later, however, the tubular changes become more marked, with cloudy swelling in the convoluted portion of the tubules and proliferation of the epithelium, whilst the tubes become crowded with leucocytes. At the same time a cellular infiltration of the inter-tubular connective tissue, interstitial nephritis, commences round the larger vascular trunks spreading into the bases of the pyramids and the cortex. The kidneys are only slightly if at all enlarged, and the texture of the organ is firm. The cortex is dark-coloured and intensely hyperæmic. The glomeruli are pale owing to the emptying of their capillaries by the compression of the nuclear masses, and appear on close inspection like white points. The contrast, therefore, between the changes in intra-capsular and those of intra-tubular nephritis, may thus be summarized :—

Intra-tubular nephritis. The kidneys much swollen, texture friable. The cortex increased in width, and rendered opaque (buff coloured) by the cloudy swelling of the parenchyma. Considerable proliferation of the epithelium with some changes in the inter-tubular connective tissue. Glomeruli extremely vascular, distended with blood, standing out as small red points.

Glomerulo-nephritis. The kidneys slightly if at all en-

larged, texture firm. Cortex, dark chocolate colour, extremely hyperæmic in the early stage, little or no cloudy swelling or proliferation of epithelium, nor marked changes in the inter-tubular connective tissue. Glomeruli filled with a number of small angular nuclei, which so compress and empty their capillaries as to render them pale, and on minute inspection to appear as small white dots.

Klein (*Path. Soc. Trans.*, vol. xxviii., p. 431), who has extended the observations of Klebs, has shown that in addition to the increase of the nuclei covering the glomeruli

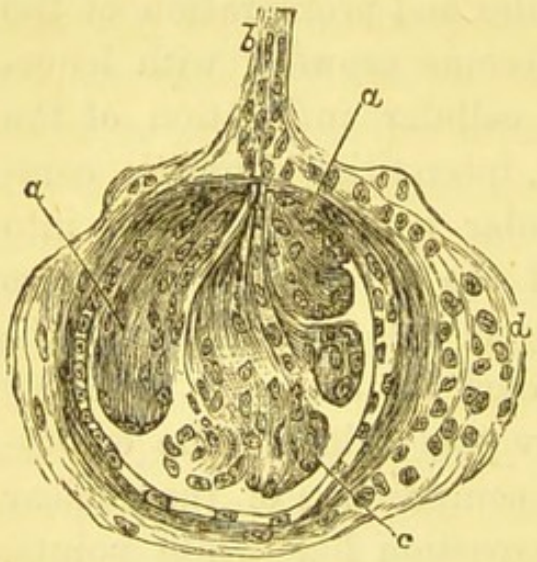


FIG. 20.—*a*. Part of glomeruli degenerated into a hyaline mass. *c*. Ditto, less degenerated. *b*. Afferent arterioles. *d*. Thickened capsule (Klein).

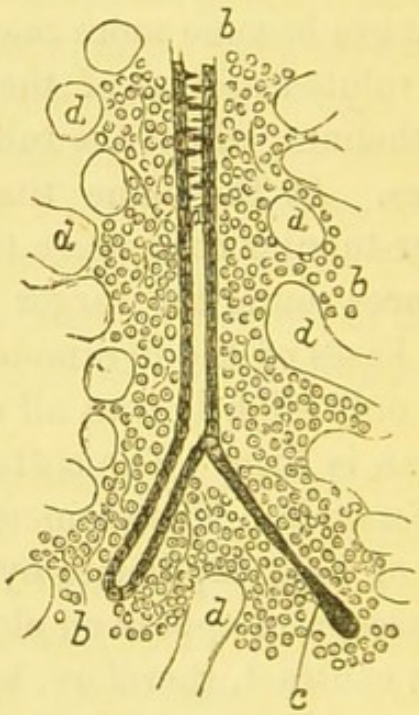


FIG. 21.—*a*. Longitudinal section of artery. *b*. Infiltration round vessels of lymph cells. *c*. Arteriole showing hyaline degeneration. *d*. Outlines of urinary tubes (Klein).

of the Malpighian corpuscles, there is hyaline degeneration of the elastic intima of minute arteries, especially of the afferent arterioles of the Malpighian corpuscles, and also a multiplication of the nuclei of the muscular coat of the minute arteries, and a corresponding thickness of the

walls of these vessels. Figs. 20 and 21 show these changes. Klein is of opinion that the anuria and uræmic poisoning that occurs in acute nephritis, when not directly to be referred to inter-tubular changes, is caused by these changes in the arterioles, in this view he differs from Klebs, who holds that anuria in these cases is due to compression of the vessels of the glomeruli by the pressure of the nuclear germination. As has been already stated, in the early stages, the intra-tubular and interstitial changes are but slight, but as the disease advances, according to Klein after the first week, these both become evident. The parenchymatous changes consist in the crowding of the urinary tubes with lymphoid cells, granular, and subsequent fatty degeneration of the epithelium, and cylinders of different kinds in the tubes. These changes in the parenchyma, however, according to Klein are not distinct till after the interstitial changes have reached a certain high degree. The interstitial changes as described by Klein are as follows:—The infiltration of the connective tissue of the kidney with round cells (lymphoid or whatever they may be called) is observable after the end of the first week, commencing round the large vascular trunks whence it spreads to the bases of the pyramids, and especially into the cortex. This infiltration of the cortex is first observed at the roots of the inter-tubular vessels, and spreads rapidly to the capsule of the kidney, and among the convoluted tubes around the Malpighian corpuscles. In the course of the process considerable parts of the cortex become converted into whitish, firm, bloodless cellular masses, in which Malpighian corpuscles and urinary tubes become more or less degenerated, and are with difficulty recognised. In some cases, the infiltration of the cortex assumes the character of adenoid or lymphatic tissue. Emboli may be

occasionally found both in the larger arterial trunks as well as in minute arteries. The more extensive the degree of interstitial change, the more marked will be the parenchymatous nephritis, and the changes in the tubules.

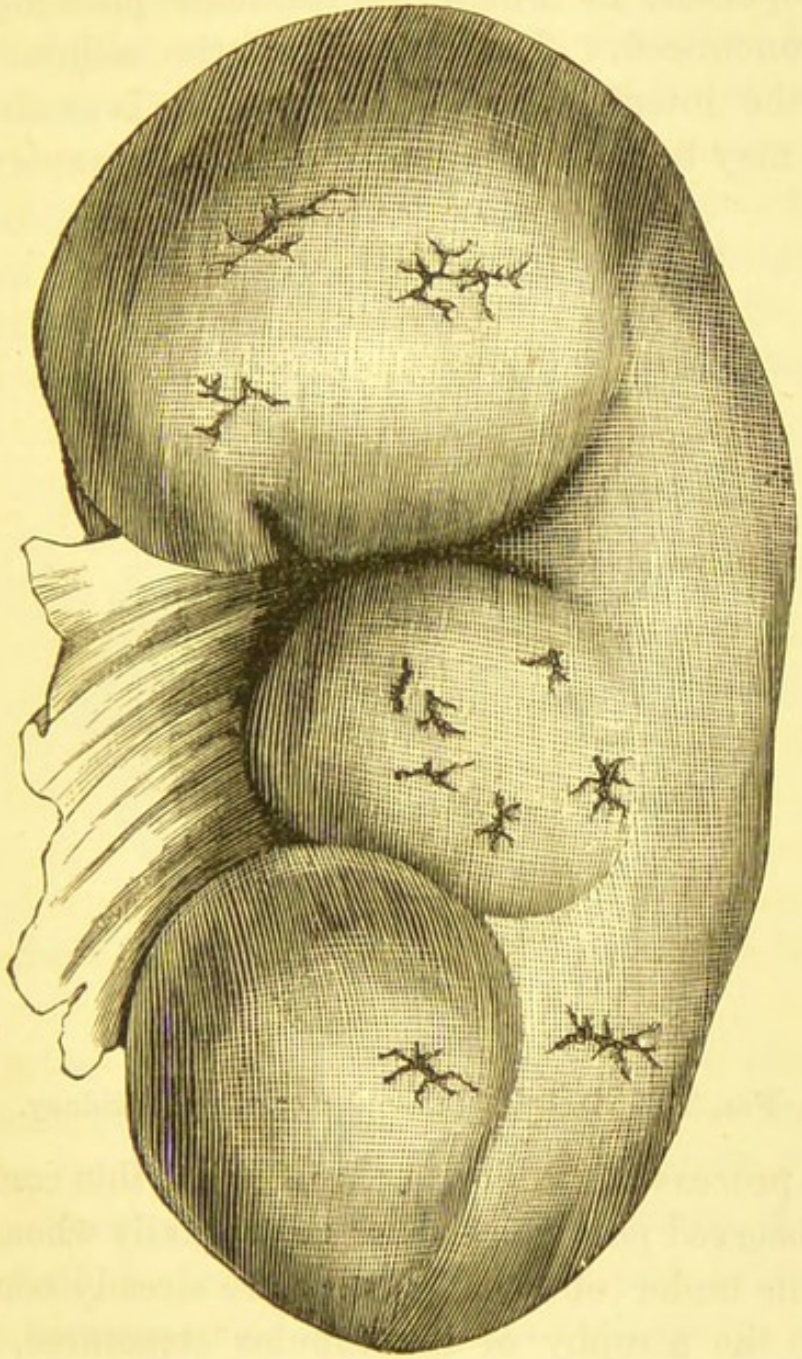
Should the attack of acute nephritis terminate in complete recovery, the epithelial changes come to an end, the vascularity subsides, and the inflammatory products are either carried off by the urine or are absorbed. If on the other hand, the disease passes into a sub-acute or chronic stage, further changes take place in the organ leading to an alteration in its appearance, such as we find in the large smooth, the pale granular, and the small fatty kidney.

Chronic Nephritis or Granular Kidney.

54. **Chronic nephritis.**—Chronic nephritis eventuates in the condition known as granular kidney. Like acute nephritis we find it existing in two forms, one in which the tubules are mainly affected, both by epithelial proliferation, and intertubular growth, and which is designated as *chronic tubal nephritis;* the second, which is essentially a chronic form, and commences with changes round the glomeruli and vessels, together with some degree of interstitial overgrowth, and which is commonly termed *chronic interstitial nephritis.*

Chronic tubal nephritis may either be a continuation of the acute form, or it may originate independently. If the patient survives sufficiently long, it passes through at least two stages, viz., that of enlargement by epithelial proliferation, and intertubular growth, in which stage it is commonly spoken of as the *large white kidney;* a stage of regression, caused by atrophic and fatty degeneration

changes taking place in the large white kidney, which changes ultimately produce what is known as the *pale granular kidney*. When the contraction caused by these



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FIG. 22.—Large white kidney showing commencing regression.

atrophic changes is carried to its fullest extent, and the fatty degeneration of the renal tissues is complete, then we have what is known as the *small fatty granular kidney*.

In chronic interstitial nephritis, the changes taking place in the kidney are so gradual in their development, that we are unable to mark their course as in chronic tubal nephritis, in which the vascular phenomena are more pronounced. In some cases if the cellular infiltration of the intertubular connective tissue is excessive, the kidneys may be slightly enlarged (*large red granular kidney*).

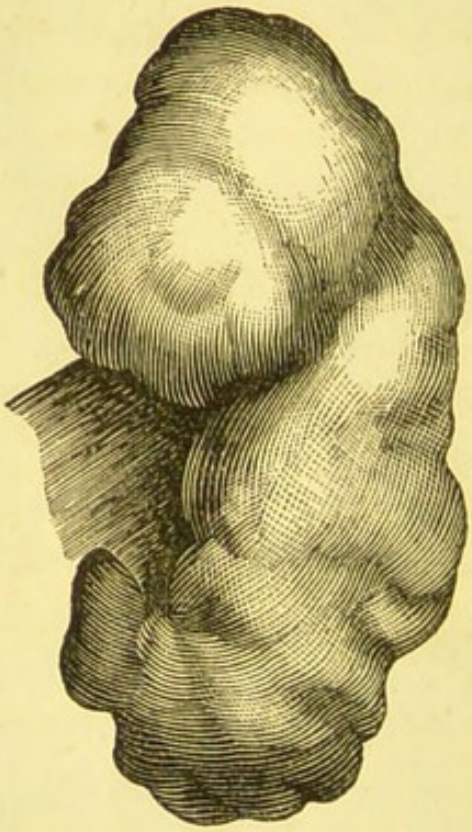


Fig. 23.—Small fatty granular or atrophic kidney.

But the process is usually so chronic that this condition is rarely observed post-mortem, so that usually when the kidneys come under observation they are already contracted, owing to the atrophy of the tubular structures, and the cicatricial contraction of the intertubular overgrowth. In typical cases, chronic interstitial nephritis leads to what is called the *small red granular kidney*, but as the condition is often associated with fatty degeneration, it is a matter of extreme difficulty, especially in cases that

have run a prolonged course, to distinguish between this form and the pale granular kidney, the result of tubal nephritis; especially as the red granular kidney becomes paler as the disease advances, owing to progressive fatty changes, whilst the pale variety on the other hand becomes darker, owing to the absorption of fat, and as the vessels on the surface become more vascular and distinct. Though a contracted and granular condition of the kidneys results from both chronic tubal nephritis and chronic interstitial nephritis it is often difficult to draw a very rigid line, histologically be-

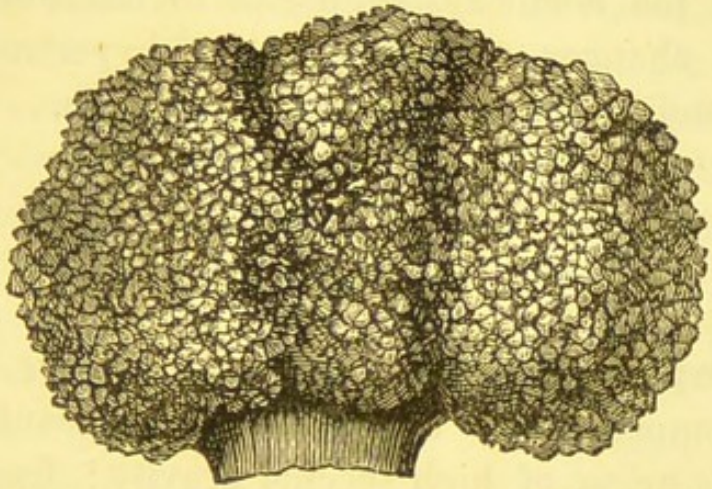


FIG. 24.—Small red granular kidney; granulations torn by removal of capsule.

tween intra- and inter-tubular changes, or clinically to distinguish between the granular condition of the kidney resulting from tubal and interstitial nephritis generally; still an attentive study of the earlier history of the case, shows that in their inception these two forms present clinical features quite distinct from each other. Thus, in chronic tubal nephritis, in the early stage we have a diminished excretion of urine with high specific gravity, an abundance of albumin, and a special tendency to dropsy; whilst uræmic symptoms, cardio-vascular changes, and arterial degeneration are not observed till the disease

has reached its height, and the contraction attendant on the secondary atrophy considerably advanced. In chronic interstitial nephritis, on the other hand, among the earliest symptoms noticed, is an increased excretion of urine of low specific gravity, cardio-vascular changes, characterised by hypertrophy of the left ventricle, and pulse of high tension, and uræmic symptoms more or less pronounced; whilst the amount of albumin present in the urine is never great, and may even in the early stage be entirely absent; and dropsy, the tendency to which is so marked in tubal nephritis, is never observed, till quite the close, when the tension in the aortic system begins to fail, owing to degenerative changes occurring in the hypertrophied left ventricle, and even then it is rarely excessive.

(A). CHRONIC TUBAL NEPHRITIS.

55. **Symptoms.**—The most prominent are, great debility accompanied by marked anæmia, scanty, highly, albuminous urine of high specific gravity; frequent micturition, and early supervention of general dropsy. These symptoms are a counter-part of those observed in the acute form, only they are more insidious in their onset. In the majority of the cases that have come under my observation for the first time, it was debility and pallor that first drew attention to the disease. In these cases, the patients only complained of malaise, but on enquiry it was found that they were frequently disturbed in the night to urinate, and that the urine was albuminous. Of the remaining cases, more or less general œdema was present, at the time the patient first applied for relief. The course these cases run, which develop in this insidious form, and do not originate in an acute attack, is as

follows. The patient for a time has been feeling languid, and has become pallid, a condition often referred by him as due to indigestion, since there is often considerable dyspepsia and sometimes vomiting. On being questioned, he will admit that of late he has had to rise once or twice or even oftener during the night to pass urine, seldom he notices whether it is darker in colour than usual, till his attention is called to that particular. Although there is no marked *dropsy*, still even at this early period there is a slight subcutaneous œdema, which is shown by the slight indentation left by the stethoscope, when applied to the chest, and also by the furrows left in the skin by creases in the clothes. The urine when collected for twenty-four hours is found to be scanty (450-600 c.c.), dark, and sometimes smoky in colour, of high specific gravity (1025-1028), and highly albuminous. The time when marked dropsy sets in is very variable, the more closely the case approaches the acute type, the earlier it is noticed. It first appears in the feet at night; or in one of the hands, the one that has been laid upon during sleep; or in the face, the eyelids especially; or in the prepuce, in fact in the parts that are most dependent, or offer the least resistance to the effusion of fluid from the capillaries. As the disease advances, the œdema becomes more diffused and general. The degree of *dropsy* manifested is very variable, if the case come under treatment early, or is not too far advanced to respond to ameliorative measures, the œdema may not become excessive, indeed may be quite relieved; in neglected cases, or in those past remedial measures, the dropsy often becomes excessive, so that rupture of the skin may occur at points where the pressure is extreme. Gangrenous inflammation may arise in the sodden cellular tissue thus exposed; it is particularly liable to occur in the scrotum, which with the penis, is in

chronic renal dropsy usually very much distended with fluid. Extensive effusions likewise occur in the serous sacs of the pleura, the peritoneum, and the pericardium. In severe cases there is also a considerable watery exudation from the mucous surfaces, the lungs become œdematous, and profuse watery discharges are got rid of by the stomach and bowels. When the dropsy disappears, either under the influence of treatment, or a tendency towards recovery, the great emaciation the patient has undergone becomes visible, in the shrunken limbs, and pinched features, whilst the ivory whiteness of the skin and pallor of the mucous membrane, testifies to the anæmia. The great debility can be accounted for by the withdrawal from the blood of large quantities of serum albumin, whilst the anæmia is no doubt owing to the watery condition of the blood, and the relative disproportion between the corpuscles and the mass of the circulating fluid.

The urine in the earlier and in the fully developed state of the disease is scanty, but as the dropsy is removed, or if the patient survives till atrophic changes take place, the discharge increases till it may considerably exceed the normal. The quantity in the early stage may vary from almost complete suppression to about 400 to 600 c.c. daily. In the fully developed stage, the usual range will be found generally, for adults, to be from 500 c.c. to 700 c.c.; whilst with the removal of the dropsy, or during the atrophic stage, it may amount to 2000 c.c. or 3000 c.c. The colour is always more or less dark, especially in the earlier stages, whilst the urine is scanty, but becomes lighter when the flow is more profuse. The dark colour is due chiefly to the presence of urates held in suspension by the quantity of albumin present in the urine, and in some few cases to the presence of blood corpuscles. Blood when it makes its appearance, must always be regarded as a sign

that the disease is assuming an acute form; it may occur at any period of the disease, and always indicates an exacerbation of the affection. There is invariably, more or less, deposit, which consists of casts, white corpuscles, epithelial cells, and granular debris, often crystals of uric acid, and red blood corpuscles if the disease assumes a sub-acute character. The specific gravity of the urine whilst the urine is scanty, is high, ranging from 1028 to 1040. It falls however in a constant proportion, as the quantity of urine increases, so that when the disease has assumed the atrophic form, or the dropsy is passing off, it falls considerably below the normal, to 1012 or even to 1008. If Trapp's formula be applied in these cases, it will be seen that in spite of these variations, the amount of urinary solids daily excreted, is always below the average. Thus a patient with a daily excretion of 400 c.c. and a specific gravity of 1040, passes 32 grms., and a patient with an excretion of 2000 c.c. and a specific gravity of 1010, passes 40 grms. of solid matter, whilst as we have seen (p. 51) the normal daily excretion of solid matters by the kidneys in the healthy adult, approaches 58 or 60 grms. This decrease of the amount of urinary solids in Bright's disease appears at first paradoxical, when we consider the amount of blood serum passed into the urine, equivalent as it is in many cases to 10 or 12 grms. of dried albumin, but it must be remembered that the specific gravity of the blood serum in chronic Bright's disease is much reduced, so that it is hardly as high as that of normal urine 1020, indeed many observations have shown it is often below it, 1018 and even 1015. On the other hand, there is a great and positive reduction in the amount of urea, which falls often as low as 18 to 13 grms., as compared with a normal excretion of 33 grms. This reduction of the chief urinary constituent more than counter-

balances the addition of albumin, even when that substance is present in large amount, and fully accounts for the diminution of the urinary solids noticed in this disease. Although the quantity of urea is always more or less reduced, still the amount excreted varies considerably day by day. This variation depends less on the daily formation of this substance in the system, as on its elimination by the kidneys, and consequent accumulation in the body. Any aggravation of the disease, therefore, by diminishing the renal function leads to decreased elimination, whilst any improvement favours its discharge. The urea formed in the body but not eliminated by the kidney is not, however, retained wholly in the blood, but in great part passes into the dropsical effusion. Thus, I have found the percentage of urea in the fluid withdrawn from a patient suffering from chronic renal dropsy, to equal that of the urine passed by the same individual on the same day.

The quantity of *albumin* passed, like the urea, varies from day to day, it is, however, during the earlier period, and during the full development of the disease always considerable, in ordinary cases it is hardly ever less than 6 grms., whilst in severe cases it may amount to 16 or even 20 grms. In the later stage, when the kidney becomes atrophic, the amount of albumin present in the urine becomes considerably lessened. Casts when the disease is established are always to be found. When the disease is recent, thin hyaline casts predominate over the broad, but as the disease advances the casts become broader and distinctly granular, whilst waxy and fatty casts increase in number (see p. 141).

Alterations in the organs of circulation are not characteristic of this form of nephritis. When they do occur it is in the later stage, when atrophic changes in the kidney become

well marked. The disease may run its course without any febrile manifestation, except that caused by secondary inflammations. As a rule the pulse is weak, soft and frequent, and the heart's sounds are feeble, as however, the disease passes into the atrophic stage, we begin to find a gradually increasing tension of the pulse, with increased cardiac impulse, and finally hypertrophy of the left ventricle. Atheromatous changes, though they may be observed, are not characteristic of this form of nephritis. The organs of digestion usually suffer disturbance, from an early date, the tongue is foul, and there is a marked disrelish, especially for animal food, though sometimes the appetite may be keen throughout. The vomiting that occurs frequently in chronic Bright's disease, may be referred to the following causes. When slight, and occurring on first rising in the morning, it probably depends on disturbance of the nervous centres, through poisoning of the blood by retained excrementory matters, *uræmia*, this form however is more generally noticed in connection with the small granular kidney. When profuse, frequent, and watery, it probably is the result of the œdema of the mucous membrane of the stomach, the more so as it is generally associated with a watery diarrhœa. A rarer form in which a glairy acid fluid is ejected, depends either on reflex irritation, or upon a subacute inflammation of the mucous surface of the stomach itself. Disorders of respiration, are chiefly those which depend either upon dropsical effusion into the cavity of the pleura, or from the mucous surface of the lungs causing œdema of those organs, though attacks of bronchitis and pneumonia are not uncommon. The uræmic convulsions which so frequently attend on acute nephritis, and are such characteristic symptoms of chronic interstitial nephritis, rarely manifest themselves in this form of the disease, when they do they are generally remarked in con-

nection with extreme dropsy, especially when the lungs are affected, or in the later stage of the disease when the kidney has become atrophied. The absence of this complication in chronic tubal nephritis is no doubt due to the relief afforded by the great œdema, which withdraws much of the toxic element from the blood, since urea is to be found in abundance in the effused serum as in the vomit and diarrhœal discharge. Uræmic amaurosis, or albuminuric retinitis are rarely met with in the early, and fully developed stages of the disease, though in the later stage when secondary atrophic changes have advanced they are of frequent occurrence.

56. **Causes.**—Chronic tubal nephritis in many cases undoubtedly supervenes as a direct consequence of an acute attack, whether produced by exposure to cold, scarlet fever, pregnancy or the like. In many instances too, it happens that though there may be no direct sequence between the acute and chronic form of the disease, still we have the history of a previous acute attack, in which recovery seems to have taken place, followed after a short interval by a return of the albuminuria, and nephritis in a sub-acute or chronic form. More frequently, however, the disease commences insidiously without any distinct initial febrile movement, and has often made some progress before the patient presents himself to the physician. In these cases the disease is induced by certain exciting causes acting on a constitution already predisposed towards renal disorder. Among the *exciting* causes exposure to cold and damp must be considered first. Here it is the prolonged action of the agency, rather than, as in the case of acute nephritis, a sudden exposure. Thus, persons residing on cold wet soils, or in ill-constructed damp dwellings, or whose occupations constantly expose them to the inclemency of the weather, and wet clothes, are

specially prone to the disease. Sub-soil damp seems to have a powerful effect in this direction, and is one reason no doubt why many writers, chiefly American and Continental, have considered that malaria is an important exciting cause in producing chronic nephritis, even without the intervention of febrile paroxysms. This, however, is not borne out by my experience at the Seamen's Hospital, where a considerable number of patients suffering from malarial poisoning are annually admitted. In these cases I failed to establish any connection between ague and chronic tubal nephritis. Indeed sailors, as a class, as has been remarked by other observers, are not, in spite of their frequent exposure to severe weather, particularly liable to chronic renal disorders. The cases of chronic nephritis associated with ague that have come under my observation, have nearly all occurred in landsmen who have resided some time in a marshy district, and though acute nephritis may often arise after recent exposure, and during the acute manifestations of intermittent fever, still I am disposed to consider the chronic nephritis in persons who have been long exposed to malarial influences, but are free from febrile paroxysms, to be due to prolonged residence on a damp soil, rather than to the specific poison of the miasm generated by it. Taking into consideration the well known fact, that sailors as a class are not specially liable to chronic renal disease, although frequently exposed to cold and wet, and also the decided improvement that the mere change of residence, from a cold clay soil to dry gravelly, or sandy, without a change of climate, often effects in these cases, I am disposed to think that telluric conditions of cold and damp, are more important than the same condition of the atmosphere or climate. Next in importance to the effect of cold and damp in the production of chronic nephritis, is the exist-

ence of affections attended either with long-continued suppuration as in diseases of the joints and bones, or in association with constitutional diseases as scrofula, syphilis or phthisis. In these cases it is usual to find lardaceous degeneration combined with the nephritis. Mercury as is well known, when its use has been prolonged, will sometimes give rise to albuminuria, but it is as yet undecided whether this is due to chronic nephritis, or as is most probable to an altered state of the blood, induced by the mineral. The albuminuria subsides after the withdrawal of the mercury, and is never attended with dropsy. Cantharides, turpentine, etc., which so readily induce active hyperæmia, apparently do not induce chronic inflammation, probably, as Dickinson has suggested, because their administration and operation is transient, and so seldom gives rise to more than temporary disturbance. Similarly it has been shown that alcohol cannot be regarded as an exciting cause. Among the *predisposing* causes the constitutional tendency towards renal disease must be taken into account; just as some persons are more predisposed to pulmonary disorders than others. Although the hereditary tendency in this form of chronic nephritis is not so pronounced as in the chronic interstitial form, still it undoubtedly exists, and in some instances it may be traced some generations back.

The predisposition is most marked during the earlier years of life. In acute nephritis the disease is most frequent between ten and twenty years of age; in chronic tubal nephritis between twenty and thirty-five years; whilst chronic interstitial nephritis, on the other hand, rarely occurs till the fortieth year is passed, and is most frequent between the fiftieth and sixtieth years. Habits of intemperance undoubtedly predispose to chronic nephritis, and whilst spirituous liquors are more concerned in the

chronic interstitial form, immoderate indulgence in malt liquors has an undoubted influence in the production of this variety of nephritis, and the large breweries at the East End of London furnish us with a considerable contingent of our renal cases annually. Overwork, long-continued mental strain, excessive sexual indulgence, may also be mentioned as occasional predisposing causes; whilst in some cases it is impossible to assign any definite cause at all.

57. **Differential Diagnosis.**—This form of nephritis may be taken for *(a) chronic interstitial nephritis*, especially in the later stage, when secondary atrophy has resulted; the features, however, that enable us to distinguish between the two forms, will be best considered when the symptoms of that form of renal disease are discussed. *(b) The cyanotic induration* of the kidneys consequent on long-standing heart disease. The urine though scanty and dark-coloured is never highly albuminous, and the casts are fine and hyaline, never broad or granular. The dropsy too, at first is limited to the area of the inferior vena cava and portal vein, so that the dropsy is confined to anasarca of the lower limbs, and the cavity of the peritoneum (ascites). It is only in the later stages that the dropsy becomes general. *(c)* To distinguish *lardaceous degeneration* from chronic tubal nephritis is sometimes a matter of difficulty, since the two conditions are often associated. When uncomplicated with nephritis, our diagnosis is guided by the following considerations. The etiological conditions, as the existence of long-continued suppuration, bone disease, etc.; the enlargement of the liver and spleen if they are affected; the small quantity of serum albumin passed. According to Senator the urine contains a larger proportion of globulin, than in any other form of chronic renal disease. Rarity of casts,

small hyaline, and not granular; the dropsy chiefly abdominal, owing to the implication of the hepatic and splenic vessels. *(d) Temporary albuminuria*, either from functional disturbance, or pyrexia, may be distinguished from chronic nephritis by the extreme variations in the amount of albumin discharged either day by day or even hourly, and which follow either marked disturbance of the digestive functions, or a rise of temperature. And that there is no marked diminution of the urinary solids, indeed in many cases the urea is markedly increased. No casts appear in the urine. The general health often is but slightly affected, and there is rarely any marked loss in weight, and dropsy does not supervene. *(e) Chronic disease of the genito-urinary organs* may be distinguished from chronic tubal nephritis by the presence of pus, and the symptoms indicating disease of the lower urinary passages.

58. **Prognosis.**—Chronic tubal nephritis may terminate in complete recovery, in temporary arrest, or may prove fatal, either at an early stage, or be indefinitely prolonged to the later stage of atrophy. Although the prognosis in this disease is not so favourable as in acute nephritis, still cases of perfect recovery do occur. In young patients, or when the disease at the outset is more or less in an acute form, and is early recognised, we may have reason to hope that the inflammation may subside without permanent damage being done to the renal texture. When the nephritis is the result of some special morbid condition of the blood, the outlook is decidedly more favourable than when it arises from exposure to cold. Thus, in the nephritis occurring in syphilitic subjects we find the albuminuria often rapidly disappears under anti-syphilitic treatment, and Bartels (*op. cit.*) has stated that the amputation of a limb affected with a fistulous opening, or incision

into a peri-pleuritic abscess, has arrested a nephritis, that without such relief would most likely have proved fatal. In the majority of cases, especially those in adults due to exposure to cold, and those which come on insidiously, and are consequently overlooked at the onset, the damage done to the kidney is so great that the secreting structure cannot recover itself, and though apparent amelioration may take place for a time under treatment and careful dietetic management, still the progress towards ultimate atrophy and contraction goes on. Sometimes this progress is so slow as to give rise to the hope that the disease is actually arrested, and the patient regains his weight and colour. But a careful examination of the urine from day to day will show that the albumin re-appears on the slightest provocation.

As a rule, however, there is no apparent respite, and though the character of the disease changes, the albumin never quite disappears, but merely lessens as the disease passes into the stage of contraction; whilst at the same time, the urine becomes more and more abundant as the hypertrophy of the ventricle becomes more marked. The diminution, therefore, in the quantity of albumin, and an increase in the quantity of water passed, is not necessarily a sign for encouragement, since it may merely imply that the kidney is passing into the latter stage of the disease. The only decidedly favourable prognostic in my mind is the urea reaching the normal rate of excretion. When this occurs, we find the quantity of urine passed daily, and the specific gravity, becoming more constant, and approximating more closely to the normal standard. With regard to the duration of the disease, when it occurs in comparatively young subjects, and is the result of some morbid condition of the blood, such as scarlet fever, syphilis, etc., complete recovery need not be despaired of even after the

albuminuria has persisted for more than a year. Bartels (*op. cit.*) relates two very conclusive cases, one a lad after scarlet fever, in whom the albuminuria continued for eighteen months, who made a complete recovery, and ten years after grew to be a vigorous man. The other a man of forty years of age, who was confined to bed for an entire year, but who afterwards recovered completely. Dickinson (*op. cit.*) relates the case of a medical student, who twenty years previously was seized with nephritis, which continued for several months. At the end of two years, the albumin entirely disappeared, but for three or four years afterwards there persisted a slowly decreasing amount of irritability of the urinary organs. In 1867, more than twenty years since the patient was first attacked, he was in perfect health, and the urine had been perfectly normal for at least fifteen years of that period. A similar case has come under my own observation, in the person of a professional friend, who some thirteen years ago had a severe attack of scarlet fever nephritis, which pursued a chronic course for fifteen months, when definite improvement set in; it was three years, however, before the renal irritability quite subsided, and traces of albumin ceased to be discovered in the urine, during the last ten years, however, his health has been quite re-established, and the urine remains perfectly normal. Cases that succumb during the development or height of the disease usually prove fatal within six months, if that period can be tided over and the dropsy relieved, we may hope either that the disease may terminate in complete recovery, or that the stage of secondary atrophy will be indefinitely prolonged. With regard to the duration of this period, much depends on the severity of the original attack, and the circumstances and surroundings of the patient. If the inflammatory stage has been much

prolonged, and there is consequently considerable infiltration of the inter-tubular connective tissue, or the Malpighian corpuscles filled by exudation, and the tubules extensively denuded, then the atrophic changes will manifest themselves at an early period and steadily progress. If, however, the exudation be slight, and limited in extent, and the patient's circumstances such as will permit him to place himself under the best hygienic and dietetic conditions, we may hope to prolong life for many years, eleven, fourteen, and even twenty years have been recorded. Even among the out-patients of the Hospital, a class most unfavourably circumstanced as regards the treatment of this form of disease, one not infrequently meets with cases that have struggled on for years, and who can refer us back to the time when they were in-patients suffering from their first attack. Should the kidney, however, become the seat, as it so often does, of lardaceous degeneration, then the case becomes almost hopeless, and the downward progress is accelerated.

59. **Morbid Anatomy.**—The post-mortem appearance varies with the stage of the disease, if death takes place during the period of development and the height (*status*) of the affection, we have the *large white kidney* (see fig. 22, p. 197) showing a variable degree of enlargement, and a surface more or less smooth. If the examination is made dur ing the later stage when secondary atrophic changes have taken place, we find the organ shrunken, or contracted, and we have the *fatty granular kidney* (fig. 23) with a nodular and granular surface. Between these two extremes we meet with kidneys of varying size and degrees of granulation according to the stage at which they come under observation. 1. *Large white kidney.* The enlargement, especially when death takes place during the height of the disease, is often very considerable. The capsule

which tightly embraces the organ is thin, and is readily stripped off, leaving the surface below quite smooth, unless the disease has been somewhat protracted, when nodulation (fig. 22), may be observed the result of commencing contraction. The surface is of yellowish-white colour, like ivory that has been long exposed to the air, and is more or less mottled in appearance, whilst scattered over the organ are stellate groups formed by distended vessels. On section we find the enlargement principally due to distension of the cortex, which is often thickened to thrice its size. This part of the organ is of the same yellow-white colour as the surface. The pyramidal portion is also enlarged, but not proportionally to the same extent as in the cortex, it is of dark reddish colour, but is not so intensely hyperæmic as is noticed in acute nephritis. The microscopical appearances are somewhat similar to those described in acute nephritis (p. 190). Of the epithelial elements, a few cells are still swollen and granular; but the majority have undergone retrogressive change and are distinctly fatty. As the disease advances, the fatty degeneration proceeds till the cells are destroyed, and the fat is deposited in a free state on the tube casts. Most of the tubules will be found dilated, a few however are usually observed of normal dimensions, and in these the renal cells may have escaped change. As a rule, the epithelium is desquamated and fills the tubule, especially the convoluted portion, and to which the distension of the cortex is mainly due; some tubules, however, when the disease is more advanced, will be found empty and stripped of their epithelium. In addition to the altered epithelium, the tubes will be found choked with casts—hyaline, granular, fatty, and waxy, granular debris, and sometimes pus corpuscles.

The changes in the glomeruli, though they may vary

in individual specimens dependent on the rapidity of their evolution, do not, as Professor Greenfield (*Path. Soc. Trans.*, vol. xxxi., p. 158) has pointed out, differ widely from those observed in the acute form of the disease. Those changes as described on p. 194, we saw consisted in the formation of nuclear masses covering the glomeruli of the Malpighian corpuscles; hyaline degeneration of the elastic intima of minute arteries, especially affecting the afferent arterioles; and a multiplication of the nuclei of the muscular coat of the minute arteries, and a corresponding thickening of the walls of these vessels. Professor Greenfield thinks that the most important changes are those found in the interior of the capsule, between the capsule and glomerulus; as when the space between the tuft and capsule is crowded with inflammatory corpuscles, and the capsule itself is thickened, such a condition leading to destruction of the function of the glomerulus.

The inter-tubular connective tissue is thickened; this may be accounted for by an increase of the connective-tissue elements, by a general albuminous exudation into the tissue, and by the presence of leucocytes (fig. 19, p. 191). This swelling of the inter-tubular substance together with the distension of the tubules accounts for the increased size of the organ. Should recovery take place the fatty products pass off in the urine or are absorbed, those tubules that have been only slightly affected recover themselves, whilst it is not improbable, that even in those most seriously impaired the epithelium may be regenerated. The inter-tubular swelling disappears, and the leucocytes are re-absorbed. Should, however, the nephritis continue, changes such as we shall see are essentially characteristic of chronic interstitial nephritis develop, and the existing connective tissue is gradually converted into fibrous tissue. The fatty degeneration of the epithelium continues, and

by its removal leaves the tubes empty, so that the kidney diminishes in volume, at the same time the inter-tubular connective tissue begins to undergo diminution in bulk. As contraction progresses we find the capsule becoming thickened and coarse, and adhering more or less firmly to the surface of the organ, so that in stripping it off portions of the renal tissue come away with it. The surface instead of being smooth or slightly dimpled becomes more and more granular (pale granular kidney), and then markedly nodular, generally preserving the yellowish-white colour (fig. 23) throughout, but sometimes acquiring a brownish-red shade, especially in those cases which have run a protracted course. In these cases, in the depressions between the granulations—the superficial vessels will be seen unduly distended and visible. On section, the substance of the kidneys will be found firm and tough, the tubules are irregularly dilated and thickened, and distributed amongst them are found numerous microscopic and macroscopic cysts. The glomeruli are found undergoing various degrees of change, many will be seen shrunk into mere fibrous knots, others less atrophied still show the remains of the capillary tuft surrounded by the thickened capsule, whilst a few still remain without obvious change (see fig. 26, p. 241). The inter-tubular space which has become infiltrated with small cells shows signs of increasing fibrillation and contraction; this change is most marked in, indeed at first is limited to, the cortical portion, and is most abundant in the region of the capsule and Malpighian corpuscles. Atrophy of the tubules, especially their convoluted portion, occurs as a necessary consequence of the compression caused by the contraction of the fibrous tissue and the obliteration of the glomeruli, and the kidneys become much reduced in size and weight. The small arteries become thickened and undergo changes

similar to those that occur in chronic interstitial nephritis, and coincidently with these changes hypertrophy of the left ventricle takes place. Indeed, at an advanced stage, it becomes difficult from a mere consideration of the morbid changes to discriminate between the two. Waxy or lardaceous degeneration frequently invades the kidney in this form of nephritis; the consideration of the changes effected by it will be found in the chapter describing the degenerative processes taking place in the kidney; it will be sufficient to state here that though lardaceous degeneration is frequently associated with nephritis it is not necessarily so, whilst when lardaceous changes are primary, nephritis is an almost invariable accompaniment. Fatty infiltration takes place in all parts of the organ. In the early and fully-developed stage of the disease this infiltration is considerable and gives the organ its rounded bulky contour and characteristic colour. As the disease advances much of the fatty deposit is removed. Liquefaction of the fatty epithelium takes place so that the fat is discharged in a free state in the urine, adhering as fine oily drops to the tube casts; some portion of the fat is directly reabsorbed. In consequence of this removal the organ diminishes in bulk, whilst the characteristic white colour is not so distinctly marked, acquiring a greyish-yellow and then a brownish-red, as the removal of the fat proceeds, and the vessels on the surface become more vascular and distinct. The fat, however, is never entirely removed, and even in advanced stages of the disease the inter-tubular growth is still to be seen infiltrated with fatty granules.

(B). CHRONIC INTERSTITIAL NEPHRITIS.

60. **Symptoms.**—When fully developed, the following are the most characteristic symptoms. A copious discharge of urine, clear and pale, of low specific gravity, containing but a small quantity of albumin, and but few casts. The pulse has a high tension, and the left heart is hypertrophied. Hæmorrhages are common especially into the retina and from the nose. Uræmic convulsions occur in nearly all cases. Unlike what happens in chronic tubal nephritis, œdema when noticed, only occurs in the latter stage of the disease. The disease is extremely insidious in its evolution, and has often far advanced before the patient comes under observation. Even in those cases in which an acute origin may be traced, a long period usually intervenes before the chronic form fully declares itself. The first symptoms usually complained of are, headache more or less persistent, dyspepsia, and a frequent desire to urinate, especially at night time. But not unfrequently a uræmic convulsion, or even an attack of apoplexy is the first announcement that a serious organic disease of the kidneys exists. The progress of a case, however, not cut short by these accidents may be thus described. The patient complains of headache, chiefly occipital, loss of appetite, and perhaps some feeling of nausea. There is usually considerable languor, but the debility is not so marked as in the tubal form of chronic nephritis. Other symptoms, but not constant ones, are often met with in individual cases, such as twitching of the muscles, and disorders of vision, itching of skin, violent neuralgic pain in the large nerves, especially of the sciatic and brachial trunks. The majority of patients become hypochondriacal and depressed, and the sexual power becomes diminished or lost. Attacks of palpitation are frequent, and asthma-

tic attacks often trouble the patient, especially at night time. It is generally for the relief of these symptoms that the patient at first seeks advice. On examination we find the pulse full and incompressible, the left ventricle of the heart hypertrophied, whilst the urine when collected for twenty-four hours, is found to be above the normal, ranging from 1800 c.c. to 2500 c.c., the specific gravity low, 1·010 to 1·012, and containing traces of albumin, which however, in the early stage may be overlooked, or be absent for days at a time. As the disease advances, these symptoms become more pronounced, uræmic convulsions assume a more distinct form, and become more frequent. Epistaxis is now often very troublesome, but hæmorrhages may occur from the stomach or other mucous surfaces, and cerebral hæmorrhage, as already stated, is a frequent termination. The visual disturbances are also more common, and the ophthalmoscope rarely fails to reveal some degree of albuminuric retinitis (p. 35); but amaurosis may occur without any ophthalmoscopic change being evident, the blindness been apparently caused by the morbid condition of the blood. Visceral complications frequently arise, and the patient may be carried off by pneumonia, bronchitis, pericarditis, etc. If the patient lives sufficiently long, the hypertrophied heart gradually fails in power, the pulse loses its abnormal tension, the quantity of urine secreted diminishes, and dropsy supervenes. We have now to consider the symptoms as they present themselves in individual cases.

The Urine, especially in this form of renal disease should be examined from day to day, for if reliance be placed on the analysis of a few individual samples taken at haphazard, the disease may be overlooked, since it may happen, as it no doubt frequently does, that many specimens so examined present very little variation from normal

urine. When therefore we have reason to suspect either from the high tension of the pulse, or from other general symptoms that interstitial nephritis exists, the whole of the twenty-four hours urine should be collected and measured, a note at the same time being made as to the amount and quality of the food and drink. From the earliest stage up to almost the very end, the amount of urine will be considerably increased, ranging from 1500 c.c. to 2500 c.c., to even 4000 c.c.; this in itself is sufficient to confirm our fears, especially if we find that the micturition is more frequent in the night than it is in the day. The specific gravity of the urine will be found to be considerably below the normal, and to be in inverse proportion to the amount of urine passed, that is to say, the greater the secretion the lower the specific gravity. On determining the amount of urinary solids by means of Trapp's formula it will be found that they are below the normal, and if a separate estimation be made of the various contituents, it will be found the decrease will be chiefly in the amount of urea and phosphoric acid excreted. The following table gives the result of an observation extended over four days, showing the amount of urine, urinary solids, urea, phosphoric acid, and the specific gravity in a typical case of interstitial nephritis, as contrasted with what might, from his age and weight of body, be considered his normal excretion.

	Quantity.	Specific Gravity.	Urinary Solids.	Urea.	Phosphoric Acid.
Normal. Approximate.	1450 c.c.	1·020	58 grms.	33·2 grms.	2·8 grms.
Disease. Calculated					
1st Observ.	2020 c.c.	1·008	32·3 grms	22·1 grms.	1·01 grms.
2nd ,,	1650 ,,	1·010	33·0 ,,	21·8 ,,	0·98 ,,
3rd ,,	2580 ,,	1·006	30·9 ,,	20·9 ,,	0·87 ,,
4th ,,	2960 ,,	1·005	29·6 ,,	19·8 ,,	0·92 ,,

Before the onset of uræmic symptoms and the later stage of the disease, or after an attack of diarrhœa, the amount of urine secreted may fall, and at the same time the specific gravity may rise slightly, but still we find the diminution in the excretion of urea maintained. This diminution continues steadily as the disease advances; at first and during the time the tension in the vessels is well marked, the diminution is never so great as in chronic tubal nephritis, and in some cases, at quite an early period it may not be much below the normal, but with the arrest of the cardiac hypertrophy the decrease becomes at last considerable. The decrease in the amount of *phosphoric acid* excreted is remarkable (Zuelzer, *op. cit.*). It cannot be accounted for by diminished ingestion, since the chlorides and sulphates are not diminished in the like ratio, nor so constantly, nor is it probable that destruction of the kidneys is sufficient to account for it. It is not unlikely, however, that the phosphoric acid is retained in the organism for some purpose of nutrition. This diminution of phosphoric acid, should any doubt exist as to the nature of the polyuria, which in the absence of albumin might arise, will serve to distinguish this form of disease from diabetes insipidus, in which the phosphoric acid if not actually increased, is certainly not diminished. *Uric acid* is said to be diminished, we must remember however, in these cases that the urine is exceedingly dilute, and the percentage yielded will be very insignificant, and likely to mislead, unless we calculate for the whole amount of urine; and again, although uric acid is highly insoluble in acid solutions, still with extremely dilute urine it may be a question whether the whole of it crystallises out when acid is added. In these cases it is advisable to concentrate the urine to half or one third its bulk, so that the specific gravity approaches the normal before adding the acid.

The amount of *albumin* found in the urine varies considerably. In some cases, especially in the early stages of the disease, albumin may be absent for days together, some physicians even go so far as to assert that the disease may run its course without the occurrence of albuminuria at all. That albumin may be absent for considerable intervals in the early stage of the disease, is a matter I think to which all will readily consent. But the cases stated to have run a course without the occurrence of albuminuria are at present too few, and the observations not sufficiently thorough to allow us to accept the statement without reservation. The case recorded by Bartels (*op. cit.*) is the strongest at present brought forward, still it is just possible that a trace of albumin may have been overlooked, or may have been present in some of the urine that was not examined, whilst absent in the samples tested. With the extremely delicate tests recently introduced, the possibility of failing to detect the minutest trace of albumin is much diminished, whilst in all cases of doubt, not only should the urine be tested day by day, but also individual samples. For this purpose, Dr Oliver's test papers are extremely handy, and the patient should be instructed how to use them. But after all, although the presence of albumin helps to confirm the diagnosis, it is not necessary to it, given a pulse of high tension, with hypertrophy of the left heart, polyuria, the occurrence of uræmic headaches, and other general symptoms, the diagnosis is already tolerably conclusive. Albumin, however, is present in small amounts in the majority of cases, but is never excessive, even in the late stage of the disease, when it becomes more apparent, the increase even then being at most relative, and due to the more concentrated state of the urine. In this it forms a marked contrast to chronic tubal nephritis, in which a very considerable amount

is passed, often amounting to more than two per cent. of dry coagulable albumin, whilst in this form the quantity rarely exceeds 0·1 per cent., whilst ·05 may be considered the average in the generality of cases. The amount fluctuates considerably, it is increased especially by exercise, it is also often increased previous to the onset of uræmic convulsions, and also after heavy meals, especially of an unsuitable kind. The *colour* of the urine is generally of a light yellow, or greenish yellow tint, and has often a turbid opalescent appearance, the amount of deposit, however, is usually slight. A few *casts* will be found, often after much search, widely distributed in the collected sediment. They are hyaline and mostly narrow, dotted with a few fine oil globules. Very rarely an occasional broad dark granular cast may be observed, when this is the case, it indicates the supervention of a nephritis of a more acute type, and which may occur at any period during the progress of the disease. Waxy casts are also infrequent, though they undoubtedly do sometimes occur, though not nearly so frequently as in chronic tubal nephritis. The *sediment* also contains renal epithelium, and occasionally pus cells, in looking for the former, we must remember that their form is apt to be modified by long immersion in the urine, so that they may be mistaken for pus cells, or for the epithelia of some other part of the urinary tract. Generally however, they can be distinguished by their cuboid form, by their being larger than an ordinary pus corpuscle, by the distinctness of their nuclei, and association with the few scattered casts. Red blood corpuscles are never found, except when the disease is complicated with some secondary affection. Crystals of calcium oxalate, with which a few fine crystals of uric acid are intermingled, are commonly observed dispersed through the sediment or attached to the tube casts.

Changes in the organs of circulation are observed early; indeed, it is from the peculiar character of the pulse, that we are often led to make an examination of the urine, and to suspect the existence of the disease. The changes consist of hypertrophy of the left ventricle, thickening of the arterioles generally throughout the body, accompanied by atheromatous degeneration. To the degenerated condition of the vessels, and the high degree of tension that exists in them, the tendency towards hæmorrhage is accounted for, the most formidable form being that from the cerebral vessels, and giving rise to apoplexy. These various changes and the conditions they give rise to, are described in the chapter on general symptomatology (p. 15). Dropsy which is such a marked feature of tubal nephritis, both in its early and fully developed stage is never observed in interstitial nephritis, except in the later stage when the arterial tension has fallen, or unless an intercurrent attack of sub-acute nephritis supervenes. Even then it rarely assumes a high grade.

Disturbances of the nervous system are also very marked, and manifest themselves early in this form of disease, and are a feature that distinguish it from chronic tubal nephritis, in which form they occur late, and are usually developed in connection with some other complication, and are due mainly to the toxic condition of the blood, and in part to the changes that are taking place in the vessels of the nerve centres. Sometimes these disturbances come on very gradually in the form of minor manifestations, at other times as a sudden outburst in the shape of uræmic convulsions. The minor disturbances are headache, neuralgia, twitching of the muscles, and itching of the skin. The headaches are generally occipital, and are extremely persistent, occasionally they are hemi-cranial. Severe neuralgic pain often accompanies the headache,

affecting chiefly the deep seated nerve trunks, and it often happens that whilst the deep seated nerves are the seat of pain, some of the superficial branches are affected with anæsthesia. Twitching of the muscles, generally confined to certain groups, is also a very annoying symptom, and usually precedes an attack of uræmic convulsions, though I have noticed the symptom in quite an early stage of the disease. The muscles most generally affected are the muscles of the calf of the leg, the quadriceps femoris, and the serratus magnus. Sometimes the patient will be woke suddenly in the night, with a general twitching of all the superficial muscles of the body. Violent itching of the skin is another distressing symptom, and which sets in towards the end of the disease; though undoubtedly mainly due to nervous disorder, it may be aggravated by the state of the skin, and the deposit on it of minute crystals of urea. The attacks of uræmic convulsions may come on without warning, but as a rule they are preceded by an aggravation of these minor nervous disorders, and by a marked change in the character of the urine.

Uræmic amaurosis without ophthalmoscopic changes, and *albuminuric retinitis* are rarely absent in a more or less pronounced degree in the fully developed stage of interstitial nephritis, in this respect they serve to distinguish it from chronic tubal nephritis, in which disorders of vision and ophthalmoscopic changes do not occur till the stage of secondary atrophy is developed. An account of the changes that are observed in the retina in this disease, is given at page 34.

Disorders of digestion are manifest throughout. The appetite fails at quite an early stage, especially as regards animal food. *Vomiting* is a very general symptom, it occurs in two forms; *(a)* that dependent upon an uræmic condition, and which usually occurs upon an empty

stomach, the ejected matters being watery, and often alkaline in reaction; *(b)* in some cases the vomiting seems to arise from gastric catarrh, consequent upon cirrhosis of the liver, which according to the statistics of Grainger Stewart and Murchison is present in about fifteen per cent. of the cases of contracted kidney. Cirrhosis of the liver may, however, be accompanied by albuminuria, without there being any disease of the kidney, owing to the pressure on the renal veins of a large quantity of fluid in the peritoneum (ascites), when this is removed by tapping, the albumin will, if there be no actual disease of the kidney, speedily disappear. In these cases there are marked dyspeptic symptoms after taking food. In addition to the ordinary dyspeptic pains, a severe gnawing radiating pain, occurring often at night or early morning, is often experienced in the hypochondriac and epigastric regions, apparently of a neurotic character, which coming on suddenly, will annoy the patient for several hours. It must not be forgotten that owing to the co-existence of hepatic cirrhosis, ascites may be present, and consequent on that, some degree of œdema of the legs. Diarrhœa, towards the close, especially when there is hepatic disease, is a very troublesome symptom, the evacuations being usually extremely fluid and frequent.

Respiration is often disturbed by attacks of *dyspnœa*, closely resembling nervous asthma, and which no doubt are caused by the circulation of blood poisoned with urea through the respiratory nerve centres. The attacks come on suddenly, especially during the night, and after lasting some hours usually subside; patients who are subject to these attacks of "renal" asthma, are however rarely quite free from general dyspnœa. Sufferers from this form of chronic kidney disease are especially liable to bronchitis and pneumonia, and those patients who insist or are

obliged to spend their winters in London, or in unsuitable situations in England, are consequently a source of perpetual anxiety to their medical attendant.

61. **Etiology.**—In a disease which commences so insidiously it is difficult to distinguish closely between exciting and predisposing causes. Among the latter, age, heredity, and residence in damp and cold climates, seem to be the most prominent; whilst gout, saturation of the system with lead, chronic dyspepsia attended with frequent deposits in the urine of oxalate of lime and urates, and long-standing disease of the genito-urinary passages, must be reckoned as among the chief exciting causes.

Age.—Many have asserted that interstitial nephritis is essentially a disease of old age, this, however, is not borne out by statistics, which unmistakably show that it is a disease of later middle age, rather than of old age, and that more cases occur in the decade between fifty and sixty than between sixty and seventy, whilst the percentage of cases met with between forty and fifty is slightly more than between fifty and sixty. In the earlier years of life, instances of the disease though rare are to be met with. Bartels (*op. cit.*), out of thirty-three cases examined, met with four instances (or eight per cent.) of the disease under twenty years of age. Taking, however, the statistics of various authors, the following table gives probably more correctly the general percentage.

Under	20	years	1·5	per cent.
Between	20-30	,,	9	,,
,,	30-40	,,	21	,,
,,	40-50	,,	32	,,
,,	50-60	,,	28	,,
Over	70	,,	15	,,

The youngest case I have observed, was twenty years of

age, though from his history he most probably had been suffering from the disease for some two or three years previously. In this case the disease was not the result of scarlet fever, which some authors are disposed to think is the cause of interstitial nephritis, when it occurs in the young, but was evidently an hereditary tendency.

The disease is undoubtedly more common in men than in women, in England it is said to be twice as frequent, but I feel disposed from my own observations to agree with Bartels, and put it at a higher figure, say 4 : 1. This frequency is no doubt accounted for by the fact that men are more liable to vesical and urethral troubles which are potent factors in the etiology of the disease.

Bartels observes that "his experience does not enable him to accuse any particular calling or occupation as predisposing to this affection." In this I cannot agree for according to my experience, the disease is more common among the well to do, highly fed, and sedentary members of the community, than among the working classes. I certainly see more of this form of chronic Bright's disease among private patients than in the out-patient department of the Hospital, whilst with the chronic tubal form, the reverse obtains. Again too with regard to particular callings, we must not overlook the frequent occurrence of the disease among workers in white lead. The question, too, how far *alcohol* habitually taken in excess tends to induce the disease, has been much disputed. The general consensus of opinion of late years, has been quite in accord with the views expressed by Dr. Dickinson, that it has no direct effect. Combined however with other conditions, especially high feeding, and sedentary habits, it no doubt plays an important part in the causation of the disease.

Syphilis undoubtedly acts as a cause predisposing to inter-

stitial nephritis, but no such direct relationship seems to exist between the two as is often observed in the sub-acute form of nephritis. When interstitial nephritis occurs in a syphilized subject, the gravity of both diseases is increased, and degenerative changes in the vessels usually proceed with great rapidity.

Cold especially residence on damp cold soils, and in marshy and malarious districts, undoubtedly has a tendency to induce the disease, though the action cannot be traced so directly as in chronic tubal nephritis. In that disease I stated, that I believed the cases said to follow attacks of intermittent fever, were to be attributed rather to "cold catching" from the damp situation of the residence, than to the influence of malaria. In this form of chronic nephritis, I believe long-continued malarial poisoning to be a direct cause, probably from the paroxysms causing frequent renal hyperæmia. In all cases that have come under observation, several years have intervened between the first attack of intermittent fever, and the discovery of the renal mischief.

Heredity.—Some very remarkable instances proving the tendency to hereditary transmission of the disease have been brought forward by many observers. Dr. Kidd in the twenty-ninth volume of the *Practitioner*, has contributed a very interesting paper on this subject; but Dr. Dickinson's account of eighteen cases, occurring in one family within three generations, with a very strong possibility that the disease had existed in the family for some generations before, must be considered the best and most conclusive evidence that can be quoted on this point. A gentleman, who I saw some few years since, informed me that four of his brothers had died of renal disease, all very nearly at the same age. He was the youngest of the family, and he was dreading the approach of the fatal

period, as he was suffering from premonitory symptoms, uræmic headaches, polyuria, etc. I subsequently learnt that he died two years after I had seen him, suddenly of apoplexy. In this case the father had died with cerebral symptoms about the same age that had proved fatal to five of his sons.

Gout.—The gouty kidney is essentially the result of chronic interstitial change. Professor Virchow (*Berl. Klin. Wochenschrift*, No. I., 1884) states he has never seen an acute nephritis, which from the presence of uratic deposit could be referred to gout. The albuminuria which is often observed in connection with acute attacks of gout, is rather to be referred to direct irritation of the whole urinary tract, the renal pelvis, the bladder, prostate, etc. Professor Virchow in the above-mentioned communication has related his own personal experience. In 1882 he had slight swelling of his fingers, and shortly afterwards began to suffer from irritable bladder, examination of the urine showed the presence of pus and albumin, on adding acetic acid to the purulent deposit, uric acid crystals separated out to an extent he had never seen before. He at once began taking alkalies, (sodium biborate) and the uric acid at once disappeared, and with it the pus and albumin. He attributed the attack to the irritating effect of the uric acid exciting a purulent catarrh of the whole urinary tract, which subsided as soon as the irritant was withdrawn. The "gouty kidney" is distinguished from simple interstitial nephritis, by the deposit of sodium urate in the tubules, in addition to the puckered and wasted condition of the cortex. But as Professor Virchow has pointed out, the chronic inflammatory change begins in the cortex, at a distance from the seat of the deposit of urates in the tubes just as in the joints, the urates occur in the cartilage and ligaments, whilst the synovial membrane is the

seat of the inflammation), and from this he argues that it is not the presence of the deposit in the tubules, but the exudation of the fluid containing the uric acid in solution, that acts as the irritant. According to this view, interstitial nephritis is the primary step in the process, and the streaky deposit in the tubules a secondary result. Whatever the process may be, the "gouty kidney" is slowly evolved, and till the later stages gives rise to no marked symptoms. No relationship exists between the degree of renal affection present, and the amount of tophaceous deposit in the joints, indeed the "gouty kidney" may be met with without their having ever been any acute manifestations of gout at all. From this it has been argued that the renal affection is the first step in the process, and it is not till the arrest of the function of the kidney, in excreting uric acid and its retention in the blood, that acute manifestations of gouty paroxysms occur. There are objections to this view however, and it is more probable that the deposit of urates in the tubules is part of the process which leads to the non-destruction and retention of uric acid in other parts of the body (see Lithuria).

Lead, when taken into the system, is eliminated chiefly by the kidneys. Ollivier (*op. cit.*) has shown that given in large doses, so as rapidly to induce plumbism, it occasionally induces acute or sub-acute nephritis, showing that the mineral is capable under certain circumstances of producing renal hyperæmia. But the most frequent form of kidney disease met with in connection with lead poisoning is interstitial nephritis. Dickinson (*op. cit.*) has shown from statistics compiled from the post-mortem books of St. George's Hospital, that out of forty-two workmen engaged in some form or other, in occupations which brought them in contact with lead, twenty-six had granular degeneration of the kidney. The relationship between

chronic plumbism and gout is equally well marked. Garrod has shown most conclusively, that the subjects of lead poisoning frequently become gouty, whilst the inheritors of the gouty diathesis are extremely susceptible to the influence of lead. There is a difference of opinion however, whether the renal affection depends on the lead or on the gout for its development. Some writers, chiefly German, have denied the direct interdependence between lead poisoning and the development of renal disease, whilst in England it is generally assumed that the first step in the process is the diminution of the excretion of uric acid. That this takes place, Garrod (*Treatise on Gout*, 3rd edit.), has shown experimentally, by administering lead in small doses to patients in hospital, and then estimating the excretion of uric acid, which in all cases showed an immediate and considerable diminution. And to this diminution of excretion, and consequent retention of uric acid in the blood, the frequency of gout in saturnine patients is generally referred. Still undoubtedly we meet with instances from time to time, in hospital practice, of lead-workers suffering from chronic albuminuria, in whom whilst living we are unable to detect any evidence of gout, nor post-mortem do we find striæ of deposited urates in the renal tubules, though the kidneys are granular. The two processes, however, are usually associated, and when that is the case the progress down hill becomes extremely rapid.

Chronic dyspepsia, attended with frequent deposits of oxalates and urates in the urine, is undoubtedly a common cause of interstitial nephritis. Thus, Murchison (*op. cit.*) regarded "lithæmia" arising from functional derangement of the liver, as one of the first links in the chain of causes tending to produce contracted kidney; and Johnson (*op. cit.*) has always maintained that the proximate cause of

chronic renal disease depends upon a morbid condition of the blood, and that the vitiated products, the result of abnormal digestion, absorbed into the blood, were to be reckoned among the chief of the toxic agencies bringing about the condition. Both Murchison and Johnson, therefore, regarded the nephritis in these cases as arising directly from the morbid condition of the blood, whereas I am inclined to the opinion, that the nephritis is provoked by the direct irritation caused by the almost constant passage through the tubules of the urinary deposits, separated from the urine, when the blood is thus morbidly charged with effete products. In cases of chronic dyspepsia, especially that form associated with deposits of oxalate of lime, a certain amount of renal catarrh and pyelitis can always be demonstrated by the presence of pus cells, and epithelium from the upper urinary tract. A catarrh that subsides when means are taken to keep the urine sufficiently dilute, although the dyspeptic symptoms remain. Indeed it is only reasonable to suppose that the constant passage of irritating particles of oxalate of lime, or of urates, along the tubules, should give rise to chronic irritation, which ultimately brings about interstitial changes, just as we find the lungs of those persons, whose occupation exposes them to the inhalation of irritating particles of dust, etc., become affected with interstitial pneumonia.

Chronic pyelitis and cystitis certainly must be regarded as one of the most frequent causes, leading to interstitial changes in the kidney. In the cases of calculous pyelitis, and chronic vesical trouble, which have eventually proved fatal, interstitial changes are usually observed, and though perhaps in some the macroscopic appearances are not well marked, still a careful microscopic examination rarely fails to reveal interstitial change. Both *pregnancy* and *valvular disease of the heart* have been assigned as causes

of interstitial nephritis. The former, however, undoubtedly is more concerned with the production of chronic tubal nephritis, and when a granular condition of the kidney is met with, the history is such as to enable us to arrive at the conclusion that the contraction is due to secondary atrophy. In valvular disease of the heart, the condition of kidney resulting from long-continued venous congestion, is generally described as the cyanotic or indurated kidney, and differs in many respects from the kidney, the result of interstitial nephritis properly so-called. An account of the cyanotic induration of the kidney, the result of passive venous congestion, is given in the section on the etiological varieties of chronic nephritis.

62. **Prognosis.**—As regards the ultimate issue, the prognosis must always be unfavourable, though when the affection is early recognised, and the patient placed under the best hygienic conditions and dietetic regulations, the progress of the disease may be so controlled, that its advance is often arrested for a considerable period. Patients who come under observation complaining of debility and general malaise, and in whose urine no traces of albumin can as yet be discovered, though the secretion is considerably increased, and the urinary solids diminished, rapidly improve in health, even if they do not entirely regain their former robust appearance, after they have been placed on a regulated diet, and under favourable hygienic conditions, but who relapse as soon as they neglect these measures, and again become polyuric, weak and debilitated. Even when the disease is more advanced, life may be prolonged for many years, when the patient is careful to carry out the instructions of the medical attendant. Life too may be prolonged for a considerable time, even after the onset of uræmic convulsions. Even after hæmorrhage from the cerebral vessels has occurred, the prognosis need

not be considered immediately in its gravest aspect, as undoubtedly many recover, more or less completely, from the results of the cerebral lesion, and may live for some years after the event. At the same time it must be borne in mind that the improvement which may set in after such grave events, as uræmic convulsions, or cerebral apoplexy, is often more apparent than real, and is only the result of the enforced rest, and increased care and attention, bestowed on the management of the renal trouble. In many instances, this has been developing insidiously and unsuspected, and the uræmic convulsion, or the retinitis, or the apoplexy, are the first symptoms, that call attention to the fact. The treatment that follows, relieves these urgent symptoms, and prevents for a time their recurrence, and though it fails to arrest the slow process of contraction going on in the renal tissue, it undoubtedly retards it. In giving an opinion of an individual case, the following considerations may help us to form an estimate of the future. 1. In gouty patients, the chronic nephritis is slowly evolved, and generally runs a prolonged course. 2. When associated with other diseases, such as syphilis, struma, general cirrhosis, etc., the disease often proves fatal, even before extreme contraction of the kidney takes place, from the early degeneration of the vascular system. 3. The most fatal combination is perhaps that of gout with chronic lead poisoning. 4. The steady persistence of uræmic symptoms, such as headache, twitching of the muscles, morning vomiting, etc., after treatment has been adopted, must be considered more ominous than a decided attack of severe convulsions. The latter may be induced by accident or some sudden complication arising, and if the crisis can be surmounted, life may still be prolonged; the former, on the other hand, announces that the disease in spite of

remedial measures, is steadily advancing from bad to worse.

63. **Diagnosis.**—There is little difficulty when the case is fully developed and is under continuous observation. The other renal affections, it may be taken for, are the small atrophied kidney of chronic tubal nephritis, and the waxy or lardaceous kidney. From the large white kidney it is distinguished by characters so marked that a mistake one would think could hardly possibly be made. The distinguishing symptoms of each, which we have already described, being as the following table shows in strong contrast.

Chronic Tubal Nephritis.	Chronic Interstitial Nephritis.
Age, more frequent in youth and early middle age.	*Age*, more frequent in later middle life.
Develops rapidly; from two to six months.	*Develops* slowly; from four to five years or more.
Chief Symptoms.—Dropsy affecting the whole body and serous cavities. Uræmic convulsions rare, as also albuminuric retinitis and hæmorrhage.	*Chief Symptoms.*—Hypertrophy of left ventricle, albuminuric retinitis, atheroma of arteries, uræmic convulsions; œdema only slight and towards the end.
Urine scanty, high specific gravity, much albumin. Casts broad hyaline, granular, and waxy. Deposit, chiefly urates, and granular débris.	*Urine* abundant, low specific gravity, little albumin. Casts, hyaline narrow, dotted with oil drops; with fine crystals of calcium oxalate sometimes adhering. Deposit chiefly oxalate of lime.

The contrast, however, between the symptoms attendant on the atrophied granular kidney, the result of secondary changes in the large white kidney, and the symptoms associated with the granular kidney, the result of true interstitial nephritis, is not so clearly marked; indeed, the symptoms have a close correspondence, and here we have to depend chiefly on the history of the case. If, therefore, we have a history of long-standing dropsy, or dropsy

coming on quite early in the illness, we may assume that the disease is not primarily due to interstitial nephritis but must have passed through the phase of large white kidney. The cardiac hypertrophy moreover is never so completely developed in the secondary, as in the primary contracted kidney. Again, although the urine in both forms is increased in quantity, and the amount of albumin is small, still the amount of urine seldom reaches the same considerable amount, and the albumin is rarely as scanty in the secondary contracted kidney as in interstitial nephritis, whilst an attentive examination of the deposit shows that casts are more abundantly deposited from the urine in the former condition, and differ from the latter by many being broad, opaque, and sometimes mingled with highly refracting waxy casts. Lardaceous degeneration of the kidney may be taken for contracted kidney, especially in those cases in which the urine is abundant and of low specific gravity, and the amount of albumin small, and the casts scanty and chiefly hyaline. In lardaceous degeneration, however, the heart is not hypertrophied, and we generally have the history of long-continued suppuration, etc., and consequent cachexia to direct our attention to the true state of things. Besides which, waxy degeneration of the kidneys is the only condition in which dropsy and polyuria are found associated together.

64. **Morbid Anatomy.**—Chronic interstitial nephritis results in what is known as the small red granular kidney. Variations from this type may be met with, as for instance, in the so-called large red kidney, probably an early stage of the disease before contraction of the connective tissue, in which the kidney instead of being dwindled in volume, is a little increased in size. Or the kidney instead of being of a reddish-brown, is of a greyish

hue, and the granulations coarse, in this case we may suspect that to the chronic interstitial inflammation, an acute attack has at some time been superadded. When the disease is fully developed we find the kidneys shrunken, about half their size may be taken as an average expression, though they may be found dwindled to the size of a pigeon's egg, or walnut. Though both participate in the process, they are not always equally affected. The capsule is thickened, adhering firmly to the surface of the kidney, and on removing it small portions of kidney substance tear away with it (fig. 24). On section the kidney cuts firmly, and its consistence is toughened, and the exposed surface of the cortex is seen covered with granulations, from the size of a millet seed to that of a mustard seed, and to be of a dark reddish hue (maroon), which colour is always more marked in the depressions of the granulations, than on their surface. Cysts usually stud the surface, in size they vary from a pin-head up to a considerable size. Irregular depressions will also be often observed on the surface, probably caused by the rupture or absorption of some former cyst. On section it will be found that the wasting of the organ occurs chiefly in the cortical portion, though the pyramidal is also considerably affected. The cut surface has a granular appearance, and the radiating lines of the cones are blurred. The Malpighian corpuscles stand out as red points, and cysts are usually abundantly met with throughout the organ. The first stage in the process consists of a cellular infiltration, which commences around the blood vessels, and the capsule of the Malpighian corpuscles, and ultimately becoming more diffused, and spreading inwards, involves the inter-tubular connective tissue. This process resembles that which occurs in glomerulo nephritis, and which has been described at p. 194 (fig. 21), only the evolution is much slower, and the cells are not so numerous.

The cellular infiltration of the inter-tubular connective tissue is shown (fig. 25). The new growth is gradually transformed into a fibrillated structure, which more or less slowly contracts, and compresses the capillaries, and the capsular bodies, so at last many of the glomeruli become shrunken to mere fibrous knots. The cellular infiltration, which commences round the interlobular vessels, and spreads rapidly into the bases of the pyramids, and around the convoluted tubules in the cortex, also undergoes conversion into laminated connective tissue, by the cicatricial

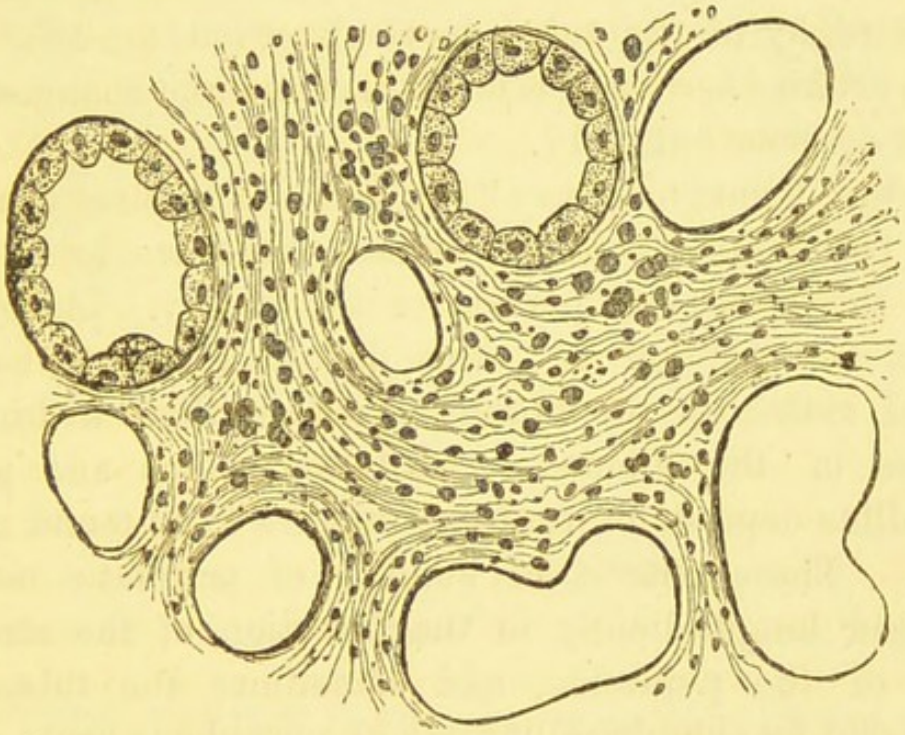


FIG. 25.—Early stage showing cellular infiltration of the intertubular connective tissue. The epithelium has fallen out of some of the tubes in the preparation of the section (Green's *Pathology*).

contraction of which the tubular structures undergo atrophy. The second stage in the process is characterised by changes in the tubules. Cloudy swelling of the epithelium, followed by desquamation and disintegration, and whilst many of the tubes are completely obliterated by the pressure of the cicatricial tissue, others are

only diminished in size, whilst some are irregularly dilated, and filled with granular and fatty débris. The irregular pressure exercised by the contracting connective tissue gives rise to cysts. Some of which appear to be developed from partially dilated and compressed tubules, their contents being transformed into a transparent gelatinous mass. Other cysts according to Klebs and Grainger Stewart, appear to be formed from dilatations of the Malpighian corpuscles. As the disease advances the glomeruli become more and more involved, and converted into fibrous knots, and the obliteration and atrophy of the tubes more extensive (fig. 26). The small arteries become thickened and undergo changes such as are described at p. 17.

In the "gouty kidney" in addition to these changes, white points and streaks of sodium urate are to be seen upon the pyramidal portion of the kidney. According to Dr. Garrod (*op. cit.*), this deposit seems to be imbedded rather in the fibrous structure, than within the cavities of the tubules. Still amorphous and partly crystalline deposits of urate sodium are to be found in the tubes. These consist of bundles of prismatic needles arranged longitudinally in the direction of the straight tubes of the pyramids, and sometimes the tubes are obstructed by cylindrical masses of amorphous urate.

In typical cases there is little difficulty in distinguishing between the small red granular kidney, the result of chronic interstitial inflammation, and the small contracted kidney, which is produced by secondary changes in the large white kidney. But if it happens that the small red kidney becomes the seat of acute inflammation, or the period of secondary contraction is prolonged, intermediate forms will be produced, so that it becomes very difficult to distinguish clearly between them. In the former case the

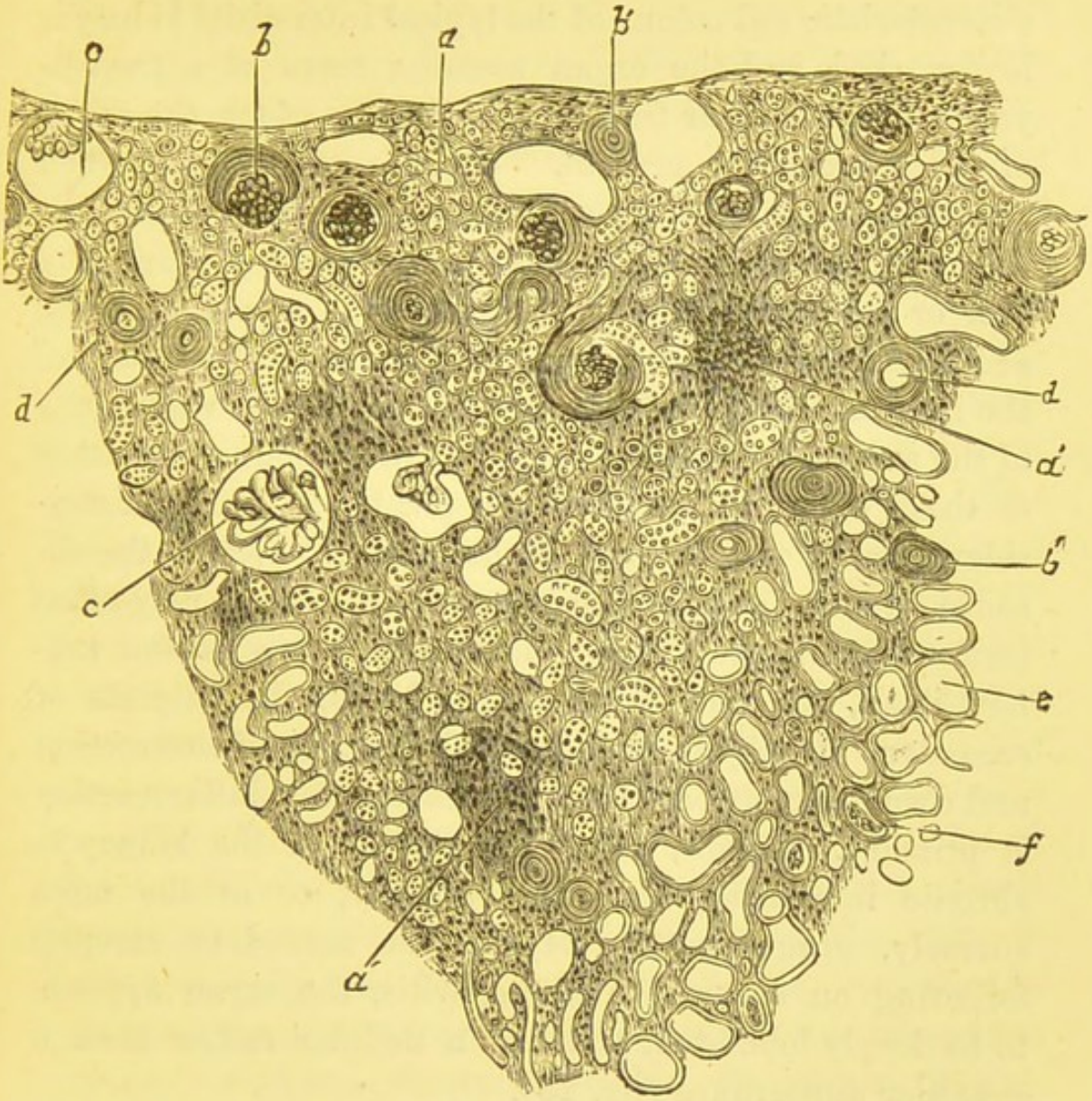


FIG. 26.—Granular contracted kidney. Segment of the cortex seen under a low power (1 inch), showing a somewhat conical patch of disease.

a. Region of convoluted tubes, occupied by an apparently fibrous tissue, composed to a large extent of atrophied tubes.

a'. Denser fibrous tissue in deeper part of cortex.

b. Atrophied glomeruli, with thickened capsule and remains of the capillary tuft.

b'. Other atrophied glomeruli, completely transformed into masses of concentric fibrous tissue.

c. A glomerulus persisting, without obvious morbid change.

d. Thickened vessels.

e. Convoluted tubules in surrounding tract, somewhat dilated.

f. Colloid casts in these tubules. (Prof. Greenfield, *Path. Soc. Trans.*, vol. xxxi.).

characteristic red colour of the typical interstitial kidney is less marked, and the organ assumes more of a greyish-yellow or buff colour from the infiltration of fat, the result of the more acute process. On the other hand, when the process of secondary contraction is unduly prolonged, the kidney loses its white colour, and acquires more of a buff or reddish grey colour, this change of colour being accounted for by the gradual removal and absorption of the infiltrated fat, and also from the increased vascularity of the superficial vessels. In forming an opinion in either of these cases, we are of course greatly helped by a consideration of the history of the case, but even in the absence of this important particular, I think we may often form an opinion from the general appearance of the kidney itself, since it is rare for kidneys, the subjects of secondary atrophy to undergo such a degree of contraction and dwindling, as occurs when the chronic inflammation is primary. Again, whilst the surface of the kidney in chronic interstitial nephritis is finely, or at the most coarsely, granular (fig. 24), in the secondary atrophy following on chronic tubal nephritis, the organ appears to be deeply lobulated, and has a nodular rather than a granular appearance (fig. 23).

Etiological Varieties of Nephritis.

65. **Scarlet fever nephritis** at first claims attention. It arises during the desquamation of skin after the subsidence of the acute attack, generally in the third week, and rarely before the eighteenth day of the disease. Dr. Mahomed has stated that it is preceded by increased tension of the pulse, constipation, the presence of the crystalloids of the blood in the urine, as evidenced by the guaiacum

test. Though I disagree with Dr. Mahomed's explanation of the cause of the phenomena, still when they are observed they are useful indications of the coming storm, and enable us to take precautionary measures. I have also observed that coincidently with the coming on of the albuminuria the urine often becomes alkaline from fixed alkali, whilst crystals of triple phosphate speedily form in the urine, after it has been passed, from ammoniacal decomposition. The albuminuria that occurs frequently during the early stage of scarlet fever must not be regarded as connected with scarlet fever nephritis. The former appears during the acme of the disease, and is a true pyrexial albuminuria which disappears as the temperature falls, and is never accompanied with dropsy; the latter sets in only during the subsidence of the specific fever, with decided evidence of renal trouble, and usually accompanied with some degree of dropsy. In favourable cases, which form the majority, the nephritis subsides in about three weeks after the commencement of the attack, and at the end of six weeks or two months the urine is found generally free from epithelium, casts, etc., though perhaps a trace of albumin may appear in the urine after exercise, or after a substantial meal. So long as this albuminuria continues, the patient must be kept under medical supervision. In aggravated or neglected cases the disease may drag on many months, dropsy and albuminuria recurring after each exposure to cold, etc., till finally the disease becomes chronic, and the stage of granular kidney entered upon. The frequency with which nephritis follows scarlet fever varies in different epidemics, and by no means depends on the severity of the original disease. Thus I have seen some of the most severe cases of nephritis follow on only slight manifestations of scarlet fever, whilst some severe cases have escaped nephritis altogether.

The fatality too varies in different epidemics, and I believe is much influenced by the sanitary surroundings of the patients. In a large school, thirty-six boys attacked with scarlet fever came under my observation, of these, thirteen had scarlet fever nephritis; of the thirteen only two had decided dropsy, though in each case some slight œdema was present. One died of acute uræmia and suppression of urine, this case had had scarlet fever so slightly that it had escaped the attention of those responsible for sending the boy to the sick infirmary, and he was still at his studies when attacked with convulsions. In twelve of the cases in which the commencement of the disease was definitely determined, albumin first appeared in the urine from the seventeenth to the twenty-first day. Since scarlet fever nephritis stands in no direct relation to the severity of the disease, as manifested by the profuseness of the rash or ulceration of the throat; whilst the theory that it is due to checking the elimination of the poison through the skin owing to "cold catching," seems to be invalidated by what has often struck me very forcibly, that the proportion of cases of nephritis following scarlet fever does not seem to be greater in the houses of the poor where the nursing is insufficient and the children sent out of doors as soon as convalescent, than among the rich whose children are nursed with solicitude, and whose convalescence is carefully attended to. The question therefore arises, to what is the post-scarlatinal renal affection due? At present no decided answer can be given to this question (see also p. 181), but the discovery of bacteria in some cases of scarlet fever and diphtheritic nephritis makes it probable, that these organisms may be concerned in the production of this form of nephritis, a supposition rendered all the more probable by Mr. Cheyne's experimental observations (*Brit. Med. Journal*, Sept. 24th, 1884), who found that when bacteria

from cultivation fluids were injected into the blood that they were mainly eliminated by the kidneys, whose tissues became crowded with them. With regard to the pathological changes that occur in scarlet fever nephritis, we have already seen that they consist primarily and mainly in an infiltration of nuclear masses within the capsule of the glomerulus (glomerulo nephritis), and that the changes in the tubules are the second step in the process; as a consequence we find therefore in quite early stages the kidney but little enlarged, and even when the changes in the tubules are well advanced, the kidneys rarely attain the volume found in catarrhal nephritis in which the tubular changes are primary. The description given of scarlet fever nephritis may be applied to acute renal inflammation following on diphtheria, small-pox, chicken-pox, measles, typhus, and the like.

66. **Puerperal nephritis.**—This has been attributed by some writers to the pressure of the pregnant uterus upon the renal vessels, others believe it due to an altered condition of the blood. With regard to the first view I must confess myself on anatomical grounds unable to accept it, for I cannot see how the pregnant uterus can compress the renal veins. Moreover, clinically the somewhat profuse albuminuria of pregnancy is utterly unlike what we meet with in obstructive engorgement of the veins, such as we find in long standing heart disease, and which leads to cyanotic induration of the kidney, whereas the symptoms correspond to those of diffuse nephritis. Nor pathologically do we find evidence of obstructive engorgement, for if we examine the kidneys from a patient, in whom the disease is recent, we find they do not differ from those we find post-mortem in scarlet fever nephritis; whilst when the disease is of long-standing, the result of continued pregnancies, or a continua-

tion of the original attack, the kidneys become pale and granular, just as occurs in oft repeated or long-continued attacks of sub-acute nephritis, and never assume the peculiar appearance characteristic of venous obstruction. On the other hand, it is more probable that puerperal nephritis depends upon some change in the blood, during pregnancy, which renders the secreting organs liable to parenchymatous changes, for we find of all the causes of acute yellow atrophy of the liver, the puerperal state stands foremost on the list. Puerperal nephritis is said to occur during the last months of pregnancy; it would be more accurate, however, to state that it is rarely met with before the end of the third month, and that it hardly ever developes after the seventh month. The period at which according to my experience nephritis usually sets in, is at the end of the fourth and during the whole of the fifth month, from then I think the tendency gradually declines till the time for delivery. It is stated that primiparæ are more liable to the disease than women who have already borne children; this statement, however, requires modification, and it should rather be that women who have not been the subject of nephritis in their first pregnancy are less liable to the disease in subsequent pregnancies, and that the risk is diminished with each successive pregnancy. Nephritis is said to occur in one out of every 150 pregnancies. This may accord with the experience of lying-in hospitals, who are called upon to attend severe cases of puerperal eclampsia and dropsy, but I am sure the proportion is far too high as regards the general run of practice. I would here distinguish between the albuminuria frequently met with in pregnant women, due to functional derangement (see Chap. XI.), and the albuminuria of nephritis, accompanied with dropsy and uræmic convulsions.

The course of puerperal nephritis usually runs a subacute rather than an acute course. The disease commences insidiously, and the urine which is diminished in quantity and highly albuminous, rarely contains blood, and as a rule but few hyaline casts. In some cases, however, the onset is awfully sudden and foudroyant in character. The considerable amount of albumin passed in this form of nephritis has been generally remarked. In a case I examined for Dr. John Williams, the urine of twelve hours contained 5·1 grms. of dry coagulated albumin, which for the whole day would represent 10 grms., a very considerable quantity. This high degree of albuminuria is to my mind an additional evidence of an altered condition of the blood in this state. In puerperal nephritis too, sero-globulin (paraglobulin) is also present in abundance, often in absolute excess of the serum albumin, this probably explains the high grade of the albuminuria. General dropsy to a greater or less degree is present in nearly every case of puerperal nephritis. Whilst uræmic convulsions of an acute character are present in about 25 per cent. of the cases (Rosenstein) of the albuminuria of pregnancy. The uræmic convulsions in this form of nephritis are particularly severe (puerperal eclampsia), and often accompanied with maniacal excitement and temporary amaurosis. The reason for the special intensity of the uræmic symptoms in puerperal nephritis has not been explained, but I believe it to be related to the excessive drain of albumin from the blood leading to an altered percentage relationship between the nutritive and effete materials of that fluid. As already stated the post-mortem examination of the kidneys, shows them to have been the seat of diffuse nephritis. In some cases severe convulsions occur without there being any evidence of albuminuria or dropsy; in these cases, I be-

lieve the convulsions are purely epileptic, and not in any way connected with the state of the renal organs. In cases when the disease is of recent origin we find glomerular and tubal changes in progress, sometimes one form being more marked than the other. As a rule the nephritis terminates with delivery, but in some instances the albuminuria may be continued to the next pregnancy when an exacerbation of the symptoms occur, or even if the patient recover between the pregnancies, the frequent recurrence of the nephritis during the puerperal state leads to the establishment of chronic nephritis, and the development of the large white kidney, and in process of time to the pale granular, or atrophied kidney.

67. **Malarial nephritis.**—In this country, at least, where the manifestations of the malarial poison are rarely intense, the form of nephritis associated with impaludism that most frequently comes under our observation, is that of purely interstitial nephritis, whilst the cases of acute or sub-acute nephritis occurring in persons residing in damp and marshy districts, which are sometimes attributed to ague, are in reality caused by the long-continued effects of cold and damp. In countries, however, where the disease assumes an intensity, fortunately now unknown among us, structural changes of an acute character do undoubtedly occur. Dr. Atkinson (*American Jour. Medical Sciences*, 1884), in a valuable contribution on the subject, thinks that the usual form of malarial nephritis is the tubal and diffuse, and that this inflammation seems to be most intense in the vicinity of the glomeruli. Kiener and Kelsch (*op. cit.*) also describe a hæmoglobinuric hyperæmia as occurring during severe attacks of ague, in which the kidneys though little altered in size and weight are intensely congested. The cortex obscured by hæmatic coloration, whilst the glomeruli stand out as red points, and the

pyramids of brighter red. The convoluted tubes are enlarged, and the epithelia swollen and discoloured, the tubes full of casts. The glomeruli are dilated, the epithelia of the capsule being tumefied and granular, and small hæmorrhages often occur within the capsule. The interlobular veins are dilated and their contents generally thrombosed. The interstitial tissue is but little modified.

68. **Syphilitic nephritis.** —There is some doubt whether acute nephritis ever developes directly in connection with syphilis. The albuminuria often met with in the tertiary stages being associated with waxy degeneration of the kidneys; and though nephritis frequently supervenes in this condition, it is doubtful, as far as syphilis is concerned, whether a nephritis, due to this specific cause, ever precedes the degenerative changes. It is a fact, however, that albuminuria does sometimes occur during the development of the secondary stage of syphilis; this is usually the case when the invasion is attended with considerable constitutional disturbance, accompanied by a marked rise of temperature, and abundant roseolous eruption, slight jaundice is often also observable in such cases. But whether this albuminuria is due to parenchymatous changes dependent upon the pyrexia, or whether a true nephritis is established I have not yet been able to decide. The albuminuria rapidly subsides on the administration of anti-syphilitic medicines. Another form of albuminuria occurs in syphilitic patients when the administration of mercury has been too long-continued, or injudiciously administered; on the withdrawal of the drug, however, the albuminuria speedily disappears.

69. **Saturnine and Gouty nephritis.**—Experiments on animals have shown that the administration of lead salts in large doses will induce an acute diffuse nephritis in which the changes are most marked in the vicinity of the glomeruli.

But the form of kidney we meet with clinically is essentially chronic in its evolution characterized by considerable interstitial changes (see also p. 231). So also with *gouty nephritis*, for here according to the view of Professor Virchow (see p. 230) chronic interstitial nephritis is the primary step in the process, and the streaky deposit in the tubules the secondary result, whilst the albuminuria that sometimes occurs during an acute attack of gout is not to be referred to acute nephritis, but to a direct irritation of the whole urinary tract.

70. **The Cyanotic induration of the Kidneys** which results from long-continued venous congestion cannot be regarded as a true nephritis, though at one time included in the list of Bright's diseases of the kidney. The appearance of the kidney differs from that which results from chronic interstitial nephritis, by the kidneys being a little larger than they should be, by the capsule being easily stripped off instead of being more or less adherent. Also the surface is smooth, not granular, only in cases in which the process has been long continued are there shallow cicatricial depressions. The surface is also marked by stellate groups of distended venous radicles. On section the kidney cuts toughly, and both cortical and medullary substances are highly vascular and deeply coloured, whilst the Malpighian tufts are not particularly distended, the vena recta on the other hand are the seat of marked engorgement. The interstitial tissue is thickened and tough, but the accumulation of lymphoid cells between the tubuli is rarely observed, except perhaps in cases that come under observation at an early period, but they are never so marked as at an early stage of chronic interstitial nephritis. The epithelium is at first unaltered, but as the disease advances, owing probably to want of proper oxygenation, from the venous stasis, the cells undergo degeneration, become fatty

and are removed. This change occurs principally in the convoluted portion of the tubules, and causes the cortex to assume a lighter colour, whilst the medullary substance still remains deeply cyanotic.

This condition of kidney results in all cases of long-standing obstruction to the return of blood by the inferior vena cava, it consequently follows on valvular disease of the heart, more especially in the mitral obstructive form; in all cases in which the muscular power of the heart is weakened, such as occurs in dilatation of the right ventricle in emphysema; or from malnutrition of the cardiac muscle. The albuminuria of heart disease can be distinguished from that of chronic tubal nephritis, by the fact that the amount of albumin in the urine in the former is extremely small, whilst in the latter it is always fairly abundant; by the absence from the former of granular and epithelial casts, or indeed of casts of all kinds, except perhaps a few hyaline ones, to which a few epithelial cells may adhere towards the end, in protracted cases. The dropsy is cardiac not renal in its origin, that is to say, it is local, being confined to the parts that are drained by the inferior vena cava. The urine is scanty, high coloured, usually extremely acid, and with a specific gravity ranging often as high as 1·035, these points distinguish cardiac albuminuria from that of chronic interstitial nephritis, whilst it is rarely associated with uræmic symptoms, which are characteristic of the latter.

Treatment of Nephritis.

71. **In acute nephritis** it should be borne in mind that much harm may be caused by the employment of a too active treatment, especially by means of cathartics, diaphoretics and diuretics. In ordinary cases, I mean those

unattended with complete suppression of urine and acute uræmia, it will be sufficient to keep the patient in bed, in a moderately warm room (60-65° F). The bowels if confined should be opened, but all violent purgation should be avoided, certainly the administration of hydragogues. I usually order a desert spoonful of castor oil, and if this is not sufficient, a simple enema of warm water is thrown up the bowel, about four hours after, to aid the administration of the oil. As the bowels have a tendency to constipation throughout the illness, they must be kept open by some simple means. For this purpose "imperial" may be used, this consists of adding ½ oz. of bitartrate of potash to a quart of lemonade, and allowing the patient to drink from time to time, till the bowels are acted upon. The diet should be light, bland, and nutritious, and should be chiefly farinaceous, albuminous principles being reduced to a minimum, eggs being forbidden in any form. In more severe forms, in which the secretion of urine is suppressed, or very nearly so, and uræmic symptoms have set in in an acute form, our measures must be more active, though here recourse to powerful purgatives, diuretics and the like, is to be deprecated. Our endeavour, in these cases, is to reduce the amount of nitrogen in the blood, firstly, by cutting off the supply, secondly, by restoring the eliminating function of the kidney. To fulfil the first indication, the patient must be placed on a rigorous non-nitrogenous diet, that is, no albuminous substance whatever is to be administered, not even a piece of toast or a tea-spoonful of milk. Dr. Aufrecht of Magdeburg (*Berlin. Klin. Wochenschrift*, Dec. 12th, 1883), who advocates the treatment of acute nephritis by this system, gives the details of a case in which suppression of urine lasted for eighty hours, and which ultimately recovered, without recourse being had to any other mode of treatment. Dr. Aufrecht ad-

vises a rigid abstinence from nitrogenous food of all kinds, even milk, till after the second week of the attack. In ordinary cases it would be difficult to enforce so severe a regimen, which practically condemns the patient to arrow-root gruel, though the benefit attendant on such a diet is great. Therefore, if the case is not very severe, the patient should be kept on an absolute non-nitrogenous diet for two days only, and then allowed a slight relaxation, if he complains of the diet, permitting the arrowroot to be made with a little milk, or some rice to be stewed in thin broth, or plain rice pudding to be given. No solid food, flesh or fish should be given, certainly during the first fortnight, and only so much milk as may be requisite for the preparation of the farinaceous articles of diet. The patient may eat at discretion, the wholesome kinds of fruit, grapes, oranges, strawberries. If the case be very severe, then the absolute non-nitrogenous diet must be continued. Our treatment has also often to be directed to the relief of complications that may arise, such as suppression of urine, followed by uræmia, and dropsy.

Uræmic convulsions in acute nephritis are usually preceded by a considerable, if not complete, diminution in the amount of urine and urea excreted. If we are thus forewarned, we may by the judicious administration of purgatives and the vapour bath prevent the attack. But we must, however, be careful not to be over active; undoubtedly many patients have been hurried into an attack of convulsions, by over purgation and the prolonged action of the vapour bath. Remember, our object is not to withdraw water from the body, and so proportionally increase the amount of extractives, but to stimulate the secreting organs, and thus ensure the elimination of urea and other matters that have accumulated in the body. Now we know that urea is, under certain conditions, eliminated by the

mucous membrane of the digestive tract, and also by the skin, and that by the latter a considerable amount of carbonic acid is also discharged. Now if our measures are too active, we obtain the maximum discharge of water both by bowels and skin, and the minimum amount of relief to the system of the deleterious agents we seek to eliminate; whilst, on the other hand, if the action is more gradual, we effect our object without the withdrawal of too much water. For purgation in these cases, I advise the administration of from one to two grains of calomel, followed in about three hours by a draught of senna and sulphate of magnesia, this generally induces bilious but not very watery motions. To promote the action of the skin, the vapour bath should not be employed at once, but the patient wrapped in blankets, and a few hot water-bottles placed round him, as soon as he begins to feel the effect of the warmth, the blankets should be supported by a cradle, and the vapour introduced from a steam kettle, the amount of sweating should be carefully regulated, and never be allowed to become profuse. The patient should be encouraged to drink from time to time some simple diluent, in order to restore the amount of water withdrawn. If, however, the uræmic symptoms have come on suddenly without warning, and the patient after a severe convulsion, passes into a state of profound coma, we must employ other measures. If the patient is strong and vigorous, and the nephritis is due to exposure to cold, or is attendant on pregnancy, then venesection affords the speediest and most sure measure of relief. If, however, the uræmic symptoms occur in patients weakened by previous disease, as often happens after scarlet fever, then the injection of pilocarpine, $\frac{1}{10}$ to $\frac{1}{5}$ grain, repeated if necessary at intervals of six hours, under the skin, must be chiefly relied on, though in these

cases, the moderate withdrawal of blood by means of leeches is also advantageous.

It is astonishing what relief is obtained by venesection in puerperal eclampsia. In a case, whose urine I examined for Dr. John Williams last year, venesection was always followed by cessation of the convulsive seizures, whilst the change in the character of the urine was most marked, the urine of the twelve hours following venesection containing only one half the quantity of albumin of the preceding twelve hours, whilst the amount of urine and urea excreted, was increased.

For the immediate relief of the epileptiform attacks, inhalation of chloroform must be employed.

Dropsy, when excessive, should be relieved by means of gentle purgatives and the vapour bath, in the manner already described. For the small dose of calomel, however, a pill which contains one grain of blue pill, and half a grain each of powdered digitalis leaves and extract of squill, should be substituted, and a mixture containing twenty grains each of sulphate of potash and acetate of potash, in ℥ iss of infusion of jaborandi, given every four hours. The sulphate keeps the bowels sufficiently loose, whilst the acetate acts as a gentle diuretic; both jaborandi and pilocarpine are useful in acute renal dropsy, though their administration in chronic renal dropsy is often followed by headache, and occasionally by more alarming head symptoms. Dropsical effusion into the serous cavities of the pleuræ and peritoneum is not of such frequent occurrence as in chronic nephritis, but when it occurs it is usually urgent; the general treatment of such an event must be on the same lines as that directed for the relief of the subcutaneous œdema. Unlike what occurs in chronic nephritis, it is rare for puncture to be required for the removal of either subcutaneous or serous effusions in

acute renal dropsy; if, however, the swelling comes on very rapidly, and the distension is very great, it should be resorted to without delay.

The gastric disturbance at the onset is often so severe as to require attention, and means have to be adopted to check the excessive vomiting. This in acute nephritis, as already stated, is generally reflex and not uræmic. Reflex vomiting, as a rule, is best treated by the administration of small quantities of morphia and opium; in this case, however, opiates cannot be administered with safety, and we have to fall back on less reliable remedies. Drop doses of hydrocyanic acid in a tea-spoonful of water every two hours, linseed and mustard poultices to the epigastrium, and iced Apollinaris water, will be found perhaps to give most relief. In acute nephritis, following exposure to cold, which is attended with considerable swelling of the kidney, and distension of the capsule, the pain is often very severe; when this is the case, relief is best obtained by enveloping the loins in a linseed poultice, and covering the abdomen with flannels wrung out in hot water, and sprinkled with tincture or liniment of belladonna. If the pain is very severe, leeches must be applied to the flank.

So long as the urine remains scanty and dark coloured, the disease must be considered acute; when, however, the urine becomes daily more abundant, of lighter colour, and lower specific gravity, even though it still contain a considerable amount of albumin, then the period of decline is reached, and our treatment must be modified accordingly. It is at this stage that iron is of the greatest benefit in preventing any further progress of the anæmia that has already occurred The choice of the ferruginous preparation must depend on the state of the digestive organs, and at first only the mildest can be borne. Griffith's mixture, the Mist. Ferri Co. of the Pharmacopœia, or the Mist.

Ferri c. Salinâ of the London Hospital, which latter contains 10 grains of ammonio-citrate of iron, and 15 grains of citrate of potash, usually agree best at first. As soon however, as the patient can take the stronger preparations, such as the perchloride, the better.

It will be observed, that I have as yet said nothing with regard to special remedies advised in acute nephritis, such as fuschine, tannin, tannate of soda, etc.; these drugs, which are much employed in Germany, are however little resorted to in this country. They no doubt, when administered in sufficient doses, diminish the amount of albumin in the urine, but that is not a matter of immediate importance in acute nephritis, our great object being to subdue the inflammation, and provide for the elimination of the urinary constituents. If employed at all, they may be of service in sub-acute nephritis, or when the acute inflammation passes into the chronic stage, and when it may be necessary to check the drain on the system, caused by the long-continued withdrawal of albumin, but even then I think perchloride of iron answers the purpose better. The only special remedy it will be found necessary to employ, is in the case of acute malarial nephritis: "Nothing," says Professor Atkinson (*op. cit.*), "can be expected to control the hyperæmia that does not bring the impaludism under subjection," for this purpose, quinine in large doses must be given, till all symptoms of malarial cachexia have disappeared.

As already stated, the employment of powerful hydragogue purgatives or active diaphoresis, should be avoided during the progress of acute nephritis, a similar caution must also be directed against the use of stimulating or irritating diuretics; nor should iron in any form be given till the acute stage subsides, whilst no practitioner would think of administering opium at any stage of nephritis.

Should it be necessary to relieve pain, chloral hydrate can be safely administered, indeed, some prefer it to chloroform for the control of uræmic convulsions.

When the stage of convalescence is reached, the patient must not be lost sight of too soon, for long after he appears to have regained his usual health, traces of albumin will be found in the urine, especially after exercise, food, or exposure to cold. Besides a relapse has to be guarded against, and as this takes generally the insidious form of sub-acute nephritis, considerable mischief may occur before it is detected. The urine, therefore, should be frequently examined, and if the albumin, however small a trace, is persistent, the patient must be kept under close medical supervision. It is at this stage that the adoption of an absolute milk diet for some weeks, or even months, may be employed with the greatest success, many patients losing their albuminuria almost as soon as placed upon it. The directions for carrying out the milk diet, will be entered upon more fully when we speak of it in reference to the treatment of chronic tubal nephritis. The patient should persist in the use of iron tonics, till the anæmia has quite disappeared. Cold should be guarded against by wearing flannel, and by avoiding exposure. Convalescence is greatly aided by a temporary residence in a warm but bracing atmosphere, with dry sub-soil. In England the best places are Folkestone, originally recommended by Dr. Bright for this purpose, Clevedon, Clifton, and Weston-super-Mare. The latter places enjoy an equable bracing air, well sheltered, and a dry sub-soil of limestone rock.

Chronic tubal nephritis, which may be a continuation of an acute nephritis, or may arise insidiously in a sub-acute form, requires but little modification from the above described method of treatment. During the development

of the disease, or in its exacerbations, when the urine is scanty and highly albuminous, the patient must be kept in bed. As, however, uræmic symptoms are not developed in this disease, till it has progressed and entered upon the stage of contraction, there is not the same necessity for an absolute non-nitrogenous diet, as in the preceding instance, and though large quantities of milk are not advisable, so long as the urine is highly albuminous, it need not be entirely cut off, but may be used in moderation. For a similar reason in the treatment of the dropsy, we need not fear the effects of withdrawing water from the blood to too great an extent, by means of purgatives and sweating, as in acute nephritis. And this is fortunate, since the dropsy of chronic tubal nephritis is generally more difficult to get rid of, than in the acute form. Ordinarily, however, it is sufficient to give nightly, till the œdema subsides, the pill already mentioned (p. 255), and during the day a mixture containing a saline aperient, such as sulphate of potash. Digitalis, too, is most efficacious in this form of dropsy, since by increasing the pressure in the renal vessels, it acts as a direct diuretic. Broom-tops, too, have long had a reputation as a diuretic, and should form an ingredient of our prescription, of which the following is a convenient form. Potassæ acetatis, gr. xv.; potassæ sulphatis, gr. xxx.; tinct. digitalis, ♏ viii.; spiriti juniperi, ♏ xv.; decocti scoparii, ad ℥ iss. Three or four times daily. The action of purgatives and diuretics should be seconded by promoting the action of the skin. Most authorities are agreed, contrary to what occurs in health, that sweating is followed by an increased flow of urine, the hyperæmia of the skin relieving that of the kidneys. For this purpose the vapour bath administered as directed for the treatment of acute renal dropsy, is the most convenient. After

sweating has been established, the action may be gently maintained by placing hot water bottles in the bed, or warm bran bags next to the patient. Pilocarpine and jaborandi, which prove so serviceable in acute nephritis, are not equally useful in chronic renal dropsy, since owing to the difficulty with which the skin can be got to act, their administration is often followed by headache, and even by alarming cerebral symptoms, and pulmonary complications have been known to follow their use. They may be employed, however, after the skin has been got to act by means of the vapour bath, when a few doses of infusion of jaborandi may be given to continue the diaphoresis. If, however, in spite of this treatment the dropsy continues to increase, or does not yield, we may try stronger cathartics, such as compound jalap powder or elaterium, but we must always remember the risk we run in exciting dangerous diarrhœa, which is especially likely to occur in patients who have already suffered from repeated attacks of dropsy. Indeed, purgatives in any form must be carefully administered if there is a tendency to spontaneous diarrhœa. Stimulating diuretics, such as turpentine, copaiba, or the like, are useful, especially when the dropsy is recurrent. Copaiba may be given, as Dr. Wilks recommends, in the form of a bolus, or enclosed in capsules, by this means its nauseous taste is disguised.

Chronic renal dropsy requires to be relieved by puncture, more frequently than that resulting from acute nephritis. As it is advisable to make as few wounds as possible, Southey's fine canula especially made for this purpose should be employed, by which means one puncture, or at the most one for each leg, is required. The canula should be allowed to remain in for about five or six hours, during which time a considerable amount of fluid will be withdrawn. Not only does this drainage relieve the distended

tissues, but promotes the diuresis, so that although only a portion of the fluid is withdrawn from the tissues by the puncture, the remainder usually disappears in the course of a day or so.

Owing to the readiness with which inflammation occurs in the cellular tissue, in these cases, it is not advisable to leave the drainage tubes longer than the time mentioned, even then it will sometimes unfortunately occur. The risk, however, may be diminished by swabbing the skin, surrounding the puncture, previously with some stimulating application, such as tincture of benzoin, and when the canula is withdrawn, the wound should be lightly covered with carbolized tow or cotton wool. The profound anæmia which occurs in chronic tubal nephritis, calls for the early administration of iron. At first whilst the urine is scanty, the citrates and tartrates are the best preparations, which can be administered with the saline salts of the same acids. Later, with a freer flow of urine, the perchloride may be more advantageously employed, this may be given in a mixture containing liquor ammoniæ acetatis, which though not a chemical, is an elegant and useful combination. Should the amount of albumin passed daily, continue excessive, so as to constitute a severe drain on the system, we may try the effect of doses of fuschine or tannate of soda. Fuschine in one to three grain doses daily, has been favourably reported on by Bergeron, Dochman and Bamberger for this purpose, and tannate of soda, originally suggested by Lewin, has also been found serviceable. However that may be, the steady administration of iron must not be superseded by these drugs.

With the disappearance of the dropsy, and with a more abundant discharge of urine, we may hope that the renal hyperæmia is subsiding, and that complete recovery is possible. Even after the process has continued a con-

siderable time, and although relapses have been frequent, we need not despair, if the patient will aid us by strictly obeying our hygienic and dietetic instructions. He must be warmly clad, flannel next the skin, and carefully shelter himself against all exposure to cold and damp, that is remain in-doors in wet weather, or during the prevalence of cold, especially Easterly, winds. He should not be permitted to fatigue himself, but should avoid long walks, long railway journeys, fatiguing business, or anything likely to depress his bodily or mental powers. If possible, he should fix his residence for some time in a warm climate with a dry sub-soil. Voyages to the Tropics have been recommended for such cases, but as it is difficult to regulate the diet on board ship satisfactorily, I think he is likely to find there is more comfort and safety in a well regulated, furnished residence at a health resort, of which in England, Folkestone, Bournemouth, Clevedon, Clifton, Weston-super-Mare, Tenby, stand in the first rank for this purpose. The diet must be light, at first chiefly farinaceous, but if the albuminuria remains persistent, even though the general health has improved, an absolute milk diet should be gradually enforced. This diet though of little use, indeed I have in one case found it positively do harm during the early period of the disease, is most advantageously employed during the subsidence of the disease. Dr. George Johnson (*Brit. Med. Journal*, Aug. 16, 1884) relates the case of a gentleman, who after having suffered from the disease a considerable number of years, adopted a milk diet for a considerable period, taking half a pint every two hours, and ultimately recovered. Dr. Embleton of Bournemouth has sent me the notes of a case we saw together last year, in which after a continuance of a milk diet for nine months, after the disease had existed for two years, the albumin almost entirely dis-

appeared. Both Dr. Johnson and Dr. Embleton have noted the remarkable fact, that if any ingredient, however innocent, such as arrowroot, or sugar, was added to the milk, there was an increase of the albuminuria. Dr. Embleton, however, found that some of the milk may be taken as curds and whey. It is usual to begin with skim milk, not that there is any special virtue in it, but that unskimmed milk taken in large quantities, is apt to make the patients bilious, till they get accustomed to the diet. After a time they may gradually replace the skimmed with unskimmed milk. Dr. Embleton has noticed that palpitation of the heart sometimes occurs during the continuance of this diet, which he thinks may be caused by the action of the potassium salts, which are particularly abundant in milk, and he advises the administration of some mineral water, rich in other bases, to correct this excess. The milk diet has no injurious effect on the general health, and can be continued for months, and even years if necessary, the patient gaining in flesh the while. Although the absolute milk treatment should never be omitted when the albuminuria is persistent, still there are many cases which get well without the necessity for employing such a rigorous measure, whilst again there are other patients who have not the fortitude to persevere with it. In these cases, good results may be obtained by keeping the patient on a light and simple dietary, which should be almost "vegetarian." The following table will indicate the kind of dishes the invalid may order.

Breakfast.—Cocoa and milk, or bread and milk; toast; rashers of bacon toasted (fat only); boiled fish with rice; sardines; boiled rice with a little sugar, jam, or stewed fruit; boiled tomatoes; fresh fruit such as grapes, strawberries, cherries, and oranges, or a soft ripe pear. Lunch or Supper.—A basin of arrowroot, flavoured with

a table-spoonful of Marsala or sweet sherry; bread and butter pudding; also varieties of tapioca, sago, rice, and custard puddings. Dinner.—Vegetable soups, like croute au pôt; or milk soups, like St. Germaine; all kinds of boiled fish, with good melted butter, but no added sauce; boiled calf's head, or knuckle of veal with bacon; boiled neck of mutton; sweetbreads; stewed calf's or pig's feet; well kept and tender game, such as grouse, pheasant, partridge, snipe, plover, or woodcock, may be permitted occasionally as a change. Vegetables of all kinds may be used except those of the leguminous order. It makes a pleasant variety in a limited dietary to have one good vegetable served by itself, French fashion, at dinner. No cheese in any form is to be permitted, instead water-cress with slice of bread and butter, or a little plain dressed salad, or laver. For the sweets, any simple kind of boiled or baked farinaceous pudding with stewed fruits, care being taken that the eggs used in their preparation should be limited, and only the yolks employed. Dessert.—Grapes, oranges, strawberries, cherries, pears if tender and of good quality. Apples, nuts, pineapples, etc., not advisable.

The patient should abstain completely from alcohol, tea and coffee. Should, however, the digestion be very feeble, a table-spoonful of Marsala in a wine-glass of water may be taken at dinner to stimulate the secretion of the gastric juice, or in a basin of arrowroot before going to bed. Eggs and cheese should be avoided, since it has been shown that egg albumin and casein, even in some healthy persons, pass more readily through the renal vessels, than does serum albumin. The meal hours should be regular, and the patient should be encouraged to rest for an hour or so after taking food. The amount of food taken should be limited to the actual requirements of the body, and the

patient should always stop far short of repletion, indeed he should leave the table with his appetite appeased, but not satisfied. The importance of regulating the quantity of the food, and not over-loading the digestive organs, is in my estimation, greater even than rigidly supervising the quality.

If the patient remains free from relapses, and will consent to follow the plan above indicated, adopting an absolute milk diet, if the modified prove insufficient, we may have good hopes for his recovery, even if the albuminuria has lasted some years. Dr. Johnson's patient recovered under the absolute milk treatment, after the disease had, I believe, existed for more than seven years. In a case which came recently under my care after the disease had existed for two years before my seeing him, five months adherence to the modified system of diet, as sketched above, cured him. If, however, relapses are frequent, and the patient will not, or cannot, take sufficient care of himself, the disease, unless cut short by some intercurrent affection, will progress to the next stage that of atrophy and contraction. The treatment of which being practically the same as for the granular condition of the kidney, arising from chronic interstitial nephritis, will be most conveniently considered together in the next paragraph.

Chronic interstitial nephritis.—In granular kidney resulting from chronic interstitial nephritis, we meet with two well marked clinical conditions. In the first, cardio-vascular changes, pulse of high tension, and hypertrophy of the left ventricle, precede, or simultaneously accompany the renal affection. In the other condition, the renal disorder is observed some time before the cardio-vascular changes are noticed. Of the two conditions the first is markedly characteristic of the small red granular kidney, and confirms the view expressed by Sir W. Gull and

Dr. Sutton, that this form of renal disorder is the outcome of a general primary constitutional condition; the second always indicates some preceding disorder of the urinary passages, such as long-continued pyelitis, cystitis, or chronic tubal nephritis. The chief therapeutic indications in both conditions are, however, the same, viz., to diminish as much as possible the vascular tension, and to restrain the hyperplasia of the renal connective tissue. The first indication is best fulfilled by insistance on an abstemious diet and rest. The ordinary diet should be the same as that recommended for chronic tubal nephritis, but should there be symptoms of extreme elevation of the blood pressure in the aortic system, the patient ought to be kept for a time on an absolute milk diet. Rest must be resolutely insisted on. Nothing aggravates the condition so much as undue exertion. This is one reason, why this class of patient generally improves so greatly when they come under the care of the physician, because then for a time they may be persuaded to give up their usual avocations. In a chronic disease like this, it is impossible to enforce absolute continuous rest, life would not be worth having on such terms, but life may not only be prolonged, but indeed fairly enjoyable if certain conditions are complied with. For instance, when the patient first comes under observation, or during an exacerbation of the disease, if he will consent to remain in bed, and keep on low diet for a few days, he may be permitted, if free from palpitation, giddiness, or oppression of breathing, at the end of that time to move about his room a little, and afterwards if there be no recurrence of the urgent symptoms to go out, and by degrees resume his general avocations, though he will do wisely to limit these as much as possible. If wealthy he should retire from business, and all exciting pursuits, if poor he should be content to earn less wages, by undertaking

lighter engagements, or doing less work. He should reside near his place of business to avoid the fatigue of the morning and evening journey, by omnibus, cab or rail, to and from the city. If possible the bedroom should be on the ground floor, at all events the necessity for mounting flights of steps, or ascending even moderate heights is to be avoided, and above all things the patient should be warned against hurry of any kind. By enforcing such regulations we shield the patient from sudden and extreme elevations of the aortic blood pressure, which not only tend to aggravate the renal disorder, but are also highly dangerous owing to the degenerated condition of the arteries that generally exists. A little gentle exercise at a slow pace on the level should not be forbidden, if the patient has no business engagements to fatigue him, otherwise those will be sufficient.

With regard to therapeutic treatment, nitro-glycerine has been recommended for the relief of the arterial tension. It is undoubtedly serviceable in cases where there is an exacerbation of the disease, especially when attended with dyspnœa (renal asthma). Iodide of potassium also has a powerful influence in diminishing cardiac action, and as it also tends to restrain the hyperplasia of the renal organs, it should form the basis of our treatment. I agree with Bartels, that in moderate doses (5-10 grains) thrice daily, it can be administered for months without any prejudicial effect. In order to act on the connective tissue, minute doses of bichloride of mercury ($\frac{1}{32}$ grain) may be given with the iodide. As however, patients with granular kidneys are extremely susceptible to the action of mercury, it must be carefully watched, and its administration systematically interrupted. Bartholow (*New York Medical Record*, June 28th, 1884,) has recently recommended in place of mercury, the double chloride of gold and sodium

($\frac{1}{20}$ grain) as having the same effect. I have had no experience of the drug as yet, but should it possess the advantage of the bichloride without its drawback, we ought to be deeply indebted for the suggestion. Great attention should be paid to the action of the bowels, since arterial tension always rises when they are constipated; whilst owing to the degenerated condition of arteries, cerebral hæmorrhage may be induced by the straining caused by a hard motion. For this purpose a dose of some aperient mineral water, Pullna, Hunyadi Janos, etc., taken before breakfast is the best. For the relief of complications special treatment is required. Of these, the chronic uræmic symptoms are the most troublesome. The muscular twitchings and troublesome itching of the skin may be controlled by chloral, and by paying particular attention to the state of the skin and bowels. As neither hot vapour or air baths are advisable in this form of renal disease, owing to the preliminary state of arterial tension they induce, prior to sweating, some other means of acting on the skin must be devised, and the best are either tepid douches of sea-water (sea-salt) or the cold pack. I prefer the former, and patients have expressed themselves most grateful for the relief afforded by it. If possible the temperature should be regulated, beginning at about 90° F., and falling to about 75° F. The saline solution powerfully stimulates the skin, whilst the douche acts, I fancy, as a kind of gentle massage. Uræmic vomiting may be often checked by the application of a cold compress across the abdomen, or a small mustard plaster to the pit of the stomach over-night. If urgent an effervescing draught containing two minims of hydrocyanic acid will often give relief. Uræmic headache is often stopped by the administration of twenty drops of dilute nitric acid in water. Uræmic asthma is best treated with nitro-glycerine, at the

onset of the paroxysms. The onset of these, as of all uræmic symptoms, points to the necessity of free action of the bowels, and if not contra-indicated, a grain of calomel followed by a saline aperient is the best agent, since it produces copious bilious stools, and thus affords considerable relief to the system. If calomel cannot be borne, then a sufficient dose of sulphate of magnesia must be given. Albuminuric retinitis must be treated on general principles. I have found that the administration of small quantities of mercury are most useful in restraining its course, and even of repairing the damage already done. An out-patient at the London Hospital, who had previously been under treatment at Moorfields for six months, taking during that time large doses of iodide of potassium, recovered, in three weeks, under the administration of one grain of grey powder twice a day, so far as to be able to walk to the hospital unaided, whereas when he first came he had to be led by an attendant.

With regard to the formidable hæmorrhages that occur in the course of this disease, our treatment must be regulated by the imminent danger they present. If the hæmorrhage occur from a cerebral vessel, and the pulse is tense, and the heart's action energetic, we ought not to hesitate, but bleed promptly. If on the other hand, the rupture occurs in a later stage of the disease, when the heart's action has become feeble, and the tension in the aortic system has fallen, and the lesion is caused not by the distension of the vessel, but by its degenerated condition, then no good will be obtained by venesection. In this case the head should be kept well raised, ice bladders applied, and a sharply acting aperient given by the mouth. In "pulmonary apoplexy" the rule should be to bleed on the first onset of the symptoms if the pulse is incompressible. In epistaxis the danger is not so immin-

ent. We may begin with milder measures, such as keeping the patient in an horizontal position, plugging the nostrils, application of ice bags over the region of the heart, the administration of gallic acid, and if these means are not sufficient, then the application of a few leeches; these latter are most advantageously applied round the anus. In cases of severe epistaxis which resist every measure, Dr. Dieulafoy (*Gaz. Hebdom.*, Jan. 18th, 1884) recommends transfusion of blood, believing that the injection of normal blood acts as an hæmastatic by restoring the composition of the impaired blood, and he relates a case in which repeated attacks of hæmorrhage were alone arrested by the injection of 120 grms. of healthy blood. Hæmorrhages from other mucous surfaces are to be treated in the same manner as epistaxis. When hæmorrhage has once occurred, it is an additional reason for enforcing rest and a spare dietary. In the early stage and during the progress of the disease, both digitalis and iron are contra-indicated, owing to their increasing the tension in the aortic system. In the later stage, however, when the heart begins to flag, and there is a tendency towards dropsy, and there is much debility and anæmia, both may be required. Opium should never be administered, since even extremely minute doses have been known to induce fatal coma. The only exception to this rigid exclusion, seems to be the simple atrophic kidney of old age, in which opium seems to be better borne than when the kidney is contracted by preceding inflammatory changes. And even here the administration of such preparations as bimeconate of morphia or nepenthe is preferable to opium or morphia. A few drops at bed-time of these preparations, will often be found advantageous to allay the annoyance caused by the frequent nocturnal micturition old people suffer so much from.

Patients with granular kidneys must be carefully sheltered from all atmospheric vicissitudes. They should be clothed with flannel, their residence should be as sheltered as possible, and all damp removed by careful attention to the sub-soil drainage. Those who can afford it should live always in a warm genial climate, with plenty of sunlight.

CHAPTER IV.

Suppurative Inflammations of the Kidney, Pelvis, Ureters, and Surrounding Tissues.

72. **Classification.**—Suppurative inflammations of the kidney differ from the diffuse form, we have considered in the preceding chapter, by the development of pus, and by their being always secondary to some exciting cause, such as impacted calculi, suppurative disease of the lower urinary passages, micro-organisms, etc., whilst both kidneys are not always affected. They have been aptly grouped by Dr. Lindsay Steven, into four classes, whose classification, with some slight verbal modification, is here adopted, viz :—

Class I. In which the septic material is carried to the kidney by means of the blood. *Metastatic abscess.*

a. The abscesses are small, multiple and symmetrical, as in *pyæmia.*

b. The abscess is large, may be confined to one side, as sometimes occurs in *ulcerative endocarditis.*

Class II. In which the suppuration originates in disease or injury of the lower urinary passages as from *pyelitis, cystitis,* etc.

a. The abscess is large, *pyo-nephrosis,* may result from impaction of calculi or foreign bodies in the pelvis of the kidney, or from injury, or suppurative disease of the lower urinary tract, with obstruction.

b. The abscesses are miliary and multiple, *pyelo-nephrosis,* so called "surgical kidney," in which the infective virus has gained access to the organ, either by the urinary tubules, or the lymphatics.

Class III. In which the infective material is brought either by the blood, or by the lymphatics, or by contiguity, but is confined to parts immediately surrounding the kidney, *peri-nephritis.*

Class IV. In which the inflammation is set up by some specific condition, as in *tubercular disease,* etc.

Class I. Metastatic Abscesses of the Kidney.

73. **Pyæmic abscesses** of the kidney are usually extremely numerous, and are more abundant in the cortex than in any other portion of the organ; they nearly always affect both kidneys. They present to the naked eye the appearance of small yellowish-white patches, often somewhat pyramidal in form; and surrounded by a zone of intense hyperæmia. This serves to distinguish them from the multiple miliary abscesses of pyelo-nephrosis, in which the zone is not present in the same degree of intensity. According to Dr. Steven, if a section of the tissue containing the abscess be examined, the walls of the abscess will be found ragged, and composed of round cells mingled with red corpuscles, whilst the tubular structure is infiltrated with inflammatory cells. Occasionally the tubules have a glassy homogeneous appearance, suggesting the "coagulation necrosis" of Weigert; whilst in the walls of the abscess, and between the tubules, the capillaries are often seen engorged. Micro-organisms are invariably found in these abscesses, and it is to them that the infective properties of the embolus are due; a point which distinguishes them from non-infective infarcts, derived from aneurisms, etc. Pyæmic abscesses of the kidney may occur during the progress of any infective disease, though as it was shown by the Committee reporting to the Pathological Society on the nature and causes of pyæmia, septicæmia, etc., they are less frequent than in the lungs or liver; they are especially observed, however, in connection with ulcerative endocarditis. The symptoms they give rise to are those general to pyæmia, viz., rigors, icteric tint of skin, and prostration, whilst the fact of the kidneys

being implicated may escape observation. In some cases, however, there may be pain in the renal region aggravated by pressure, and the urine may become scanty, dark coloured, and albuminous, whilst epithelial and granular casts make their appearance, occasionally the cast is studded with pus cells, which display the characteristic reaction with acetic acid. The urine is generally acid, a condition which serves to distinguish pyæmic abscess from pyelonephritis, which is alkaline.

74. **Large Pyæmic Abscess** of the kidney is of rare occurrence, it occasionally happens, however, that a larger embolus than usual is detached, of sufficient size to block one of the larger renal arteries. In these cases, however, necrosis rather than purulent destruction is generally the result. Thus in a case, recorded by Bartels, of a boy eight years old, the left kidney was completely necrosed from an extensive embolism caused by large thrombus masses existing in the left ventricle of the heart. If, however, the embolism is infective, as in ulcerative endocarditis, it will give rise to abscess instead of necrosis. Thus in a case related by Vogel, the whole of one kidney was destroyed by suppuration, without any other anomaly being found in the uropoëtic system. Maier also records a case in which it was noted that a large embolus had plugged the right renal artery, leading to the formation of a large renal abscess, in which numerous bacteria were discovered. No special treatment is called for when pyæmic abscesses, either large or small, form in the kidneys, it is the general septic condition that must be combatted. The strength must be supported by beef tea and stimulants, whilst antiseptic medicines, such as quinine, boracic acid, sulpho-carbolates, etc., should be administered.

Class II. Pyelitis and Pyo-nephrosis.

75. **Symptoms.**—Inflammation of the mucous membrane of the pelvis of the kidney is termed *pyelitis*. Should, however, the ureter of the affected kidney become blocked so that the discharge of urine is prevented, a collection of purulent fluid mixed with secreted urine, takes place above the obstruction, greatly distending the pelvis of the affected kidney, and forming, more or less, a palpable tumour, this condition is spoken of as *pyo-nephrosis*. The change in the character of the urine is the leading symptom. In an early stage, the urine is generally acid, and varies but little in quantity and specific gravity, it is, however, turbid, and on standing, yields an abundant sediment, consisting of epithelial cells, pus globules, and in acute cases, or those associated with renal calculus, blood corpuscles. At this stage it is possible to make out by microscopic examination, the characteristic epithelium cells of the renal pelvis. These are (fig. 15, p. 136) spindle-shaped, caudate, and laminated, and are usually more swollen than normal, a condition which distinguishes them from somewhat similar cells from other portions of the genito-urinary tract. As the quantity of pus increases with the progress of the disease, this characteristic epithelium is lost sight of. The urine contains albumin, which however, unless there is co-existent kidney disease, is derived from the pus and the blood, when that element is present. In old standing cases, especially in those in which the disease originated in the mucous membrane of the lower urinary organs, and has crept upwards, the urine may become ammoniacal. This alkaline condition of the urine dissolves the pus corpuscles, and they are no longer deposited in a creamy layer, but the whole urine becomes opaque and

viscous, whilst abundant crystals of ammonium-magnesium phosphate (fig. 10, p. 96), together with numerous bacteria, form in it. If no obstruction exists at the orifice of the ureter, the purulent urine is passed continuously, the desire to micturate being frequent. But when any obstruction occurs in the urinary passages, the discharge is either entirely suppressed, or it comes intermittently, as the obstruction from time to time is overcome. The accumulation of pus in the pelvis of the kidney, leads to the formation of a renal tumour, which generally is most prominent in the flank, extending downwards and forwards. When with this tumour we have an intermittent discharge of muco-purulent urine, or there has been such a discharge, the diagnosis of pyo-nephrosis is not difficult, and it only becomes so, when we have no evidence of a previously existing purulent state of the urine.

The pain in pyelitis is not generally severe, and is usually limited to an aching feeling across the loins. It is, however, often reflected, and irritability, which in some cases may amount to strangury, may be felt in the bladder, and along the urethra. The pyrexia in simple pyelitis is rarely high, but when pus accumulates in the pelvis as in pyo-nephrosis, the rigors become more marked, and recur more frequently.

76. **Etiology.**—Exposure to cold and wet, especially if there be any existing disease of the lower urinary organs, as gonorrhœa, or chronic vesical catarrh. The administration of irritating medicines in large doses, as turpentine, cantharides, copaiba, etc., though these in moderate quantities are often given as remedies in the complaint, may induce pyelitis. But the two most fertile causes of the disease, are to be found in the irritation of foreign bodies or growths in the pelvis of the kidney, and obstruction to the regular flow of urine. In the first category,

renal calculus is the most frequently observed, whilst less rarely the irritation is caused by malignant growths, tubercular deposits, hydatids, or blood clots, the result of hæmorrhages. In the second list, any obstructive disease of the lower urinary passages, such as stricture of the urethra, enlarged prostate, chronic vesical catarrh, phimosis, sooner or later induces inflammation of the mucous surface of the renal pelvis. In spinal disease attended with paraplegia, the mucous surface of the pelvis of the kidney participates in the change, common to the whole of the mucous membrane of the genito-urinary tract, and which is attended with ammoniacal decomposition of the urine (p. 65). Pyelitis occurs in many constitutional affections. Thus it is often noticed in gouty individuals, caused no doubt by the lithatic condition of their urine. Scrofulous deposit in the mucous tract gives rise to the most intractable form of pyelitis. In Bright's disease, and in diabetes, slight inflammation of both renal pelves is generally present. It may also develop during the progress of enteric, scarlet, and typhus fevers, small-pox, measles, cholera, scurvy, and pregnancy.

77. **Diagnosis.**—We have to distinguish first between pyelitis and vesical catarrh ; secondly, when the latter is present, to ascertain whether the renal pelves are affected as well. The discovery in abundance of the swollen epithelial cells, peculiar to the renal pelvis, in the urine, affords a tolerably certain indication of the existence of pyelitis, but when they are no longer to be found, we must rely on general symptoms to distinguish between inflammation of the upper and lower urinary tract. In pyelitis the urine is decidedly more purulent and acid than in vesical catarrh, which is usually muco-purulent and frequently alkaline, from ammoniacal decomposition of the urine. When both pyelitis and vesical catarrh co-exist,

the amount of pus passed with the urine is more considerable, and in addition to lumbar pain symptoms of vesical irritation are present. In pyo-nephrosis, when a tumour is formed, we have to distinguish it from malignant growths, hydatids, and hydro-nephrosis. In these there is an absence of pyrexia; whilst the cessation, or intermittent discharge, of previously existing purulent urine, also serves to distinguish it.

78. **Morbid Anatomy.**—In the earlier stages, the mucous membrane of the pelvis of the affected kidney is reddened and swollen, and covered with a muco-purulent discharge. In cases when the disease is secondary to some constitutional disturbance as for instance in puerperal fever, small sloughs, which appear as minute yellow spots, may form on the surface of the mucous membrane. When the disease has become chronic, the mucous membrane will be found thickened and of an ashy colour. This condition may last a considerable time without the renal structure being affected, but ultimately the effects of pressure become manifest, and the infundibula become dilated, and the papillæ flattened; whilst the process of dilatation may proceed to the complete obliteration of the cortex, and the conversion of the kidney into a mere bag of pus. The rapidity and extent of this change depend of course on the degree and amount of obstruction that exists at the outlets of the renal pelvis. When this arises only from the thickened state of the mucous membrane and is not complete, the dilatation and destruction of the kidney take place slowly, and never proceed to an extreme degree. On the other hand, when a calculus or other foreign body absolutely obstructs the flow of purulent urine down the ureter, the destruction of the kidney is generally rapid and more or less complete. The effect of pressure in the urinary tubules is first, to cause an over-

growth of the connective tissue, a conservative process which enables the kidney for a time to resist the stretching which its tubular structure undergoes; gradually, however, absorption of the pyramidal portion of the kidney proceeds, the situation of the absorbed portion being represented by the expanded calix. The cortex resists the pressure some time longer, owing probably to considerable overgrowth of interstitial connective tissue. This ultimately becomes thinned and stretched, so that the whole kidney resembles a large cyst. The tumour, thus formed, may be converted into a semi-solid mass by the drying up of the purulent fluid which mingled with the urinary salts forms a putty-like material; or the purulent fluid may be absorbed, in which case the tumour becomes reduced in size if not altogether shrivelled up; or the tumour may burst, posteriorly into the renal cellular tissue and thus set up peri-nephritis or anteriorly into the bowels, or pass downwards into the iliac fossa along the psoas muscle and form an abscess in Scarpa's triangle; or what is far less common may find its way upwards to the lungs and burst into the bronchial tubes, whilst equally rare is rupture into the peritoneum.

79. **Prognosis.**—Idiopathic pyelitis when properly treated is rarely an obstinate or prolonged affection, it is only when associated with long standing disease of the lower urinary organs, or the presence of foreign bodies in the pelvis of the kidney, that it becomes formidable. The improvements in renal surgery of late years, however, have considerably diminished the fatality of these cases, and operations for the relief of pyo-nephrosis are readily undertaken at a period when there is the best chance for the patient's recovery, and before the complete destruction of the kidney has taken place.

80. **Treatment.**—In the treatment of pyelitis its

origination must hold the foremost place of consideration. If due to simple catarrh, or to any temporary constitutional disturbance, rest in bed, diluent drinks and alkaline saline remedies are sufficient to subdue the inflammation. If after the pain and fever has subsided the urine still continues cloudy, the chronic catarrh will be best removed by the administration of benzoic acid and terebinthine remedies. I have found these more reliable and more efficacious than either tannic acid, iron, or the mineral acids which have been recommended. In calculous pyelitis our object must be to remove the foreign body as quickly as possible, this can either be done by attempting its solution by medical means or by operative interference. In pyonephrosis, if the discharge from the kidney is intermittent we may hope the obstruction will pass; for this purpose, the renal passages should be got into as healthy a state as possible, and turpentine given with biborate of soda if the urine is acid, or with boracic acid if it is alkaline, is undoubtedly the most efficacious; whilst diluents, of which distilled water is as good as any, owing to its diuretic action, should be freely given. At the same time the patient should have complete rest on a sofa or better still on a specially constructed couch. If a tumour should form, the question of operative procedure must be raised at an early period. Should it be objected to by the patient, we must hope by maintaining the general health, that the contents of the tumour may solidify or become absorbed. The chronic pyelitis of gouty individuals, or those suffering from oxaluria, and which often runs an insidious course, is greatly benefitted by direct treatment of the digestive organs, such as alkalies in the one case, and nitro-muriatic acid in the other, and by drinking the mineral waters of Vichy and Contréxeville respectively. Should an operation be decided on for the relief of unilateral pyo-

nephrosis, the question of the condition of the other kidney has to be considered.

The best means of ascertaining whether this is in a healthy condition or not, and this is required in cases in which nephrectomy or nephrotomy is called for, is I believe, by introducing Mr. Davy's rectal lever into the rectum, having previously emptied the bladder, and to compress the ureter of the diseased side, so as to prevent the passage from it of even a small quantity of purulent urine, then the urine passed during that period by the other kidney will furnish us with a very tolerable idea of the state of things there. If normal, no further enquiry need be made, but as it sometimes contains traces of pus, and albumin, derived from the bladder, a more rigid examination into its constitution may be required. Diminution in the amount of urea excreted must not be regarded in itself as sufficient to debar an operation, since in most chronic diseases the elimination of urea is diminished, but what is of serious import, is for the urea to be diminished out of proportion to the inorganic constituents. Thus, in normal urine of the twenty-four hours, the relationship of urea to the inorganic constituents may be stated as 2·3 : 1·6, but suppose we find in any given case the percentage of the urea falls considerably below this, whilst the inorganic are relatively but little affected, we may fairly assume that structural alterations in the kidneys exist, which are the cause of the deficient elimination of nitrogen, whilst the salts and water are still transmitted. Even this cannot be entirely relied on, though taken in conjunction with other evidence it often affords us assistance in arriving at a right conclusion.

Pyelo-Nephrosis (Consecutive Nephritis, Beck).

81. **Etiology.**—The morbid conditions of the kidney, the consequence of vesical or urethral disease have been classified by Beck as follows:—1. The effects of pressure caused by obstructions of the urinary passages. 2. Diffuse interstitial inflammation. 3. Interstitial inflammation with scattered points of suppuration. 4. The cicatricial kidney, noticed in cases that recover. Although these conditions are readily distinguishable from each other, still it is more common to find them existing together, and therefore they must be considered as forming one disease. These conditions, which till Beck's masterly description, were very imperfectly understood, have in consequence of their frequent association with pyelitis, been classed together under the term *pyelo-nephrosis*. This designation is retained here for convenience, though the name consecutive nephritis as proposed by Beck is undoubtedly more correct. The changes in the kidney are distinguished from those occurring in pyæmia, by their being confined to the renal structure, and by being invariably associated (with one exception), to disease of the lower urinary organs, so that they may be regarded as the result of a local infective process. They constitute the most frequent terminations of old urinary cases, and recently special attention has been drawn to them by Sir Andrew Clark in his paper read before the Medical Society, Dec. 1883.

The chief causes concerned in the production of secondary renal disease, are according to Beck:—1. *Increased urinary pressure*, causing chronic interstitial inflammation, and gradual absorption of the structure of the pyramids. This pressure rarely arises from regurgitation from the bladder,

but is invariably connected with obstruction of the ureters, the most common form being, the pressure on the ureters of the thick bundles of muscular tissue of an hypertrophied bladder, such as we find in old standing stricture of the urethra, enlarged prostate, or from vesical calculus. If in these cases the pressure came from in front, we should find the changes similar in both kidneys, but as they are frequently different, it is natural to assume that the cause of the difference lies in the unequal degree of obstruction existing at the orifices of the two ureters. 2. *Reflex irritation of the kidney.*—A close nervous relation seems to exist between the trigone of the bladder, and the prostatic and bulbous portions of the urethra. Irritation of the nerves of these parts, therefore, probably sets up a certain degree of hyperæmia. This, if the kidneys are healthy, is comparatively harmless, but if they have already become the seat of diseased action, then the irritation tends to aggravate any inflammatory changes that may have been set up. 3. *Presence of septic matters.*—In the majority of cases, the presence of decomposing urine in the pelvis of kidney is the immediate exciting cause of the acute attack, and the mode in which it acts, is as Beck suggests as follows: the pelvis of the kidney, and probably also the straight tubules for a greater or less distance are filled with putrid urine at some degree of pressure, the contact of this irritating fluid, damages the epithelium, and causes its desquamation, the septic matter then passes into the inter-tubular lymph spaces of the kidney, and excites diffuse inflammation, which spreads rapidly towards the cortex and between the tubules. But it may occur, as Klebs has pointed out, without there being any continuity of the inflammation with that in the bladder, and the question then arises how the infective matter reaches the kidney. Klebs has accounted for it by showing that

organisms might spread up into the tubules of the kidney, and so excite the suppurative action. Whilst Dr. Lindsay Steven has shown how the infective virus may gain access to the kidney from the bladder, apart from the route by the tubules, viz., by means of the lymphatic spaces through the bladder wall, the organisms gaining access to the lymphatic channels in the walls of the ureters, and thus gradually spread upwards. At length the organisms reach the pelvis of the kidneys, and then pass into the lymphatic spaces of the capsules, giving rise to small abscesses. The fact that abscesses are so frequently met with, situated between the capsule and the kidney, and the elongated and pyramidal shape assumed by the inflammatory processes when extending through the cortex are, as Dr. Steven remarks, strongly suggestive of the infective material being disseminated through the kidneys by the lymphatic vessels. It is not improbable that the frequency with which, according to Mr. Doran's recent observations, pyelo-nephrosis is found post-mortem after operations on the internal generative organs, may be due to this cause.

Catheterism is often the immediate exciting cause of pyelo-nephrosis, and the danger resulting from its employment is certainly greater when the practice is first begun, than when the patient has become habituated to its use. Pyelo-nephrosis also frequently follows on operations performed on any portion of the lower urinary tract. Mr. Alban Doran (*op. cit.*) has also shown that it not infrequently follows on operations on the internal genital organs, in these cases the renal mischief may be excited by reflex irritation, since a close connection seems to subsist between the kidneys and internal organs of generation and their appendages, as shown by Dr. Matthews Duncan (*Med. Chir. Trans.*, 1884) in the frequent associa-

tion of albuminuria with parametritis. But as in most of Mr. Doran's cases, chronic interstitial changes were noticed, it is not improbable that some degree of obstruction to the flow of urine had previously existed, due to pressure of the tumour on the ureters, which may have predisposed to the intense renal hyperæmia which ensued when operative procedures were undertaken. In some cases, however, though this has not been actually observed, septic virus may have been conveyed by the lymphatics of the ovaries, etc., to the kidneys.

But it is not always necessary for operative procedures to excite the secondary renal mischief, given obstructive inflammatory disease of the lower urinary passages, any slight disturbing influence may start the process. Thus I have seen it follow upon a chill, caught by sitting in wet clothes, in a patient suffering from gleet, and who also had a stricture of the urethra. And in another instance, which I saw last summer with Mr. Elliot of Belvedere, the immediate cause appeared to be enforced retention during a long railway journey.

82. **Morbid Anatomy.**—The chronic interstitial nephritis, which results as we have seen (p. 279) from the effect of pressure, is intermixed in different degrees, in the kidney, which has become the seat of suppurative nephritis, with diffuse interstitial inflammation, more or less acute, and scattered points of suppuration. The kidney is enlarged, often only slightly, and its substance softened. The capsule strips off easily, but tearing the surface in places, especially over the seat of small collections of pus. Scattered over the surface of the organ are yellow spots, surrounded by a red zone, either containing pus or excessively soft; between these yellow spots the kidney substance is of a palish-yellow colour, mottled with red. On section, purulent soften-

ing will be observed, giving the cortex a mottled appearance. The small purulent collections, like yellow streaks, extend from the superficial abscesses into the cortex, whilst others are observed in the pyramids, which follow the course of the interfasicular veins, and are therefore in the line of the lymphatics. This purulent softening has a somewhat wedge-shaped appearance, and may have distinct centres of suppuration; they may also be surrounded by a slight zone of hyperæmia, but this is never so intense as with embolic abscesses. Another point that serves to distinguish them from embolic abscess, is that in the latter the width of the base is seldom less than half its length, whilst in these abscesses the base showing on the surface may be only the width of a pin's head, while the length of the wedge may be an inch or more. Yellowish lines may also be observed, extending from the papillæ to the base of the pyramids, which correspond to small foci of suppuration, extending in the direction of the uriniferous tubules. The pelvis of the kidney is often intensely inflamed.

On microscopic examination, areas of interstitial inflammation will be found both in the cortex and pyramids. In the parts most distant from the centre of suppuration, only small round cells will be observed between the tubules; the epithelium is slightly swollen and cloudy, but the nuclei of cells are readily seen without reagents. In the next stage the tubules are invaded by the round cells, the renal epithelium being still distinctly recognisable. Finally all trace of tubule and epithelium disappears, their place being occupied by small round cells, which after the breaking down of the intercellular substance, become pus (fig. 27).

A careful microscopic search according to the method described by Dr. Lindsay Steven, will generally reveal

micro-organisms, either disseminated or grouped together into colonies or zooglœa. The colonies are usually associated with one of the inflammatory foci, although sometimes there is no apparent relationship, and they are often as abundant in the pyramidal as the cortical portion, but in the former situation the zooglœa are elongated, in the



FIG. 27.—Showing, on one side, the inter-tubular infiltration, and invasion of tubules with round cells; on the other, the breaking down of the intercellular substance (Erichsen's *Surgery*).

latter, somewhat circular in shape. When the virus is situated within the uriniferous tubules, the colonies may often be seen to be directly continuous with epithelium, or, in transverse section, surrounded by it, as is shown in fig. 28. When the organisms are contained in the lymphatics no such evidence of intra-tubular situation is to be found. No micrococci have been found in the glomeruli or other vessels, a fact which Dr. Steven believes distinguishes this condition from the state of matters observed in metastatic abscess of the kidney.

Should the process subside, the kidney becomes shrunken, toughened, and irregular in form (*cicatricial*

kidney), closely resembling the granular contracted kidney. Occasionally cicatrices are to be observed on the surface, probably the scars of former abscesses. Kidneys that have undergone this change, may, however, become the seat of another acute attack, so that chronic and acute changes are found variously combined.

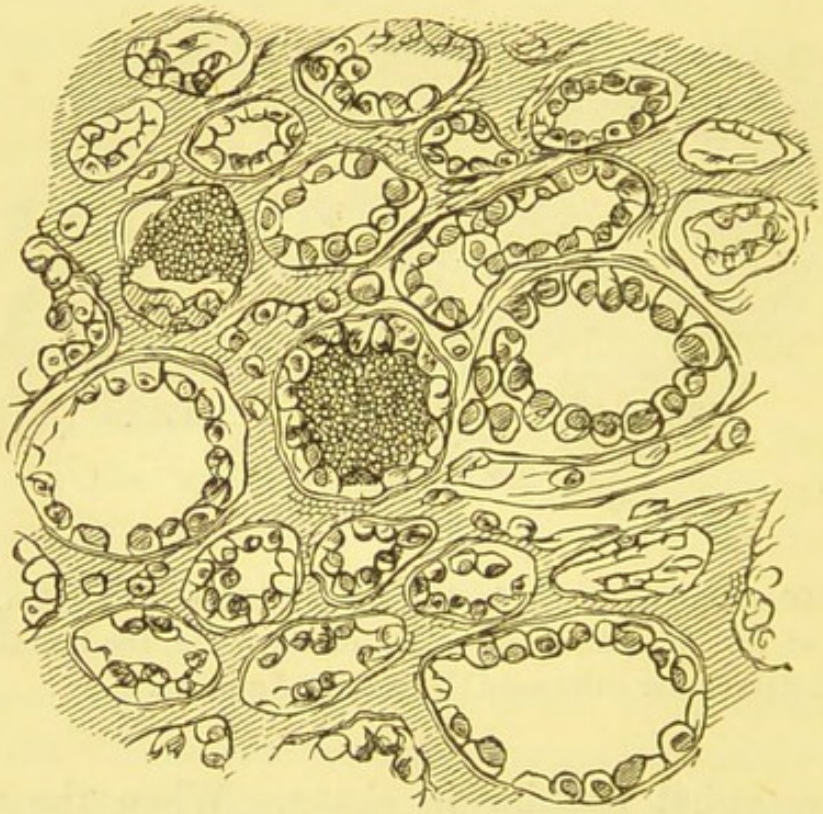


FIG. 28.—Transverse section showing colonies of micrococci in two of the tubules of the kidney (Dr. Lindsay Steven).

83. **Symptoms.**—Suppurative nephritis is ushered in with marked rigors, sometimes so severe as to simulate an attack of ague. Indeed, in a case I saw recently with Mr. Parsons of Hackney, we had some little difficulty at first in arriving at a decision. The patient had suffered much from ague, he had also an enlarged prostate. As the urine contained pus, the question arose whether the rigors were associated with renal mischief, or were purely malarial.

The latter conclusion was arrived at since the amount of urea excreted was in excess, and the reaction of the urine acid. What added to our difficulty in this case was the fact that in addition to the rigors and pyuria, the patient was decidedly heavy and drowsy, and had somewhat an icteric tint; he, however, recovered. Following the rigor, uræmic convulsions may ensue; though according to Beck uræmic convulsions or coma are usually absent in these cases. In one case, however, I was called to see, complete coma lasting several hours, followed the initial rigor; the patient survived this attack fourteen days, during the interval he lay in a dreamy state, but not quite unconscious. The urine is not usually diminished in quantity, but the amount of urea excreted if altered at all, is below, rather than above, the normal, whilst the reaction is almost invariably alkaline. Albumin, unless there is much pus or blood, is not abundant. The urine deposits much epithelium, renal and vesical, occasionally hyaline and granular casts, sometimes pus casts. Pain in the loins may be complained of, especially on pressure, but is rarely severe; when it is, it points to extension of the inflammation to the cellulo-adipose tissue—peri-nephritis. Among the general symptoms may be noted rapid emaciation, gastric disturbance, nausea, sometimes urgent vomiting, and diarrhœa, an icteric tint of the skin is developed early. As the end approaches, the tongue becomes brown and dry, the pulse remarkably rapid, feeble, and intermitting, the patient lies in a dreamy state, sometimes accompanied with a muttering delirium, and often bathed in a profuse sweat, the temperature sometimes before death becomes sub-normal. In this state he may remain many days, it is rare, however, for the patient to survive three weeks from the first rigor, more frequently death occurs within a few days. The disease when it comes on insidi-

ously may be taken for general pyæmia, typhoid fever, septic peritonitis, or ague. In all cases an examination of the urine will help to decide the question. If the urine be ammoniacal, purulent, and the urea not in excess, and there is also existing disease of the lower urinary organs, the matter ought not to be doubtful.

84. **Treatment.**—Since in the cicatricial kidney, old scars the result of past abscesses in the kidneys have been found post-mortem, we may infer that the disease is not always immediately fatal. We must not therefore abandon these cases in despair. The indications for treatment are twofold, first to support the patient's strength, and secondly to combat the local septic conditions. The first indication is best fulfilled by dietetic measures, and attention should be paid to the condition of the alimentary canal, and the bowels should be freely relieved. If diarrhœa exists, the administration of a purgative is not contra-indicated, since the diarrhœa is evidently eliminative, and not due to inflammatory conditions in the intestines, but mild purgatives must be employed, such as castor oil, to which a few drops of laudanum may be added. Should there be vomiting as well, then three or four grains of calomel dusted on the tongue is indicated. After the action of the oil or calomel, the tendency to diarrhœa will often diminish, whilst the patient will be less drowsy. With regard to antiseptic remedies, our chief reliance must be placed in quinine and boracic acid. The latter has the advantage possessed by few other antiseptic remedies of passing unchanged through the kidneys, it therefore acts upon the whole urinary tract. It can be given in large doses. As it is very insoluble, the following prescription will be found the best mode of administering it. Dissolve boracic acid ʒ ij., in glycerine ℥ j., add to this hot water ℥ viii., flavoured with syrup of orange peel. Of this mixture take one ounce

four times daily. Turpentine may also be advantageously employed with boracic acid. It certainly improves the condition of the urine, whilst its administration, for a time, seems to rouse the patient. Owing to their toxic action, iodoform and the salicylates, should not be given. The question whether the bladder, if diseased, should be washed out after consecutive nephritis has occurred, may arise. Some have thought the introduction of the catheter keeps up reflex irritation, and thus adds to the renal hyperæmia. But it seems to me that there is less risk in completely emptying the bladder, than in allowing foul urine to accumulate, and if a catheter be introduced I do not see why, when the urine is withdrawn an antiseptic should not be introduced. For this purpose, thirty grains of boracic acid in four ounces of water, or a 0·2 per cent. solution of hydrochloric acid, or quinine are the best solutions to employ. The patient's strength must be supported, but in order to diminish the excretion of nitrogen by the kidney, albuminous constituents must only be given sparingly. The yolks of eggs freed from the white, beaten up with brandy, arrowroot flavoured with Madeira, white broth, made with veal stock, and thickened with cream and arrowroot, boiled sago or tapioca, with a little milk added, furnish a diet containing a maximum of starchy with a minimum of nitrogenous elements.

With regard to prophylatic measures, patients with chronic disease of the lower urinary passages, should ascertain for themselves the character of the reaction of their urine, and should be taught to regard the persistence of an ammoniacal condition as highly dangerous. They cannot be too highly impressed with the importance of thoroughly carbolizing all instruments they may employ for the relief of retention or incontinence of urine. And never under any circumstances subject themselves to en-

forced retention, but always be provided when on long journeys, or attending public meetings, etc., with a commodious india-rubber urinal. The patient also should be careful about exposing himself to damp and cold.

Class III. Peri-Nephritis.

85. **Symptoms.**—The term peri-nephritis is applied to the inflammation of the loose connective and adipose tissue surrounding the kidney. It usually occurs on one side only, but in rare instances it may be bi-lateral. The kidneys themselves may or may not be involved in the inflammatory process, but when they are, the disease will generally be found to have originated in them. The cellulo-adipose tissue which surrounds the kidney is continuous with the layers of cellular tissue, which connect all the organs in the neighbourhood of the kidneys together, but the most intimate connection subsists between it and the upper portion of the cellular tissue of the iliac fascia, and the cellular tissue of the lumbar region beyond the quadrati lumborum, and between the margins of the latissimus dorsi and external oblique muscles. These connections must be borne in mind when considering the direction peri-nephritic abscess is likely to take.

The disease often commences insidiously. At first only pain is experienced in the lumbar region, and is often mistaken for colic arising from renal calculus or gravel. Examination of the urine, however, unless the kidney is previously diseased, shows nothing abnormal. The pain too, is usually more deep seated than that which attends renal colic, and is rather of a dull pricking character, than tearing and crushing. A marked rigor followed by sweating is often an initial symptom, but may not be noticed

till pain has been complained of some two or three days. When once noticed the rigor recurs at least once a day, usually in the evening when the temperature rises to 102-3° F., becoming nearly normal towards morning. Vomiting may be an early symptom. The bowels are constipated. In this stage, the disease, when on the right side, has been taken for enteric fever in the first week, and for peri-typhlitis. The severity and seat of the pain will distinguish it from the early stage of typhoid, whilst the pain and swelling in peri-typhlitis is more anterior, and situated lower down than in peri-nephritis. The swelling in the lumbar region may develop slowly, sometimes quite rapidly, but at the end of a week, however, in the generality of cases, firm pressure with the hand in the lumbar region elicits a feeling of resistance, and then if the other hand is placed firmly on the abdomen, and a slightly swaying movement made with both hands, a mass can often be made out. This may be taken for a collection of fæces in either the ascending or descending colon, or if on the right side for tumour of the liver; from the first it can be distinguished by no diminution occurring on complete evacuation of the bowels, and from the latter by the tumour not being affected by the ordinary respiratory movements, and by being covered by the colon. The tumour may increase slowly or rapidly. About this time an œdema accompanied by a slight redness of the skin usually occurs in the lumbar region, and extends to the hips. The thigh also becomes more or less flexed upon the abdomen from pressure on the psoas muscle. When suppuration commences there is an exacerbation of all the symptoms. The pyrexia is more continuous, and of a higher grade, and though there are still remissions in the morning temperature, they are not so marked. The swelling now rapidly increases, and if the pus is not evac-

uated, it will endeavour to find a passage towards the surface by burrowing in the neighbouring layers of cellular tissue. Thus, it may invade the cellular tissue of the lumbar region, and point in the situation that surgeons have shown to be the position where lumbar herniæ make their appearance, viz., between the margins of the latissimus dorsi and external oblique muscles. Here it may be localised as an abscess, or it may spread subcutaneously over the back and hip. Or the matter may find its way downwards, passing from the renal region to the cavity of the pelvis, from thence it may pass below Poupart's ligament and present in Scarpa's triangle, or even discharge into the hip-joint, or it may open into the bladder, the vagina or intestines. More rarely the direction taken is upwards, and the diaphragmatic cellular tissue becomes involved, so that pleurisy and pneumonia are developed, or the abscess may even burst into the bronchial tubes. Very rarely indeed, the abscess opens directly into the peritoneum. The reason why this event is so uncommon, though it might at first sight be naturally expected, is as Trousseau has explained, in consequence of perinephritic abscess being generally situated behind the kidney, where that organ separates it from the peritoneum; moreover, when the inflammation does approach the peritoneum, peritonitis is induced, but the resistance caused by the false membranes, serves to turn the pus in another direction. Of all possible events, pointing of the abscess in the lumbar region is, in the case of adults, by far the most frequent; in children, however, the direction of the abscess is quite as frequently downwards, either forming in Scarpa's triangle, or passing even into the cavity of the hip-joint. When the pus takes this direction, the peculiar flexion of the thigh on the abdomen, which is more or less observable in most cases as soon as the tumour is of any magni-

tude, becomes more marked, and even partial extension becomes an impossibility. The urine, except in those rare cases when the inflammation extends to the substance of the kidney, or the tumour compresses the renal veins, is not albuminous.

86. **Causes.**—The disease is frequently attributed to exposure to cold when the body is in a heated condition. Though this may be a potent exciting factor, still it may be doubted if in itself it is sufficient to cause the disease, unless there be some predisposing cause, as for instance some constitutional taint, or injury, recent or remote, to the lumbar region. Strains and blows across the loins often give rise to it, and it may result from incised wounds in the renal region, though less frequently than from contusion. But in the majority of instances peri-nephritis is secondary to disease of other organs and tissues. Thus, (*a*) it is not uncommon in calculous pyelitis for peri-nephritis to develop and for the calculus to be discharged by lumbar abscess; (*b*) as an extension of inflammation of the pelvic cellular tissue upward, as following upon wounds of the lower part of the uterus and vagina, or after child-birth, and after operations on the testicle or spermatic cord or rectum; (*c*) sometimes, but this is a comparatively rare event, a psoas abscess bursts into the renal cellular tissue, and thus gives rise to peri-nephritis; (*d*) or inflammation of the renal cellular tissue of pyæmic character may develop in enteric fever, typhus, small-pox and scarlet fever, in these cases it usually happens that the peri-nephritis is on both sides. Trousseau would attribute simply to pain in the urinary organs, a large share in the causation of some of these abscesses, this however is doubtful. It is generally stated that peri-nephritis is more frequent in men than in women, whilst some German writers assert it to be extremely rare in children. My own

experience gathered from Hospital practice, is that cases of peri-nephritis are more frequent among women, consequent on the puerperal state, then in delicate ill-nourished and strumous children, and least of all among men. The reason why peri-nephritis has been considered to be of rare occurrence with children is that it is often overlooked in the earlier stage, whilst later, owing to the abscess taking a downward direction and presenting in Scarpa's triangle, or else actually bursting in the hip-joint, it is mistaken for psoas abscess, or disease of the hip.

87. **Diagnosis.**—In the early stage when the inflammation is on the right side, the disease may be mistaken for enteric fever in the first or second week, or for peri-typhlitis. It may be distinguished from these by the seat and severity, of the pain, by the absence of gurgling in the iliac fossa; by the swelling, if it can be detected, being in the lumbar region. When a tumour is formed we have to diagnose peri-nephritis from those diseases which cause renal enlargement, cancer of the kidney, hydro-nephrosis, hydatids, pyelitis and pyo-nephrosis. In the first three, the disease is chronic and unaccompanied by pyrexia, whilst in cancer there is usually hæmaturia; in hydro-nephrosis there is often an intermittent discharge of watery urine; and in the case of hydatids, hooklets may be passed *per urethram*, and oftentimes the hydatid fremitus can be produced on percussion. In pyelitis and pyo-nephrosis the purulent condition of the urine usually affords sufficient indication, since the urine in peri-nephritis is clear, unless it is associated with kidney disease; but here the fact that the urine was previously purulent or albuminous, enables us to attribute to the right cause the increase of swelling, pain and fever, that occurs when the cellular tissue becomes involved. Psoas abscess may be distinguished by the fact

that in that disease forcible flexion of the already flexed thigh, gives great pain, and little is given by firm pressure over the lumbar region, whilst in peri-nephritis the reverse obtains.

88. **Prognosis.**—Idiopathic peri-nephritis under prompt treatment may subside in the course of a few days, otherwise it proceeds to suppuration. This commences from the end of the first to the end of the second week, distinct fluctuation rarely occurring till the end of the third week. When the abscess is opened early, and the disease is uncomplicated, the result is usually favourable. In peri-nephritis secondary to calculous disease, the results are not quite so satisfactory; still since surgeons have paid more attention to the surgical diseases of the kidney, and operations are undertaken earlier than formerly, the number of recoveries have greatly increased. The least favourable results follow the treatment of peri-nephritis when it follows on the puerperal state or in septic conditions. But even in these cases when the disease is recognised early the proportion of recoveries is more considerable than the statement of some authors would lead us to suspect. Even in neglected cases, where the abscess has been permitted to burst into the bowels, or into the lungs, cases of recovery are recorded. In forming an opinion in any given case, we must be guided more by the constitutional powers of the patient, than the extent of the disease. And our success in treatment will be, in a given number of cases, directly proportionate to the early application of remedial measures, and the immediate evacuation of the abscess the moment fluctuation is perceptible.

89. **Morbid Anatomy.**—The walls of the abscess are sometimes ragged, sometimes smooth, the latter conditions being generally observed in cases of long-continuance. Its shape is irregular, especially if there has been a tendency to

burrow. The pus in idiopathic cases is yellowish and creamy, but in septic conditions is thin and of a greyish-yellow colour. The kidney in some cases seems to have been little affected by the contiguous inflammation, but in most there is evidence of some compression of its substance. Rarely, minute abscesses are observed on the surface of the kidney, beneath the capsule; sometimes it is somewhat softened. If the disease has been of long-continuance, especially in septic cases, cloudy swelling is observed. Otherwise except in those cases were pyelitis or pyonephrosis primarily existed, the organ has sustained no serious mischief. When the abscess has opened internally its course can be readily traced.

90. **Treatment.**—In the earlier stages absolute rest in bed. If the patient is robust, and the disease idiopathic or the result of direct injury, leeches should be freely applied to the affected side, and an antimonial saline, with a sufficient dose of opium to relieve pain, given from time to time. As the bowels are generally obstinately constipated, and as this condition adds to the discomfort of the patient, and the pressure of a loaded colon on the kidney increases the pain, they should be promptly relieved. For this purpose a full dose of calomel followed a few hours after by a small dose of Epsom salts has the most decided effect. By thoroughly clearing the bowels at first, the patient need not be troubled again for a day or so, an important consideration, whilst a sharp purge has almost the effect of venesection. These measures applied early may lead to resolution of the inflammation. In delicate persons, as in females in whom the disease has supervened after parturition, or in ill-nourished strumous children, or when the disease occurs in the course of small-pox, scarlet fever, typhus, etc., the treatment must be less active. Pain

must be relieved by opium, and the best form of administering it is as Dover's powder, whilst the bowels must be opened by means of castor oil. Inunctions of belladonna to the affected side prove very serviceable and afford considerable relief. These cases rarely if ever terminate in resolution. When the pyrexia becomes more continuous, and the rigors more marked, indicating that suppuration has commenced, and if a definite swelling can be made out, puncture and the withdrawal by means of the aspirator of some of the contents will afford considerable relief, even if no pus be met with. At the same time large poultices should be frequently applied. As soon as fluctuation is perceptible the surgeon should be requested to evacuate the pus by means of a free incision. The necessity of calling in surgical assistance early cannot be too emphatically insisted on; a few hours delay may lead to formidable burrowing of pus, and an extensive destruction of the soft tissues.

Class IV. Specific Conditions.

The instances in which suppurative inflammation is excited in the kidney by specific causes, as for instance, in tubercular disease of that organ, will be referred to in a subsequent chapter, and require no special mention in this place. (See Scrofulous Infiltration of the Kidney).

CHAPTER V.

Degenerations and Infiltrations of the Kidney.

Lardaceous Degeneration.

91. **Etiology.**—Waxy or lardaceous degeneration of the kidney was formerly considered to be a stage of Bright's disease, indeed even at the present day when the exact nature of the process is fully understood, many writers on Bright's disease still include it in their classification. Lardaceous degeneration, however, is a process quite independent of nephritis, although the two conditions are often associated together. Thus a waxy kidney may become the seat of nephritis, or lardaceous degeneration develop in a granular kidney. Lardaceous degeneration when it occurs is hardly ever limited to the kidney but affects other organs as well, especially the liver, spleen and intestines, indeed the kidney is generally the organ least affected. According to statistics collected by Dr. Charlwood Turner (*Path. Soc. Trans.*, 1879), the spleen was affected 48 times, the liver 30 times, the kidneys 15 times, and the intestines 10 times out of 58 cases. Waxy degeneration of the kidney therefore must be regarded as a general affection of the system.

Lardaceous degeneration is usually secondary to long-standing suppurative disease, whilst it is also frequently associated with constitutional syphilis, scrofula, or cancer. Dr. Charlwood Turner out of 58 cases collected by him, found that 43 occurred in association with prolonged suppuration. These included 20 cases of phthisis, 13 cases of bone disease of which six were due to caries, four to necrosis and three to disease of the joints. Of the re-

maining 15 cases, 8 were found in association with syphilis, six with malignant disease, and one in a patient suffering from the hæmorrhagic diathesis. In one of the cases associated with syphilis, and two of the cases associated with malignant disease, there was a history of ague. The connection between ague and waxy degeneration has been disputed, but Sir Joseph Fayrer has recorded as the result of his experience that apart from the long-continued suppuration of dysentery, waxy degeneration is an occasional result of tropical malarious disease. I have recorded (*Path. Soc. Trans.*, 1879, p. 537) an instance, confirming this statement, in an old Greenwich pensioner, aged 90, who died apparently from old age, but whose liver and spleen were enormously enlarged from infiltration of lardaceous matter. All his other organs were sound, there was no evidence of old abscesses or other cause of suppuration, nor of any dysenteric attack, nor of syphilis, but he had been much exposed to malaria in the West Indies. In chronic Bright's disease, the long-continued drain of albumin is supposed to be the main cause of the infiltration of lardaceous material that so frequently occurs. Whilst in phthisis, chronic nephritis follows on previous waxy infiltration, the result of the chronic suppuration from pulmonary cavities. Lardaceous degeneration, in some rare instances, may be quite localized, depending on a long-continued suppuration limited to the affected organ, an instance of this is occasionally seen, when one kidney, which has been the seat of calculous pyelitis is found after death to be infiltrated with waxy material. Neither age nor sex have any special bearing on the etiology of the disease, given long-continued suppuration, or the constitutional cachexia of struma, syphilis or cancer, lardaceous changes follow independently of age or sex.

92. **Symptoms.**—When in the course of an exhausting disease, connected with prolonged suppuration or syphilitic or other cachexiæ, we find the urine becoming profuse, of low specific gravity, of nearly neutral reaction, and containing a small quantity of albumin, and depositing a fine white deposit, which on examination is found to consist of lymph corpuscles, a few fatty epithelial cells and fine hyaline casts, whilst with these symptoms there is no hypertrophy of the heart, we may conclude that the kidney has become the seat of lardaceous infiltration. In uncomplicated cases this character of the urine is maintained throughout, only the albumin frequently becomes more abundant as the case progresses, though the amount passed on successive days is extremely variable. The paraglobulin often exceeds the serum albumin. The casts, too, in long-standing cases, may stain with iodine; this, however, is not always observed. If the case become complicated with acute nephritis, the urine becomes scanty, and dropsy may ensue; if on the other hand chronic nephritis supervene, cardio-vascular changes will be observed, though owing to the debility of the patients they never attain a prominence as marked as in uncomplicated interstitial nephritis. Though general dropsy is not a symptom of uncomplicated lardaceous infiltration, still a little puffiness round the ankles, especially in the later stages of the disease, will frequently make its appearance, this no doubt is owing to the hydræmic condition of the blood that is so marked in these cases. As the liver and spleen are nearly always affected as well, any enlargement of these organs will aid our diagnosis, though it must not be forgotten that both may be the seat of extensive infiltration without their being perceptibly increased in volume; when, however, the liver and spleen are infiltrated to a considerable extent, abdominal dropsy (ascites)

makes its appearance. The appetite is rarely affected, often the patients crave for food, and digest with comfort, though if the intestines be also affected they are troubled with diarrhœa, and as this is apt to follow on the ingestion of food, it is advisable to give it in as nutritious and easily digestible form as possible. Owing to the debilitated condition of the patients, they are extremely liable to secondary inflammation, especially of the serous membranes, and they are also extremely liable to thrombosis. Patients suffering from lardaceous degeneration of the kidneys become rapidly pale, and complain of fatigue on the slightest exertion.

93. **Prognosis.**—The duration of the disease in its various stages is very variable, depending in great measure on the individuality of the patient, the circumstances in which he is placed, on the development of the disease, and the secondary complications that it may give rise to. Dr. Goodhart (*Path. Soc. Trans.*, 1879, p. 535) has made some observations as to the length of time that must elapse between the commencement of suppuration and the production of the disease. According to his experience at Guy's it appears that three months is the shortest period in which the disease is known to have occurred, and also that the duration of the suppuration necessary to produce lardaceous disease depends in great measure upon the duration and intensity of the fever. If either in suppuration, or syphilis, the pyrexia be great or perhaps prolonged without much intensity, other things being not adverse, the lardaceous change will be produced rapidly. In hot climates not only is the disease very rife but its progress is also rapid. Death, however, as the result of mere lardaceous degeneration of the kidney is rare, the event being due to either the exhaustion caused by the original disease, or

to the general extension of the infiltration to other organs leading to marasmus from impairment of nutrition, or from secondary inflammations or thrombosis. On the other hand in cases where the originating disease is removable, as in caries or necrosis of bone, the health of the patient is often materially improved for a time by the relief of these conditions. Whether a cure is ever possible is still a disputed point. Dr. Dickinson (*Path. Soc. Trans.*, 1879) relates a case following on constitutional syphilis in which a cure seemed certainly to have been effected. He also relates a case which lived for eight years after the first appearance of the disease, the greater part of which was passed in apparent good health.

94. **Diagnosis.**—In lardaceous disease we have to distinguish between it and other conditions leading to albuminuria. It is most likely to be taken for granular contracted kidney, in both we have a profuse flow, low specific gravity, and only a small amount of albumin. In contracted kidney, however, the polyuria is more marked, and the specific gravity is often much lower, (in waxy kidney Bartels says it probably never falls below 1·006) the urea is more reduced than is the case in lardaceous degeneration of the kidneys, whilst in the latter instance there are no cardio-vascular changes, and uræmic convulsions are very rare. It is distinguished from tubal nephritis by the difference in the character of the urine, and absence of general dropsy; the œdema of waxy disease of the kidneys, unless associated with nephritis, being confined to the abdomen and lower extremities. In waxy degeneration of the kidney, the urine does not become scanty and high coloured, unless there is some febrile complication, whilst in tubal nephritis that is the ordinary condition of the secretion. The supervention of tubal nephritis on waxy degeneration is consequently marked by the transition from an abundant discharge of urine of

low specific gravity to a scanty discharge of high coloured urine of high specific gravity. The albuminuria of pyrexia can generally be distinguished from that of waxy infiltration by its dependence on the course of the temperature, by the previous history of the case, but in cases of hectic dependent on phthisis, or long-continued suppuration, the differentiation between the two often becomes exceedingly difficult. On the other hand the albuminuria from extra renal sources can usually be readily made out, by reference to the morbid conditions existing in the urinary passages. The diagnosis between functional albuminuria and that due to waxy infiltration, as a rule, is not difficult. In the former there is generally no very marked increase of the urine secreted, the specific gravity is rarely lowered, indeed is often more than normal, the urea is generally in excess, whilst there is an absence of that remarkable pallor and emaciation so characteristic of the victims to lardaceous degeneration. In all cases our diagnosis will be aided by a careful consideration of the etiological details of the case.

95. **Morbid Anatomy.**—Lardaceous infiltration usually affects both kidneys and generally equally. Degeneration of one kidney is exceptional, though it may be observed if the organ has been the seat of long continued suppuration from calculous pyelitis, or of cancer. The affected kidneys in the early stage are only slightly, if at all enlarged, in appearance they may be slightly paler than usual, whilst on section the glomeruli may appear prominent and sparkling. No apparent change, however, may be noticed, till the cut surface is washed with iodine or methyl aniline violet, when the degenerated glomeruli acquire a stain from these reagents, and stand out like spotted points. As the disease advances, and the waxy infiltration affects other vessels of the kidney besides the

glomeruli, and the vasa afferentia, such as the vasa recta, vasa efferentia, and the inter-lobular vessels, an increase in the size of the kidney takes place, which may be very considerable. The surface of the organ is smooth and the capsule readily removed. The enlargement is most marked in the cortex, which is of a pale yellow colour, and contains but little blood, whilst the pyramids are usually red, it being only in an advanced stage of the disease that the pyramidal portion of the kidney becomes involved and the cut section of the kidney assumes an homogeneous aspect. The Malpighian tufts stand out from the translucent wax-like surface, like glistening points, "dew-drops," as Meckel has poetically described them. If the surface be now washed with iodine or methyl violet, it will be seen how extensive is the infiltration, all the vessels exposed to the action of the reagent acquiring a stain, and bringing them out as prominently as if injected. A third or final stage of waxy kidney has been described, but it is evidently due to the association of other processes such as tubal or interstitial nephritis. In these kidneys, the homogeneous wax-like appearance of the cortex is often streaked with a number of minute yellowish white lines, the result of the fatty changes in the epithelium of the tubules. The superficial cortex is diminished in volume, the capsule is more or less adherent to the surface of the organ, and becomes marked with irregular depressions. If in addition to this diminution of bulk from atrophic changes in the tubules, there has also been an increase of the inter-tubular connective tissue, the shrinking will be more considerable. In these kidneys the staining with iodine and methyl violet often takes place in a very irregular manner, little or none taking place in the cortex, whilst the papillæ stain deeply, stained lines running up from the apex into the pyramid.

The staining of this part of the kidney, which is not noticed during the earlier period of waxy infiltration, is probably accounted for by the fact that the hyaline walls of the tubules have become affected, whilst the disappearance of the staining in the cortical portion may be explained by the breaking up of the waxy matters by fatty degeneration. In connection with this latter circumstance Dr. Moxon (*Path. Soc. Trans.*, 1879) has remarked that under typhoid fever he has known lardaceous organs recover themselves; it may be that pyrexia, as well as local inflammation, leads to molecular degeneration of the infiltrated material, and thus facilitates its absorption and removal.

The deposit of waxy material commences in the Malpighian bodies, and then affects the afferent arteries,

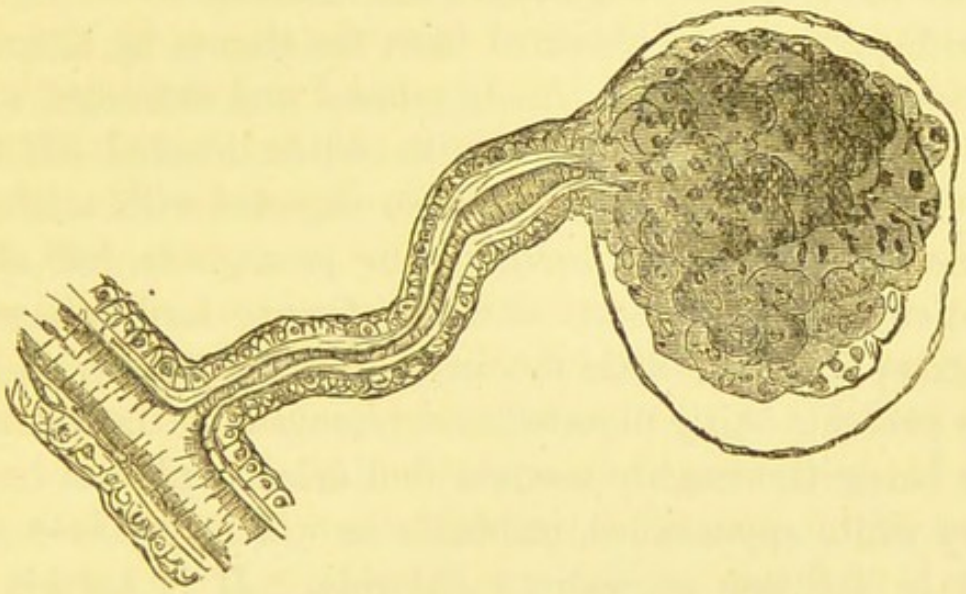


FIG. 29.—Lardaceous degeneration of the Malpighian tuft and small arteries (Green's *Pathology*).

(fig. 29). The vasa recta are next involved, the vasa efferentia and the inter-tubular vessels being usually the last attacked. At a very late stage of the process the urinary tubules may become involved, when this

is the case it is the hyaline wall of the lower part of the collecting tubes of the pyramids that first become the seat of this deposit. The epithelium at an early stage of the disease is normal, but later on it undergoes fatty changes. Cysts are often observed, they may be caused either by the irregular compression of the infiltrated material; or as is more frequently the case, from the shrinking of the inter-tubular connective tissue the result of associated interstitial nephritis. Casts are not numerous, when found in the tubules they are hyaline, sometimes covered with fatty epithelium. The majority are simply the result of exudation, though sometimes they seem to be composed of lardaceous material, and stain with iodine and methyl violet; these, however, are only met with in the later stages of the disease, when the tubules have become the seat of the infiltration.

Lardacein may be obtained from the tissues by Kühne's process. The kidney is finely minced and extracted with cold water and subsequently with dilute alcohol till the mass becomes colourless, it is then digested with artificial gastric juice for several hours. The precipitate, left after filtration, consists almost entirely of pure lardacein with the exception of a little mucin and elastic tissue, all the other proteids being digested and removed by the filtrate. After being thoroughly washed and dried, lardacein has a snowy white appearance, insoluble in water, and does not swell in solution of sodium chloride. It is soluble in dilute ammonia from which it can be precipitated by dilute acids. With iodine it stains a mahogany-brown, and this reaction was supposed to be peculiar to it, but I have shown (*Path. Soc. Trans.*, 1879) that casein, syntonin and dried fibrin equally develop the reaction, though not coagulated serum albumin. Methyl aniline violet stains lardacein a rosy red. A blue colour is developed by the

joint action of iodine and sulphuric acid, but this coloration can be caused by the admixture of iodine and sulphuric acid, without the intervention of lardacein, or any other substance, the blue colour being probably due to the volatilization of the iodine by the sulphuric acid.

Some difference of opinion exists, as to the real nature of the deposited material, whether it is the result of chemical changes in the tissues themselves, or whether it is a morbid material derived from the blood. When first discovered it was, from the blue colour given with iodine and sulphuric acid, supposed to be allied to starch, hence the term amyloid substance applied to it. Chemical analyses, however, have proved it to contain nitrogen, and by its exhibiting the xantho-proteic and Millon's reactions it is shown to be a proteid substance. Its composition is as follows:—carbon 53·6, hydrogen 7·0, nitrogen 15·0, oxygen 23·1, sulphur 1·3. Dr. Dickinson regards it as de-alkalised fibrin, and maintains that he has obtained it artificially by digesting fibrin in dilute hydrochloric acid, he believes the de-alkalization is caused by the withdrawal of potash salts from the tissues, the result of long-continued discharge of pus. In proof of this, he quotes analyses made by Dr. Dupré, which show that the potash in healthy liver tissue is 0·209, and in the spleen 0·311 in 100 parts, whilst in lardaceous degeneration of these organs the potash is reduced to 0·151 and 0·196 respectively. Dr. Dickinson also considers the fact, that the brown stain caused by iodine with lardacein is removable by the action of dilute solutions of potash, but is restored by the action of an acid, is an additional proof that the reaction with iodine is associated with the condition of acidity that is with the removal of alkali. In answer to this view, it is maintained that the action of dilute hydrochloric acid on fibrin can have no other effect than to con-

vert it into syntonin, and yet we know that syntonin is not lardacein, since the former is soluble in acids and alkalies, and digestible in gastric juice, which the latter is not. Syntonin only resembles lardacein by the fact that both give the same coloration with iodine, a circumstance that has perhaps led Dr. Dickinson to regard both products as identical. Again, as Dr. Pye Smith (*Path. Soc. Trans.*, 1879) has observed, the decolorizing effect on the iodine reaction is not caused by its action on lardacein but on the iodine, since the same effect occurs when we use liquor potassæ to efface stains of iodine on the finger, the unstable coloured compound of iodine is decomposed, and potassium iodide is formed, which is in turn decomposed, and the colour restored by the addition of acid. I have also shown (*Path. Soc. Trans.*, vol. xxx.) that the iodine reaction does not depend upon the withdrawal of alkali from the fibrin, since alkali albumin, if all traces of free alkali are carefully removed, made by treating fibrin with liquor potassæ, developes the reaction as well as acid albumin made by treating fibrin with dilute acid. Lastly, the deficiency of potash existing in the affected tissues, may be accounted for by the increase of fat in them, since we know that tissues that have undergone fatty degeneration become poorer in saline constituents.

With regard to the actual nature of the product it is impossible as yet to express anything like a definite opinion, still there are many points which indicate that lardacein is a mixture of a proteid with a fatty body, of which we have a physiological example in vitellin, which Hoppe Seyler considers to be an admixture of globulin with lecithin. However this may be, Dr. Stephen Mackenzie in the debate on lardaceous disease at the Pathological Society, made an important suggestion, in pointing out a probable connection between hyaline and

lardaceous degeneration. For though the hyaline material gives no definite reaction with iodine, still the further study of this condition may throw considerable light upon lardaceous degeneration being associated with alterations in the blood, for it might be that the difference between the hyaline and waxy is only one of degree, the hyaline being the first step in the degenerative process, brought about by pyrexial conditions, which, if long-continued, leads to waxy deposit. Looked at in this light, Dr. Goodhart's observations made at the same debate, and to which allusion has been made in speaking of the symptoms of the disease, with regard to the relation between the production of lardaceous disease and the intensity of fever, acquire additional interest. In any further inquiry that may be undertaken to investigate the exact nature of this product, and to put its composition beyond doubt, I would suggest that the nature of the fatty changes occurring in the organs in this disease should also be considered. No one can view the peculiar translucent waxy appearance of the cut sections without at once recognizing the fact that the fatty matter, to which it is undoubtedly due, is present in a form unlike any other kind of fatty deposit, suggesting the idea that it is either some peculiar kind of fat, or else ordinary fat mixed with some other constituent.

96. **Treatment.**—In all cases we must enquire into the originating conditions and endeavour to relieve them. If due to suppuration from diseased bone, means must be taken to check further discharge by the removal of the dead bone, etc. If from phthisis, scrofula, or syphilis, by proper constitutional remedies. With regard to the treatment directed towards the infiltrated organs, iodide of potassium has often proved of great service, especially when dependent on constitutional syphilis. It should be given in large doses, from 15 to 20 grains, three times a

day. The administration of cod-liver oil at the same time improves the patient's general condition. In cases, however, independent of syphilis, I prefer the use of iodide of iron, to iodide of potassium, and I believe its efficacy to be greatly increased by the addition of arsenic ($\frac{1}{20}$ grain arseniate of iron). In a patient recently under my care at the London Hospital very great improvement followed the combined administration. The liver and spleen, which were considerably enlarged when the treatment was commenced, at the end of three months were nearly of normal dimensions, whilst the urine became nearly free from albumin. Although a course of mercury cannot be ventured on, yet great benefit ensues from an occasional dose, not only in cases associated with syphilis but in others, especially when the liver is implicated and ascites is present. A grain of grey powder combined with digitalis and squill may be administered, for many nights following, and its use is attended by increased excretion of urea, and often prodigious diuresis, and relief to the ascites, if present. In those cases where the intestines become the seat of lardaceous deposit, and there is considerable diarrhœa, bismuth proves most serviceable.

Cystic Degeneration.

Under this head we have to consider:—1. *Congenital renal cysts*; 2. *Renal cysts in adults*, primary and secondary; whilst 3. *Hydro-nephrosis* or the dilatation of the pelvis with destruction of kidney substance, is also most conveniently studied in this place.

97. **Congenital Renal Cysts.**—Both kidneys are usually affected, and sometimes attain such a size as to impede delivery. Their usual size, however, ranges from three to six inches in length, and two to four inches in

width, and weight from three and a half to five ounces. Their surface is studded with numerous projecting cysts, whilst on section it is found that nearly the whole of the kidney structure has disappeared, being replaced by a congress of cysts of different sizes, these being generally filled with a darkish coloured fluid, which contains urea, and is more or less albuminous. Virchow, who was the first to thoroughly investigate the nature of the disease, showed that it was caused by an embryonic inflammation of the tubules, which occluded the papillæ, and he thought that the inflammation originated from the infarcts of uric acid and urates so frequently deposited in the straight tubes during fœtal life (see calculous disease of kidney). This, probably, is the explanation in the majority of cases, but in some it is probable that increased connective tissue formation plays a part in the causation, whilst others may be referred to the metamorphosis of the epithelium, in some portions of the tubules, into colloid matter (Förster, *Pathological Anatomy*, p. 468). Dr. Ewart has recorded (*Pathological Society's Transactions*, 1880) a case of cystic degeneration of the left kidney and ureter in a new-born infant, in which the obstruction was due to a valvular fold of mucous membrane in the ureter, which allowed the passage of a probe upwards, but not downwards. Congenital cystic degeneration of the kidney has also been found associated with hydatids, an interesting case of which is recorded by Dr. Cayley (*Pathological Society's Transactions*, 1874). The subjects of congenital cystic disease have generally some other congenital defect, club-foot, webbed fingers, transposition of viscera, imperforate anus, encephalocele, are among the most frequent examples, whilst Ebstein relates a case in which with cystic kidney on the right side, the right lower extremity and right half of the female genitals were absent, whilst

nothing abnormal was found on the left side of the body. Most of the children with cystic disease are born prematurely, and either are still-born, or else die soon afterwards. In some where the disease is limited to one kidney, life may be prolonged, Mr. Knowsley Thornton and Dr. Day have recorded a case of this kind, which was believed to be congenital, in which the kidney was removed, and six months afterwards the patient was reported to be much improved in health, and to have grown considerably (*Lancet*, June 5th, 1880).

98. **Cystic Degeneration after Birth.**—1. *Primary cystic formation* is most commonly observed during middle life. Both kidneys are usually affected, though as a rule to an unequal extent. It is twice as frequent in men than women (Ebstein). The disease runs a very insidious course, with often a sudden termination in uræmic convulsions. In some cases a history of a blow, or a strain can be obtained, otherwise there is no special etiological condition associated with the disease. The symptoms are usually obscure, if there be great enlargement of the kidney, a tumour will be felt in the loins, whilst an intermittent hæmaturia and albuminuria, and the discharge of urine of abnormally low specific gravity, are the most constant phenomena observed, but even these may be absent, and we may remain unaware of the existence of any renal mischief till after death. The kidney when removed from the body presents a remarkable lobutated appearance, owing to the projection of the numerous cysts. These vary in size from minute points up to that of a fair sized orange, and their colour may be either dark and purplish, reddish-brown, or greenish-yellow, so that the whole appearance of the transformed organ has the resemblance to a bunch of unequally ripened grapes. On section it will be found that the cysts

are independent of each other, and that, with the exception of a few that may have been ruptured, their walls are closed. Their contents are usually limpid, sometimes gelatinous; whilst serum albumin, altered blood, crystals of cholesterine, and oxalate of lime, are the chief constituents, true urinary products being rare. The cysts are lined with flat polygonal epithelial cells, and are surrounded with a thick bed of coarse connective tissue. In spite of the apparent destruction of the kidney tissue, it is remarkable to find on microscopic examination how many tubules have been spared. With regard to the origin of the disease, some refer it to an alteration in the Malpighian bodies, others to occlusion of the renal tubules. Mr. Eve (*Pathological Society's Transactions*, 1880), who, in a case reported by him, paid attention to this point, states positively that the glomeruli were not perceptibly altered in sections, which showed distinct dilatation of immediately adjoining tubes; whilst the stages of transition from simple dilatation of the tubule to the formation of cyst-like cavities, could be so plainly observed, as to leave little doubt that cyst development took place from the tubuli uriniferi. In most cases, as in this, the disease is, however, too far advanced to permit of conjectures as to the original cause of the retention, though it is probable it consists in a chronic inflammation of the interstitial tissue, leading at first to occlusion of the ducts of the pyramids, and then causing dilatation higher up, till the whole kidney is involved. When the disease involves the glomeruli, it will be generally found that the contents of the cysts are not limpid and albuminous, but colloid, in this case the capsule becomes distended with colloidal matter, and thus forms a more or less solidified cyst, but these cases, which are less frequent than the limpid variety, ought to be considered rather as colloidal than a true cystic degeneration.

2. *Secondary Cystic Formations.*—These are the clear transparent looking cysts so constantly present in granular kidney. They vary in size from a pin's-head to a pigeon's egg, the largest contain albumin, and sometimes uric acid crystals, they all have minute masses of a gelatinous character floating in them, their walls are thin, and are generally distinct from each other. The view generally held with regard to their formation, is that they are formed by the irregular compression exercised by the contracting fibrous tissue on the urinary tubule, or by distension of the capsule of a Malpighian corpuscle, owing to obstruction of its outlet by compression, from contracting fibrous tissue, or blockage by a cast. Recently a view has been advanced (Greene, Heitzmann's *Morphology*), which considers cysts as products of secondary changes of medullary bodies. The first step, according to this account of the process, is the formation of inflammatory corpuscles in the cortex, and pyramidal substance, apparently derived from the tubular epithelia. These bodies swell, become pale, and by a process of liquefaction form a hyaline mass, in which may be found fine granular fibres, like those of myxomatous tissue. This mass is bounded by unsoftened inflammatory corpuscles. As the cysts enlarge, these gradually liquefy, till a cavity containing a sero-albuminous fluid is formed, bounded by flattened medullary corpuscles, from this a fibrous basis substance originates, which forms the wall of the cyst.

Hydro-nephrosis.

99. **Etiology.** — It has been objected that hydro-nephrosis ought not to be classified in connection with cystic disease of the kidney, which is supposed to refer

only to microscopic degeneration of the organ. But as Dr. Pye Smith (*Path. Soc. Trans.*, vol. xxiii.) has justly replied, that an obstruction to the ureter producing either a large single cavity, or a multilocular one, may be fairly described as cystic disease, and that every gradation in the form and character of cystic development may be observed between a simple hydro-nephrosis and a granular kidney full of microscopic cysts.

Hydro-nephrosis then, may be defined as a cystic disease of the kidney, following on dilatation of the ureters and the pelvis of the kidney, and attended with more or less destruction of the renal tissue. The obstructions that produce the original dilatation of the ureter and pelvis of the kidney are numerous. Out of forty-seven cases collected by Mr. Henry Morris (*Med. Chir. Trans.*, vol. lix.), twelve were due to impaction of calculous matter; in five the obstruction was caused by the abnormal course of the ureter; in five, it was impervious; in two, simply narrowed, probably from congenital causes; in two it was compressed, one by tumour, and in the other by an abnormal branch of the renal artery; in two, the obstruction was caused by a valvular flap of mucous membrane at the orifice of the ureter; in one case, the compression was caused by a band of fibrous tissue passing from the brim of the pelvis to the sacrum; whilst in nineteen cases, the cause of the obstruction was not mentioned or not discovered. Ebstein lays a particular stress on the connection that subsists between hydro-nephrosis and the pathological conditions of the female genital apparatus as caused by pressure from tumours, etc. It may also be caused, not by direct obstruction by pressure, but by displacement and traction on the ureter by the tumour. Obstruction to the flow of urine from the bladder by enlarged prostate, or from stricture, has been spoken of

as causing hydro-nephrosis; but the condition is rather one of sacculation than the formation of a cyst containing fluid.

100. **Symptoms** depend very much upon the mode of origination. Thus when it follows upon uterine disease no symptoms may be noticeable during life. As Mr. Morris observes: "Numerous cases of cancer of the pelvic organs are treated annually in the Middlesex Hospital, yet none of the present surgeons can remember to have seen a single instance in which distension of the pelvis of the kidney could be detected by an abdominal swelling during life; yet hydro-nephrosis is almost weekly seen in the post-mortem room." This, no doubt, is owing to the fact that the ureter in these cases is never quite occluded, and therefore the pressure effects do not lead to extreme distension of the kidney so as to be detected during life. It is when the occlusion is more or less permanent and complete, and has come on suddenly, that the hydro-nephrotic distension of the kidney acquires a considerable size, and these cases are those in which the obstruction is high up in the ureter, rather than when it is situated near the bladder. Mr. Morris is of opinion that when an abdominal swelling can be detected, there has been either sudden and complete obstruction to the urine secreted by a kidney in full function, or else after one kidney has undergone compensatory hypertrophy, some obstacle has arisen to the flow of urine in the hypertrophied organ. The tumour thus formed may be enormous, and seriously compress both the thoracic and abdominal viscera. By its pressure on the colon it often causes serious obstruction of the bowels. The tumour is painless when handled, though often the seat of cutting, stabbing pains; fluctuation can generally be determined, and frequently after handling by the physician or surgeon,

the contents are discharged into the bladder, causing an abundant flow of urine. Hæmaturia and albuminuria may be occasionally present, but they are by no means constant symptoms. The urine is not diminished in quantity unless both kidneys are affected, the sound organ doing the work of the obstructed one; indeed, the discharge is often over-copious from the contents of hydro-nephrosis discharging into the bladder.

101. **Diagnosis.**—During the whole progress of the disease the urine may remain unaffected in quality, but the diagnosis is tolerably certain, if, with a renal tumour, we have intermittent discharges of pale aqueous urine. The tumours likely to be taken for hydro-nephrosis are ovarian cysts, hydatids of the kidney, and ascites. The former may generally be determined by examination by the vagina and rectum. This latter examination should be performed by introducing the hand into the rectum, and exploring with the finger the whole of the upper pelvic region. By alternately compressing the ureters with Davy's rectal lever we can also learn whether urine is being discharged by both, or whether it is obstructed in one. If the urine is *quite* obstructed in one, we may be tolerably confident that the case is one of hydro-nephrosis, and not ovarian. The history of their development, and a careful consideration of the relation of the tumour to the intestines, will also aid in forming our opinion. Withdrawal of small portions of the contents of the tumour will decide if there should be doubt, as also will be the case with an hydatid tumour. In ascites, dulness will always be found in the most dependent part, whereas in hydro-nephrosis the dulness always remains localized, in whatever position the patient may be placed. Solid tumours of the kidney may be distinguished from hydro-nephrosis by the want of

fluctuation and their irregular and nodulated contour. It is sometimes difficult to determine between pyo-nephrosis and hydro-nephrosis. In the former, however, we have generally the history of preceding pyelitis and the occasional discharge of pus and blood, considerable constitution disturbance, and often a fluctuating temperature; whilst in hydro-nephrosis the early history is often obscure, the symptoms have come on insidiously, there is little constitutional disturbance, and the discharge, when it occurs, is aqueous.

102. **Morbid Anatomy.**—The degree of dilatation of the pelvis of the kidney, and the destruction of its tissue, depends on the completeness of the obstruction, whilst the form of the tumour is determined by the position of the obstruction. If situated low down, as in the bladder, the distension of the ureter, pelvis and capsule assumes a somewhat fusiform shape, the ureter in some instances resembling small intestine both in size and sacculated appearance. When the obstruction is higher up in the ureter, the tumour assumes a rounded pyramidal shape, the apex being formed by the obstructed part of the ureter. The tumour may consist of only one single cavity, more frequently of several, each opening into the pelvis of the kidney and corresponding to the dilated calyces. When the obstruction is complete and long continued, every vestige of renal tissue may disappear and nothing left but a membranous sac. The first change in the renal tissue is flattening of the papillæ and dilatation of the calyces, whilst the medullary substance atrophies, till at length under the long-continued pressure of the confined secretion the cortex dwindles and disappears, though this process is slow, owing as we have seen (p. 279), to the overgrowth of the interstitial connective tissue, which, for a time

resists the undue pressure in the tubules. When the obstruction at first is slight and only gradually increases, no great dilatation may ensue, and may proceed, supposing the obstruction never becomes quite complete, no further than to atrophy of the medullary substance. Even then if complete obstruction sets in, and the kidney structure is absolutely wasted, the hydro-nephrosis never attains considerable dimensions, because the destruction of the secreting structure has gone hand in hand with the obstruction. It is sudden and complete obstruction that leads to large hydro-nephrotic tumours. The fluid of hydro-nephrosis is of low specific gravity 1·004 with a neutral or slightly acid reaction, never alkaline unless it has been kept, it generally contains traces of urea and uric acid though these may be absent. It does not contain albumin, though Dr. Schetelig of Hamburg has found par-albumin in the fluid of a hydro-nephrosis, cholesterin has also been found. The fluid contains an abundance of sodium-chloride. In many respects it resembles the fluid of an hydatid cyst, that however has usually a higher specific gravity, 1·009 to 1·013; its reaction is usually faintly alkaline; the sodium-chloride is much more abundant than that found in hydro-nephrosis or any other fluid in the body, whether healthy or morbid; lastly, it never contains urea or uric acid, whilst the presence of hooklets can generally be made out. The fluid of a hydro-nephrosis often contains pus, sometimes it becomes rapidly purulent so that the condition becomes that of a true pyo-nephrosis.

Hydro-nephrosis is usually confined to one kidney, the other becoming hypertrophied in consequence of the double duty thrown on it. If both kidneys are affected they are generally unequally so. When the disease results from congenital malformation of the ureter, there is usually some other abnormality of development noticed,

as club-foot, webbed toes and fingers, hare-lip, cleft palate, etc.

103. **Treatment.**—If the disease arises from sudden obstruction as from the impaction of a calculus, we may hope if the obstruction is speedily removed, that beyond dilatation of the pelvis of the kidney, no great damage has been done to the renal tissue. Even in cases where it is impossible to effect the removal of the obstruction, great good may result by endeavouring to relieve the pressure or tension on the ureter. Thus in cases of hydronephrosis arising from tumours in the pelvic region, the thorough emptying of the lower bowel every day; supporting, when possible, the tumour, as in prolapsed uterus or fibroid of that organ, by means of pessaries, etc., introduced into the vagina; by keeping the patient in a posture that shall diminish the pressure or traction of the tumour on the ureter, to the greatest possible degree. In those cases in which the obstruction is so great as to resist the onward pressure of the accumulated fluid, but not so complete as to resist any additional force, such as may be produced by pressure with the hand, great relief, and in a few instances a cure, has been effected, by daily emptying the sac by gently squeezing it, and then applying a flannel roller firmly round the abdomen. In applying this mode of treatment, care must be taken not to apply the pressure too suddenly but gently and uniformly, otherwise there is danger of rupturing the sac. Lastly, if the tumour is rapidly increasing and cannot be emptied by ordinary pressure, surgical means must be employed, mere puncture and withdrawal of the fluid gives sufficient relief in some of these cases, but in others, especially if the cause of the obstruction be an impacted calculus and the sac after having been tapped speedily refills, it is advisable to have recourse to more effectual

means and to make an incision through the loin into the distended pelvis of the kidney, when the calculus may be removed, or possibly even a stricture due to an abnormal fold of mucous membrane at the upper orifice of the ureter may be dealt with; or the entire organ may be removed. The details connected with the operative procedures required for puncture, nephrectomy or nephrotomy belong entirely to the province of surgery, and cannot be discussed in this work. In making, however, an exploratory puncture with an aspirator for the purpose of withdrawing fluid for examination, we should, unless there is a decided prominent fluctuating spot where the skin is discoloured or the sac thin, in the case of the left kidney, insert the trocar in the interval between the two last ribs near their anterior extremities, a situation originally proposed by Mr. J. Thompson of Nottingham. Whilst for the right kidney, Mr. Morris proposes a spot half-way between the last rib and the crest of the ilium, between two inches, or two inches and a half, behind the anterior superior spine of the ilium.

Dermoid Cysts.

104. **Dermoid Cysts,** although frequently discharging into the urinary passages, are rarely found actually existing in the kidneys or walls of the urinary passages. Their structure is peculiar, consisting of an outer coat or fibrous envelope, and an inner layer of cuticular tissue. This is smooth, but having irregular prominences scattered throughout. The epithelium consists of layers of cells, the superficial are flattened and nucleated, the deeper polygonal and rounded. Occasionally under the epithelial layer, papillæ may be observed in the cutis. Between this

layer and the external coat is a little fine adipose tissue. The contents of the cysts are composed of a dirty yellowish pultaceous fluid, consisting of fatty and sebaceous matter, epithelial cells, and crystals of cholesterin. Imbedded in this will be found remains of bone, teeth, hair, and sometimes stripped muscular fibres and nerve-tissue. In a case brought under my observation, the cyst was apparently connected with the right spermatic cord, forming a hernia-like protrusion in the inguinal canal, in fact it was at first taken for a hernia and was found to be irreducible. The child became ill and feverish and the urine thick and albuminous, and the swelling disappeared. The urine then cleared up and ceased to contain albumin, no teeth or bone were discharged, but when the urine became clear it was noticed that from time to time an abundance of fine hair was passed with the urine. This hair collected and examined, consisted of three varieties of hairy matter mingled together; very fine, short straight hairs closely matted together by a sticky sebaceous substance and having somewhat the appearance of felt, short crisp curly hairs somewhat resembling wool, and some longer fibres, resembling in all respects human hair. These latter varied in length from about a quarter of an inch to two inches, and were coloured either a deep coal-black or else a bright vermilion-red, they comprised about one-tenth of the whole mass of hair. The amount discharged varied considerably, for some days no hair would be deposited and then an abundance would come away. This discharge of hair caused the patient no discomfort, and the child had no apparent irritability when it passed water. I therefore advised the parents not to trouble about the matter at present, but to keep the child under medical supervision, when if any chronic irritability of the bladder arose, either from the irritation produced by the constant

presence of foreign bodies in the bladder, or from calculous deposit round any hairs that had not come away, surgical interference might be required. The peculiar character of the hairy matters discharged is sufficient to indicate the nature of the case, and to distinguish them from hairy substances purposely or accidentally introduced into the urine. The peculiar felt-like substance, in which woolly and long straight hairs are intermixed, and the peculiar bright-red colour of some of the latter, are alone characteristic of hairs discharged by dermoid cysts.

Fatty Degeneration.

105. **Fatty Degeneration** of the kidney epithelia may be either acute or chronic. The most acute forms are those associated with phosphorus poisoning, and other toxic agents, such as sulphuric acid, oxalic acid and carbonic oxide; certain morbid conditions, as in ulcerative endocarditis of acute rheumatism, after extensive burns, pernicious anæmia, and diabetic coma, and that condition not yet determined, which leads to acute yellow atrophy of the liver. The chronic forms are the fatty changes that occur in the epithelium in Bright's disease, and the fatty infiltration observed in chronic phthisis and other wasting diseases.

The *acute fatty changes* occur chiefly in the convoluted portion of the tubules, and is often so limited to them that a distinct line of demarcation can be made out between the straight and convoluted portions of the tubules. Though the straight portion may be affected it is not so marked. The swelling of the epithelium

causes some slight enlargement of the organ at first, but as desquamation proceeds the kidney diminishes in bulk from the discharge of the degenerated cells. On making a section of a kidney undergoing acute fatty changes, the cortex presents a greyish-yellow colour, often much mottled, the pyramids congested. In septic cases the organ is very much softened throughout, and in some cases, as in embolism of the renal artery, necrosis of the kidney may result. In this case, the whole of the cortical substance, and some portion of the pyramidal, are converted into a dry greyish opaque mass, in which dark red spots irregularly distributed may be observed. These spots correspond to the Malpighian corpuscles, which are the only vessels in the kidney that contain blood in sufficient quantity to cause distension; the veins of the kidney either being empty, or containing only a little thin bloody fluid. No special symptoms indicate the occurrence of acute fatty degeneration of the kidney. Albuminuria may be present, but it is not infrequently absent (see p. 163). Fatty cells may appear in the urine if the patient survive the attack a few days, but they are rarely noticed in the early acute stage, though I have seen free fat in small quantities, in the urine of a patient dying of acute diabetic coma (acetonæmia). As acute fatty degeneration of the kidney is generally associated with fatty degeneration of other organs, especially the liver, we often find the character of these derangements expressed in the urine. Thus, in acute yellow atrophy of the liver, or after phosphorus poisoning, we find the urine containing bile, and products of imperfect proteid metabolism, to wit, leucin and tyrosin. With respect to these constituents the composition of the urine varies at different stages of the disease. At first, during the period of hyperæmia, we find the urea either normal in quantity

or perhaps slightly augmented, whilst both bile pigments and bile acids are present in the urine and but rarely leucin and tyrosin. As the destruction of the liver cells advances, the amount of urea rapidly diminishes, till only a fourth of the normal quantity may be observed, and it is then that leucin and tyrosin are most abundant, whilst the quantity of bile considerably diminishes; the pigment being only represented, the bile acids being usually absent; the dark colour of the urine observed at this stage being due to a very great relative and absolute excess of urates. Albumin may or may not be present in these cases.

The nature of the changes, in *chronic fatty degeneration* of the kidneys, is described in connection with the atrophic changes observed in chronic nephritis (p. 217).

106. **Parenchymatous Degeneration,** or as it is sometimes called, molecular or granular, consists in a "cloudy swelling" of the renal epithelium, similar to what is observed in acute tubal nephritis. Indeed most authorities consider the two conditions identical, and that cloudy swelling is the first step in acute Bright's disease. Professor Greenfield defines the relation between the two in perhaps a more exact manner, when he says, that whilst parenchymatous degeneration occurs at the onset of acute Bright's disease, and other morbid conditions, it is not the essence of the disease but only the common result of different processes. This "cloudy swelling" is noticed in those who have died of febrile diseases, such as pneumonia, typhus, enteric and scarlet fevers acute rheumatism, in which the temperature is raised for some time above the normal. It may give rise to no symptoms during life, though a trace of albumin is nearly always present in febrile urines, and which no doubt results from the disordered function of the renal

epithelium. It is interesting to observe in these cases how a rise in the temperature is followed by an increase of albumin in the urine. Cloudy swelling is also found in other specific diseases, giving rise to albuminuria as in cholera, diphtheria, erysipelas, etc.

The kidneys in febrile cases are more or less swollen, especially the cortex which is generally slightly congested and of a pinkish colour. The epithelium of the convoluted tubes is swollen and granular, whilst the epithelium of the straight tubes is rarely found to have undergone any apparent change.

Some, however, drawing their conclusions from the result of experiments on animals, in whom the pyrexial state was artificially induced, deny that renal hyperæmia is occasioned by the pyrexial state, but on the contrary they maintain the condition to be one of anæmia, and that instead of the kidney being slightly swollen it undergoes a diminution in bulk. This condition they consider is brought about by contraction of the walls of the blood-vessels, and is constant and progressive, being proportionate to the amount of the fever; the contraction of the vessels is brought about, they believe, by a stimulus originating in the central nervous system, probably the hot blood circulating there. This view has received considerable support, and is very ably stated by Dr. Mendelson in an article on the Renal Circulation during fever (*American Journal of the Medical Sciences*, No. 172, 1883).

107. **Calcareous Degeneration.**—In old persons, or in patients suffering from osteomalacia, deposits of carbonate of lime are often found in the straight portion of the urinary tubules, and in the inter-tubular tissue, giving rise to white streaks extending from the papillæ to the basis of the pyramids, very much re-

sembling the infarcts of sodium urate observed in the kidneys of newly-born infants, and the sodium urate in the kidneys of gouty patients. They are distinguished from these by effervescing when treated with dilute acid, and not giving the murexide reaction. The carbonate of lime is generally arranged in small nodular masses, in the form of small balls, and usually contains in addition some phosphate of lime mixed with organic matter. Another form of calcareous deposit, is described, as occurring in the walls of the renal vessels and surrounding fibrous tissue, which becomes infiltrated with a gritty material resembling sand.

Syphilitic Infiltration.

108. **Syphilis** is an important etiological factor in relation to the development of lardaceous disease (p. 301), but syphilitic deposits are not so common in the kidneys as in other organs. When met with they occur in roundish irregular nodulated masses rarely exceeding half an inch in diameter, situated in the cortex of the organ, they have a yellowish appearance, and are somewhat tough and hard, owing to caseous changes, yielding little or no fluid, though in an early stage they may be more gelatinous; they consist of a number of small cells imbedded in an obscurely fibrillated tissue. In the central portion the cells are for the most part broken down and converted into granular debris and fat granules, whilst the fibrillated tissue is scanty. The outer portion of the gumma is highly cellular, and the fibro-nucleated structure more evident, the cells are mostly small, like white blood corpuscles, whilst some are larger and nucleated; between the cells is a scanty homo-

geneous substance containing new blood vessels, which rapidly become obliterated as the process advances. The central portion of the growth may become calcified, but more usually the degenerated products are absorbed and nothing is left but the external fibrillated structure, which by contraction forms a fibrous cicatrix. These scars are generally present in the kidneys the seat of gummatous deposit and are evidences of previous formations, the kidneys too are almost always the seat of lardaceous degeneration. Syphilitic disease of the arteries of the kidney may be observed in association with gummatous growths or independent of them. Syphilitic disease of the arteries consists in the infiltration of the inner coat of the vessel with a cellular growth of small round and spindle-shaped cells, resembling ordinary granulation tissue, this infiltration of course diminishes very considerably the lumen of the arteries, and by interfering with the circulation leads to softening of the parts supplied by them. The obliteration of the new blood-vessels of a gumma is effected in this manner, and their destruction is followed by the rapid softening of the centre of the growth. Syphilitic disease of the kidney may exist without giving rise to any symptom; as, however, it is nearly always associated with lardaceous degeneration, albuminuria will generally be observed. Albuminuria, occurring in a person the subject of syphilis, requires specific treatment, for this purpose large doses of iodide of potassium are generally relied on, commencing with ten and gradually rising to twenty grains three times a day, but I have often known the albuminuria to continue till mercurial preparations have been employed. They must, however, be given with extreme care, since mercury is badly borne when the kidneys are the seat of waxy degeneration, the best plan is to give it in the form of grey

powder combined with Dover's powder, one grain of each twice a day, stopping it as soon as any tenderness of the gums is experienced and resuming it as soon as its influence seems to have subsided. In this way I have been able to maintain a course of mercury for several weeks, with most satisfactory results. With the mercurial, cod-liver oil and syrup of the iodide of iron should be given.

Scrofulous Infiltration.

109. **Etiology.**—Scrofulous inflammation of the kidney may occur at any period of life. According to Roberts it is most frequent during middle age. This is contrary to my experience, which would lead me to fix from twelve to twenty-five years of age as the epoch of life during which it is most likely to occur. But my cases occurred for the most part among sailors at the "Dreadnought," lads from training ships, and the inmates of a workhouse infirmary, which no doubt accounts for the difference. It is very much more frequent among males, for two reasons: first, because males are more exposed by their occupations to causes likely to set up inflammation; secondly, because in the male the liability of secondary extension from the generative organs is more frequent; whilst in the female, though scrofulous disease of the urinary organs may extend to the generative organs, it is an extremely rare event for scrofulous inflammation after attacking the generative organs, to involve the bladder and kidneys. The predisposition to scrofulous inflammation is no doubt usually inherited, though it is often difficult to trace a direct history; whilst the exciting cause is generally attributed to cold. Indeed, cold is the only cause alluded to by Roberts and Ebstein.

In cases, however, in which the disease was unilateral, I have known it follow on strumous deposit in the testicle and cord of the same side, in one case; after a blow, or strain of the loin, in two cases; after over-distension of the bladder for some hours, the result of compulsory retention, in this case there must have been some previous tubercular deposit in the bladder or prostate; and, in one case it followed immediately on the disappearance of an eczema affecting the inner sides of both thighs. This patient subsequently died of phthisis.

110. **Symptoms.**—When the kidney is the organ first attacked, the earliest symptoms are those of pyelitis, usually followed, sooner or later, by cystitis. There is pain in the loins, but this, unlike what occurs in calculous pyelitis, is rarely reflected downwards into the thighs or testicles, nor has it the paroxysmal character, being mostly dull, aching, and continuous. Should the pain become, at any time, paroxysmal, it is generally associated with a diminution of the amount of pus in the urine, and indicates a blockage, temporary or otherwise, of the ureter, on the side the pain occurs, with some of the cheesy mass. When the disease involves the bladder, symptoms of cystitis set in. No reliance, however, should be placed in mere increased irritability of that organ, since, as with renal calculus, a considerable degree of vesical irritability and even strangury may be present without the bladder being in any way diseased. The only reliable sign is the character of the urine, which from being acid and almost entirely purulent, may become alkaline, and the pus mixed with an excess of mucus. When the disease commences in the bladder, and then extends upwards to the kidney, it is often very difficult at first to determine that it has occurred, and it may indeed escape observation entirely. The enlarged kidney may usually

be felt in the loins and flank, though in ordinary cases if the ureters are free it rarely attains a large size. If, however, the passage of the purulent fluid be arrested, and pyo-nephrosis result, a considerable tumour may form. If the obstruction be temporary, the size of the tumour will vary inversely with the amount of pus and cheesy matter discharged. Manipulation of the swelling generally aggravates the pain. Fever of hectic character is always present, the elevations of temperature being ushered in by chills followed by sweating, whilst the apyretic periods are of irregular duration. Owing to the continuance of the fever, the patient rapidly emaciates, the skin becomes dry, harsh and branny; digestion becomes affected, and diarrhœa is easily provoked, and checked with difficulty. The urine from the first is always more or less turbid with pus, which comes away uniformly, or else in sudden discharges, according to the degree of obstruction in the ureter; and when the kidney is the sole seat of the disease, the reaction is mainly acid. Blood is usually observed during the early progress of the case, it is rarely, however, as excessive, or as constant as in calculous pyelitis, nor does it depend so closely on undue movements on the part of the patient. The epithelium of the pelvis of the kidney, in a swollen condition, can generally be recognised in the urine. Albumin is always present, being usually derived solely from the pus, and is proportionate to the amount discharged. In some cases, however, true albuminuria has been noticed preceding the onset of the disease; or as the disease progresses, diffuse nephritis, with the appearance of tube casts, may occur. The urine contains in addition to the pus and blood, much granular detritus, often fragments of cheesy matter insoluble in acetic acid. In these fragments the tubercle bacillus has been observed. Also occasionally when the

disease is advanced, elastic fibres from the destroyed connective tissue. When the bladder is affected the urine becomes muco-purulent, and an alkaline reaction generally developes.

111. **Diagnosis.**—Scrofulous disease of the kidney may be taken for calculous pyelitis, cancer of the kidney, or an hydro-nephrosis which has become purulent. If the bladder is also affected, chronic prostatic abscess may be mistaken for it. From the first it may be distinguished by the higher degree and character of the pyrexia, the less paroxysmal and radiating character of the pain, by the hæmaturia being less frequent and not following necessarily upon exertion. From cancer, by the abundant discharge of pus and by the pyrexia. From a hydro-nephrosis that has become a pyo-nephrosis, by the history of the case, by the hectic character of the pyrexia. The presence moreover in the urine of small portions of caseous matter, insoluble in acetic acid will in all cases when observed determine the diagnosis in favour of scrofulous inflammation; especially if the tubercle bacillus be likewise observed.

112. **Morbid Anatomy.**—The inflammatory process, which, in persons of a scrofulous habit, tends to the formation of cheesy masses, may commence at any point in the urinary tract. Thus the disease may begin in the papillæ of the kidney and by extension upwards destroy the pyramidal and cortical portion of the organ, and by invasion downwards the mucous surface of the pelvis of the kidney and the ureter, or the disease may commence in the bladder and spring upwards, involving successively the ureters, the pelvis of the kidney, and the kidney itself. When the disease is fully established the kidney presents a nodular and lobular appearance, the capsule thickened and adherent in places, whilst scattered over its surface are numerous cheesy deposits. On making a section of the organ

we find it converted into a thickened sac, irregularly divided by a few septa, all opening freely into the pelvis of the kidney. The kidney tissue may be completely destroyed if the disease is extensive and of long standing, but usually some remnants may be made out. In some cases, a fibrillated and granular substance, attended at a certain stage of its progress with the formation of masses of cells round some of the vessels, occurs in the cortex (*Path. Soc. Trans.*, 1875, p. 132). The pouches formed by the membranous septa are filled with yellowish cheesy masses, undergoing softening in the centre; or with a pultaceous fluid consisting of pus; broken down caseous matter insoluble in acetic acid; occasionally small cysts containing dark yellowish fluid of urinous odour, and containing pus cells, with triple phosphate and granular matter, may be observed. The mucous membrane of the pelvis of the kidney is greatly thickened with infiltrated caseous matter, and irregularly ulcerated where this has broken down. Portions of the destroyed mucous membrane, together with fragments of the subjacent connective tissue, are constantly removed by the urine. If the ureter is affected it will be found greatly thickened, and irregularly nodulated on its exterior, whilst its lumen is encroached upon by the deposit of tubercle in its walls; the mucous membrane may be ulcerated in patches and its upper portion widely distended by plugging of the canal by a portion of tubercular matter. Both kidneys were affected in forty per cent. of observed cases, in the remainder, the right and left kidney were attacked with about equal frequency. Roberts gives the right kidney as affected in seven cases, and the left in six; whilst Meckel declares the left to be more frequently attacked. The disease rarely causes great enlargement of the kidney, when this is the case, it is due to obstruction of the ureter, and the consequent

retention of the caseous and purulent fluid, so as to form pyo-nephrosis; on the other hand, if the destruction and removal of the caseous matter is rapid, the kidney may be only slightly enlarged, or may even be somewhat collapsed and shrunk.

113. **Treatment.**—The termination of these cases is usually fatal, either by the exhaustion caused by the original disease; more frequently by secondary tubercle in other organs. Dr. Roberts has expressed a hope, that if the tendency toward fresh formation of caseous material could be checked, evacuation of the deposit already formed in the kidney might occur, as is sometimes witnessed in the lungs, and quotes a case of Dr. Bennett's, in support of this view. In a case under my care a few years ago, of pyelitis of the right kidney, followed by cystitis, which existed several months, the urine after the formation and discharge of a pelvic abscess, cleared up, and presented nothing abnormal; nor had there been recurrence of the urinary affection, when he consulted me a few years subsequently for an affection of the chest, which proved tubercular. I have only the assumption to offer that the case in the first instance was due to scrofulous inflammation, having no opportunity of examining the kidney post-mortem, but the whole course of the disease indicated it, whilst he passed masses closely resembling caseous material during the progress of the renal affection. Indeed it was only the fact of the patient's recovery from the attack that shook my belief in the opinion I strongly held from the first, of the scrofulous character of the inflammation. It may have been a case in which the scrofulous material was discharged, as suggested by Dr. Roberts, from the urinary passages, whilst the inflammation in the pelvic cellular tissue, may have arrested further deposit taking place in the kidney or bladder. Such a termina-

tion, however, is extremely rare, though every such case encourages us to hope that by attention to the treatment of the tuberculous disease, a recovery may be effected. This is best effected by the continued administration of cod-liver oil, and iodide of iron, the pyrexia controlled as much as possible by cold sponging, and the employment of food as nutritious and digestible as possible, whilst any diarrhœa that may arise should be promptly checked. When the disease is limited to one kidney, and there is as yet no disease in other organs, the question of the removal of the affected organ should be discussed. Even if the organ is not removed, incision into the inflamed and thickened pelvis is a procedure likely to afford great relief; and lastly when the bladder is extensively affected cystotomy should be performed. In a case of mine, great relief was given by the operation, and though the patient ultimately succumbed, his life was undoubtedly prolonged by the operation.

Tubercular Infiltration.

114. **Tubercle** may be deposited in the kidney, in the general tuberculosis which invades many organs of the body simultaneously. It is, however, less rarely observed in the kidney, when only one organ is the seat of the process, than in the lungs, brain, spleen, etc. The tubercles are scattered throughout the kidney substance, being most numerous in the cortex, they appear as minute yellowish granulations, from about the size of a pin's head, to small yellow nodular masses, the size of a cherry-stone. The kidney tissue appears healthy, except that round the larger deposits, a reddish zone of congestion may be observed. The presence of tubercle in the kidney gives

rise to no symptoms. If there is much pyrexia there may be albuminuria, but that depends on the fever, as does also the concentrated condition of urine. Violent lumbar pains accompanied by severe rigors, occurring in patients already the subject of tubercular disease, may lead us to infer that deposition of tubercle is occurring in the kidney.

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CHAPTER VI.

New Growths in the Kidney.

Cancer.

115. **Etiology.**—Cancer attacks the kidney less frequently than any other organ of the body, though the statements regarding its infrequency are perhaps somewhat exaggerated. Cancer of the kidney, occurring as it does at the extremes of life, does not present itself so frequently at our general hospitals, as diseases affecting the kidneys during adolescence and middle age. It is met with rather in the hospitals set aside for the treatment of sick children, and in our workhouse infirmaries. In order therefore to obtain a definite idea of the frequency of renal cancer, the statistics of children's hospitals, and workhouse infirmaries should be incorporated with those of the general hospitals. In the following remarks, attention will chiefly be drawn to primary cancer of the kidney, which runs a definite course, attended with characteristic symptoms; whilst secondary cancer, the result of infection from primary cancer elsewhere, or of general cancerous manifestations, and which is rarely attended with definite clinical symptoms, will only be alluded to incidentally.

Cancer of the kidney is undoubtedly more frequent in the first and last decades of life, than at any other period. Out of 123 collected cases of primary cancer of the kidney, 45 occurred in children under ten; 19 cases in persons between fifty and sixty; and 25 cases between sixty and seventy; whilst only 24 cases are noted as occurring between

the four decades, between ten and fifty. Contrary to the usual experience of cancerous disease, renal cancer in adults is more frequent among men than women. It is difficult to account for this, for though men may be more liable to blows and injuries, still it might be thought that pregnancy, if it exercises the injurious pressure effect on the kidneys, that certain writers on renal disease contend it does, would place the sexes on a level in this respect. Dr. Roberts' supposition that cancer in the female prefers the generative organs to the kidneys, may therefore be correct. An hereditary predisposition can be traced in the majority of cases, especially in the more elderly, in children it may be absent, because as Sir James Paget has pointed out, the cancerous tendency has not yet declared itself in the parents (*Path. Soc. Trans.*, 1874, p. 317). Calculous disease of the kidney may induce cancer of that organ, since post-mortem we often find renal concretions in cancerous kidneys, though it is certainly not such a frequent clinical sequel as in the case with biliary concretions. A good clinical instance of cancer following calculus is given by Dr. Norman Moore (*Path. Soc. Trans.*, 1882), and also by Mr. Pollard in the Transactions for the current year 1885. Moveable kidneys, too, not infrequently become the seat of cancerous deposit. Blows and injuries are often referred to by the patients as having caused the disease. In some cases the blow seems to have rendered the disease—already present, but latent—active. In others, as in the case recorded by Dr. Brinton, in which cancer of the kidney appeared two years after a blow sufficiently violent to cause hæmaturia, it may be fairly attributed to injury. In a young sailor who died in my ward at the Seamen's Hospital, from primary cancer of the left kidney, no deposit being observed in any other organ, the only possible cause that

could be assigned was a strain received during reefing, when as well known sailors mainly support themselves by pressing the belly against the yardarm.

116. **Symptoms.**—The two characteristic symptoms, tumour and hæmaturia, depend as regards their prominence, mainly on the age of the patient, the nature of the cancerous growth, and the circumstances favouring its development. The earliest symptom is often the *hæmaturia*. It may be noticed before a tumour is felt in the loin, or pain is complained of. On the other hand the kidney may become much enlarged before the urine becomes bloody. According to my experience, hæmaturia usually precedes the detection of the tumour in elderly patients; whilst in children the presence of the tumour generally first draws attention to the disease. The *pain* may be very severe, but it is by no means a constant symptom, and many cases run their course without experiencing more than slight discomfort from the weight of the tumour, in others severe pain may be followed by a long period of quiescence. The *tumour* usually presents the following characters. In its growth it takes the path of least resistance, and tends forwards towards the navel, making its way upwards towards the hypochondrium, and downwards towards the pubes. In this direction it meets only with the soft and yielding intestines, instead of the firm lumbar muscles and fascia. The relation of the tumour to the intestines depends on its size. If small the natural position will not be much interfered with, but if the tumour acquires considerable dimensions, then the relative positions become somewhat altered. If the right kidney be enlarged, then the cœcum and lower portion of the ascending colon are pushed back to the outer side of the tumour, whilst the upper part of the ascending colon passes somewhat obliquely in front of it, the duodenal portion of the small intestine being pushed

over towards the navel. On the left side the descending colon lies well in front of the tumour, though if the enlargement be great it will be compressed, and may then only be felt as a thick cord passing somewhat obliquely over its surface. Owing to this relationship of the large intestine to the anterior surface of the tumour, a tympanitic note can generally be elicited on percussion over some portion of the tumour; though in some rare cases this may be absent, owing on the right side to the ascending colon being entirely pushed downwards, and on the left to the descending colon being so stretched and compressed, that on percussion it does not yield a tympanitic note. In this last case, however, it can be usually felt like a cord obliquely crossing the tumour. In some exceptional cases, the large intestines are found altogether behind the tumour, in these cases growth has usually been very rapid.

The cancerous tumour feels smooth, rounded and elastic, somewhat nodular, and irregularly hardened in places. It does not descend on deep inspiration, and is rarely moveable. Their elasticity sometimes leads one to suspect fluctuation, whilst many instances of pulsating tumours have been recorded, see case by Mr. T. Holmes (*Path. Soc. Trans.*, 1873, p. 149). These cases may be mistaken for aneurism. The largest and most rapidly increasing growths usually occur in children.

Hæmaturia, though a very constant symptom, is absent in about one-half the cases observed (Roberts, 28 times in 58 cases; Ebstein, 24 times in 50 cases). According to my experience, hæmaturia is more frequently absent in children than in adults. In elderly persons hæmaturia often precedes the tumour. Repeated urinary hæmorrhage, therefore, in old persons accompanied with loss of flesh, and in whose bladder on

careful examination no stone, growth, or enlarged prostate can be detected, should be regarded with suspicion. In these cases there may be no pain in the region of the kidneys, and the tumour may develop but slowly. Hæmaturia when present, follows no constant course. It may be present during the early stage, and then be absent for months, returning towards the end, or it may not occur at all till quite the later stage of the disease. Unlike the hæmaturia caused by renal calculus, it does not necessarily follow upon increased movement on the part of the patient, nor is it usually accompanied with increase of pain, unless a clot passes down the ureter, and gives rise to colic. The amount varies considerably, and though not always profuse or exhausting, it must be remembered that no disease of the kidney can give rise to such a profuse hæmaturia as cancer; especially if it has been excited by a blow or injury to the diseased organ.

The *urine* in cancer of the kidney is generally increased; it may be diminished by temporary obstruction of a ureter by a clot of coagulated blood, or temporarily obstructed by blockage of the urethra by a similar cause. It is rarely albuminous, except in connection with the hæmaturia. When albumin is constantly present, it shows that either nephritis or waxy degeneration co-exists. In some rare cases, pus has been observed in the urine. The older writers speak of the presence of cancer cells in the urine, but more recent investigations have proved this to be an error, the cells observed being probably the caudate cells of the pelvis of the kidney much swollen. Cancer cells might, however, appear in the urine, if a portion of the growth became detached, in which case the alveolar structure would be recognised as well. Disturbances of digestion are frequent in renal cancer, there is usually nausea and loss of appetite. In rapidly growing cancer,

however, there may be boulimia and thirst. Owing to compression of the colon, there is usually constipation, but diarrhœa is easily provoked, and when it sets in it is exceedingly troublesome to deal with. Cancer of the kidney, unless there be some complication, does not give rise to pyrexia. Renal cancer runs a more rapid course in children than in adults. In the former, few cases are recorded, extending over eighteen months from the first manifestation of the disease; in the latter, life may be prolonged for three or four years, cases giving even a longer period have been recorded. In forming an opinion, however, as to the probable duration of life in any individual case, account must be taken of the degree of cachexia existing, and whether other organs are implicated.

117. **Diagnosis.**—A cancerous tumour of the kidney may be taken for an enlargement of some other organ of the abdomen. The rules on which the differential diagnosis in these cases is based, have been already given (p. 8). When however, cancer of the kidney co-exists with cancerous enlargement of some other organ of the abdomen, the diagnosis becomes very difficult, if not in some cases impossible. Thus, in cancer of the right kidney with cancerous deposits in the liver and peritoneum, or of the left kidney with secondary deposits in the omentum. When ascites co-exists with renal cancer, the difficulty of diagnosis is undoubtedly increased, though unless the cancer fills the entire cavity of the abdomen, there ought to be no hesitation in distinguishing ascites from a tumour of the kidney. Enlarged masses of lymphatic glands in young children may be taken for renal cancer, they, however, are usually to be found on both sides of the abdomen, whilst renal cancer in children is almost invariably unilateral. Moreover, a careful consideration of the clinical

conditions ought to be a sufficient indication to prevent us mistaking a tabes mesenterica for cancer of the kidney. Other renal enlargements may be taken for cancer, such as hydatids, renal cysts, enlarged moveable kidney, peri-nephritis, and pyo-nephrosis. In the former, if the cyst has opened into the urinary passages, a careful and systematic examination will detect either vesicles or hooklets. If the cyst be intact, the more elastic feel, fluctuation, or fremitus if present, the absence of hæmaturia, and the fact that the patient's general health is but little impaired, usually enable us to exclude cancer. If is often, however, a matter of extreme difficulty to distinguish extensive and rapidly developing cystic disease of the kidney from carcinoma, if the growth be soft. As a rule, however, cancer has a more nodulated surface, and on manipulation, irregular, hard and soft patches can often be made out, whilst a cystic tumour is usually more elastic than a cancerous growth. In hydro-nephrosis and pyo-nephrosis, the intermittent discharge of watery urine or pus, generally enables us to form an opinion. Tumours, too, containing fluid, are usually more elastic, fluctuate, and are more globular than solid ones, moreover, whilst a solid tumour usually makes its way forwards, towards the navel, and then spreads equally upwards towards the hypochondrium, and downwards to the pelvis; the usual course of a fluid tumour is to extend towards the navel, and then more rapidly upwards, and more slowly downwards. An enlarged, painful, moveable kidney can be distinguished from cancerous growth of that organ by its greater movability, and the want of distension in the corresponding loin; whilst if the moveable kidney has acquired adhesions, and is fixed in its new place, then the latter sign can alone be relied on. It must not be forgotten, however, that moveable kidneys not infrequently become the seat of cancerous deposit.

118. **Morbid Anatomy.**—Primary cancer is almost invariably unilateral, secondary cancer bilateral. The frequency, when the disease is unilateral, with which the disease affects the kidneys is a matter of some dispute. Ebstein out of 54 cases found the right affected 31, and the left 23 times; Dr. Roberts in 60 unilateral cases found each kidney affected an equal number of times; whilst Klebs maintains the left kidney to be most frequently attacked; and Dickinson found 11 belonging to the left, and only one to the right kidney. My own experience is in accord with the last named observer, indeed, excepting moveable kidney and renal calculus, I have found in all diseases of the kidney, that are generally unilateral, a preponderance of cases in which the left kidney is affected.

A satisfactory classification of malignant growths of the kidney has still to be made.

Cancerous growths of the kidney originate either in the pelvis of the kidney, or in the kidney tissue proper.

1. In the former we meet with the ordinary villous growth, so common in the bladder, and which is regarded as a *papilloma*, whilst formerly it was classified as epithelioma. This form is always attended with profuse hæmorrhage. True *epithelioma* is extremely rare, Dr. Windle forwarded to the Liverpool Committee of the British Medical Association, who reported on "New Growths of the Urinary System," 1883, a specimen showing some squamous evolution, with slight bird's nest formation; Robin and Rindfleisch have each recorded a case. *Colloid* cancer springs also from the pelvic mucous membrane, as well as from the substance of the kidney. At Liverpool, an excellent specimen from Guy's Hospital was exhibited by Dr. Goodhart.

2. The cancerous growths of the kidney proper are

scirrhus, colloid, and encephaloid. The *scirrhus* growths are rare, and only one case has come under my notice, it was found post-mortem, and its existence was not suspected during life, as there was neither pain, tumour or hæmaturia, the patient died of chronic dysentery. The left kidney was affected, a portion of the organ presented a hardened yellowish-grey appearance, cutting with a fibrous section, yielding little juice on scraping, and the whole growth intersected by numerous bands. *Colloid cancer* of the kidney apparently arises from dilatation, and the infiltration of the Malpighian corpuscles with colloid material. It is rarely distinct, and is usually associated with other growths, especially with medullary cancer. *Encephaloid* or medullary cancer is by far the most frequent form of cancer met with in the renal organs, and is the variety that runs the most acute course, and also attains a considerable size. Tumours weighing 25 to 30 lbs. have been met with, even in young children, but these very large tumours are, however, generally of a mixed character; pure encephaloid growths rarely exceeding 12 to 15 lbs. Encephaloid cancer varies in consistence, in some places being soft and semi-fluid, in others harder portions are to be found even somewhat resembling scirrhus in firmness. The irregular softness and hardness often give to the tumour a feeling of fluctuation. It sometimes happens that one part of the tumour developes more rapidly than another, so that the growth becomes very irregularly shaped. The whole of the kidney is usually involved, but if only a portion is attacked, a fine line of connective tissue, will usually be observed dividing the renal tissue from the deposit. The secreting portion thus spared is, however, rarely quite healthy, the urinary tubules being usually enlarged and the epithelium undergoing granular degeneration. Owing to the abund-

ance of wide thin-walled vessels, often showing aneurismal dilatations in the growth, hæmorrhage is of frequent occurrence, so that these tumours have been called "fungus hæmatodes." Secondary deposits in other organs, especially in the liver, lungs and lumbar glands are most frequent with encephaloid cancer. *Mixed cancerous growths.* The most frequent is a mixture of encephaloid with sarcoma, Dr. Dowse (*Path. Soc. Trans.*, 1874) has recorded an example of this kind. Schueppel (*op. cit.*) describes a kidney weighing 28 lbs., which showed in part the characteristics of an encephaloid in a state of fatty degeneration, and in part those of an alveolar colloid carcinoma. Fatty cancer (carcinoma lipomatosum) has been described by Dr. Hilton Fagge (*Path. Soc. Trans.*, 1876). Under the microscope in the fresh state the growth showed large fatty globules, and looked as if only made up of fat. The fat globules, however, were really contained in the interior of cells of very irregular form, with large oval nuclei. Some of the cells were quadrilateral, some pear-shaped, and in some the form of the cells was cylindrical. Hardened with chromic acid, the section showed a portion of the growth to be composed of the characteristic structure of a carcinoma. This form is extremely rare, the only other description is by Cornil and Ranvier (*carcinome lipomateux*) who observed it in two cases, one being a carcinoma of bone.

Cancerous growths of the kidney generally form adhesions with the surrounding tissues, and so become firmly fixed. They may extend to neighbouring organs and compress and even perforate the intestines. If the compression of the intestines takes place rapidly we may have symptoms of acute obstruction. Enlargement of the right kidney has been reported as having caused dilatation of the stomach by compression of the duodenum (Ebstein). The renal

vein is also generally involved, and in this way the growth may reach the inferior vena cava or even the vena azygos, portions of the growth are thus liable to be carried into the circulation. When the disease originates in the pelvis of the kidney it may spread to the renal tissue, and *vice versa*.

119. **Treatment.**—The treatment can be only palliative, though my colleague, Mr. McCarthy, recently removed a carcinomatous kidney, weighing 2 lbs. 5 oz., in a man aged 45. The operation was performed on March 18th, and by April 13th the wound was healed and the patient sitting up. The patient must be placed under the most favourable conditions as regards food, rest, pure air, etc. Pain, if present, relieved by morphia injections. The hæmaturia is best controlled by gallic acid, given in ten grain doses every four hours during its continuance, and if very active by the application of ice in a bladder to the abdomen. Ergot combined with iron may be employed if there is repeated hæmorrhage associated with great pallor. The tumour if large should be prevented from dragging as far as possible by the careful application of a flannel roller to the abdomen. Constipation, which is often such a distressing complication, must be overcome with the greatest care, since purgatives even in moderate doses, often excite the opposite extreme, and lead to a profuse diarrhœa most difficult to check. Castor oil, colocynth, and saline purgatives, had best be avoided, whilst enemas aided with a pill composed of grey powder and rhubarb, are undoubtedly the safest, and as an effectual means as any for the relief of this form of constipation. If the clots and coagula formed by the hæmorrhage are retained in the bladder, they must be removed as speedily as possible by gently washing out the bladder.

Miscellaneous Growths.

120. **Sarcoma.**—Many of the tumours formerly described as cancerous, would now undoubtedly be classified as belonging to this class of new formations. The sarcomata are tumours, consisting of the progressive formation of connective tissue, which retains throughout its growth its embryonic state. The sarcomata are divided into three varieties, according to the form of the cells, round, spindle or fusiform, and myeloid. According to the Liverpool Report on new growths of the urinary organs (*Brit. Med. Jour.*, Jan. 12th, 1884), these growths have been classified as congenital and adult, since it was felt that a distinction should be drawn between a growth distinctly the result of a developmental error, and one, which arising later in life, might have a different source. Congenital sarcomata are by far the most frequent, as may be imagined from their typical origin, and invariably prove fatal during the first few years of life. They are encapsuled growths, but as they increase, there is a tendency to general infiltration. They are either extra-renal, spreading from without, generally from the neighbourhood of the hilus, to the substance of the kidney, or sub-capsular, originating immediately beneath the capsule of the kidney. The extra-renal variety is usually round-celled, and both kidneys have, in the majority of cases recorded, been involved. Dr. Abercrombie has recorded three examples (*Path. Soc. Trans.*, 1880), of sarcomatous growths invading both kidneys from without; in all three cases, the pelvis of the kidney was enlarged, the lining membrane being red or purplish, whilst without near the hilus, a new growth, mainly composed of loose connective tissue, with masses of small round cells, interspersed in the masses

was observed pushing its way towards the kidney. The sub-capsular growths may consist of round or spindle cells, or both mixed. Mr. Paul, in the report already alluded to, thus describes a specimen of his own, consisting of two kidneys, weighing twelve ounces, from a seven months' fœtus. Externally they appeared quite normal, and when the capsules were stripped, the surface was kidney-coloured and minutely lobulated. On section, the medullary portion of each was made up of lobules of white new growth, and the cortex was mottled by the same; but there remained, at least, twenty to thirty times the normal amount of renal tissue. Under the microscope, this renal tissue was more embryonic in character than that of a fœtus of full time, but it is doubtful whether it is the correct equivalent for a seven months' fœtus. The lobules of white growth consisted mostly of round cells, but in many parts they arranged themselves as though attempting some higher evolution. The same report also furnishes an account from Dr. Osler of Montreal, of a specimen taken from an eight months' fœtus, in which both kidneys were equally enlarged, and which like the preceding case has been classed as an *adeno-sarcoma*, the description is as follows:—"On microscopical examination at the cortex, the tubuli uriniferi and Malpighian bodies were easily distinguished, but separated by much interlobular tissue, composed largely of spindle cells. Towards the pelvis, the entire substance was made up of these spindle cells closely compressed together, and amongst them coils of epithelial cells, some resembling dilated tubuli, others irregularly shaped Malpighian capsules. The sections showed many irregular small and large spaces (cysts) through the entire substance."

Virchow has described a variety of very small round-

celled sarcoma (glioma) as springing from the neuroglia of the nerves of the kidney. They appear as small translucent knots in the cortical part of the kidney.

Myo-sarcomata are sarcomata containing muscular fibres of an embryonic character. Of the recorded cases that have come under my notice, the disease has been unilateral and bilateral in an equal number. The case reported by Dr. Dawson Williams (*Path. Soc. Trans.*, 1882, p. 317) may be taken as a typical example of this kind of growth, and will serve best for a general description. The tumour, together with the left kidney, the ureters, and the bladder, were removed *en masse*. Section of the tumour revealed a smooth, indistinctly lobulated surface, of a general yellowish-white hue, but with pinkish mottlings; the consistency was everywhere soft, and towards the upper part the substance was almost diffluent, so that after the specimen had been washed a ragged-walled cavity was left. The right ureter could be traced into the tumour, and a director passed along it led into the mass. No vestige of the natural kidney substance could be distinguished by the naked eye. The tumour weighed 1 lb. 13½ oz., equivalent to about one-sixth of the total body weight. Sections made through portions of the tumour taken from various parts and hardened in bichromate of potash showed an unusual structure. The greater part of each field was occupied by fibrillated bundles; these bundles were made up of cylindrical fibres, having a direction generally parallel to each other, but the bundles were arranged in the most diverse planes, crossing and intersecting one another at every angle; tracts of small-celled tissue, chiefly of the spindle-shaped variety, were also encountered, as well as sections of the kidney tubules, and in one or two instances masses which were regarded as altered Malpighian bodies. Being at a loss to under-

stand the nature of this fibrillated structure, some of the sections were submitted to Dr. Klein, and he immediately expressed his opinion that they were composed of muscular fibres of the voluntary type. Mr. Frederick Eve's account of specimens of tumours, composed of stripped muscle and sarcoma tissue from the kidneys, in the same volume of the *Pathological Transactions* (1882), gives an excellent description of the general characters presented by these tumours.

Melanotic Sarcoma.—These growths no doubt from their high degree of malignancy were formerly regarded as carcinomatous, there is now, however, but little doubt that the majority of specimens, if not all of them, are sarcomatous. The prevailing character is the spindle-shaped cell, though round or oval cells may be present, the pigment, melanin, is deposited within the cells. This pigment at first has a brownish colour, but rapidly acquires an inky blackness on exposure to air. The pigmentation is generally very unequally distributed. Melanotic sarcoma of the kidney in adults is usually secondary to deposits in other organs, in children it may occur as a primary affection and then is congenital.

121. **Adenoma.**—Adenoma of the kidney, owing to the smallness of the growth, may escape observation, and this has probably given rise to an idea that they are rare. In the report (*Brit. Med. Jour.*, Jan. 12th, 1884) already referred to, two varieties are recognised, the one tubular, the other intra-cystic. The former consists of tubes, much like convoluted renal tubes, but larger, and containing more epithelial cells; the latter has a villous appearance, the stalks being clothed with a single layer of cubical epithelium. They are almost invariably bilateral, and generally multiple, and rarely exceed the size of a pea. Many new growths of the kidney, however, are accom-

panied by an increase of the gland tissue, and an adenomatous appearance is given them, thus we may have an adeno-sarcoma, adeno-myxoma, adeno-carcinoma, etc.

122. **Lymphadenoma** of the kidney occurs as part of the general disorder, deposits of a similar nature being found in the lymphatic glands elsewhere. The deposit which is of a yellowish-white colour is distributed through the kidney, especially in the cortex, and occurs in irregularly ovoid masses, from the size of a mustard seed to that of a bean. They consist of a fibrous net-work, blended with the interstitial tissue, in which are dispersed numerous lymph corpuscles, some of these are granular and contain no nucleus, others, larger, are multinuclear. A very good description of this affection is given by Dr. Coupland (*Path. Soc. Trans.*, vol. xxviii.). *Leucæmic growths.*—The deposits consist of an accumulation of white corpuscles and a delicate net-work of lymphoid tissue, distending and enlarging the blood-vessels, giving rise to small marrow-like masses, varying in size from a poppy seed to that of a hazel nut. They are also part of the general disorder, and when met with in the kidney are found as well in the spleen and liver.

123. **Lobulated Fatty growths,** apparently originating from the capsule of the kidney, are occasionally met with. They have been mistaken for multiple supra-renal capsules. The whole organ may be transformed into a fatty mass, or only a portion. In the majority of instances some other lesion exists, generally of a calculous nature. A case of this kind is reported by Dr. H. Browne (*Path. Soc. Trans.*, vol. xii., p. 132), by Dr. Whipham (*Path. Soc. Trans.*, vol. xix.), and by Dr. Rickards (*Brit. Med. Jour.*, July 7th, 1883); whilst in Mr. Heath's case (*Path. Soc. Trans.*, vol. x.) the renal artery was obliterated. Fatty growths may also arise from the pelvis of the kidney.

Extra-renal fatty tumours, springing from the outside of the capsule, or originating from the adipose cellular tissue surrounding the kidney are by no means infrequent; in most of the cases the organ is atrophied by the pressure. These fatty growths of the kidney, which are comparatively common, must not be confounded with that extremely rare affection we have already spoken of (p. 348), carcinomatous lipoma.

Fibroid tumours are occasionally met with, either as small fibromata, in the form of small nodules composed of dense fibrous tissue in which may be found atrophied urinary tubules; or as large fibro-cartilaginous growths, which evidently originate from the fibrous tissue of the capsule, and by their growth, gradually destroy the renal tissue. Some of these tumours, which may attain the size of a cocoa-nut, have a somewhat cystic appearance, caused by the distension of the pelvis of the kidney.

CHAPTER VII.

Parasites in the Kidney.

Hydatids.

124. **Etiology.** — Echinococci cysts are about five times less frequent in the kidney than in the liver. As regards the lungs, an equal frequency subsists; whilst with respect to the other organs and tissues, the kidney is more often the seat of the disease. The tendency to the disease is very marked in some countries, as in Iceland, South Australia, and in some parts of Germany and Silesia. In these countries the disease seems to be transmitted by means of dogs, who harbour the tænia echinococci in considerable numbers. In Iceland and South Australia the agricultural class live in close contact with their dogs, whilst in Silesia it is probable that the disease may be actually communicated by eating dog's flesh, a practice often resorted to by the poorer classes. It is said that the disease is more frequent in man than in woman, but discordant statements have been made with regard to this point. In Iceland it is said that every seventh person dies of hydatid disease of some organ or other. When the kidneys are attacked, the disease is usually unilateral, the left kidney being the one most frequently affected.

125. **Symptoms.** — Unless the cyst ruptures at an early date a tumour will slowly form; this may attain the size of an orange or cocoa-nut. It presents the character-

istic relations of renal tumours generally (p. 8), and by this means it can be distinguished from enlargements of other organs. It is usually more rounded than other tumours of the kidney, often fluctuates obscurely, rarely distinctly, whilst fluctuation is sometimes absent. Occasionally the so-called "hydatid fremitus" can be made out, and when present it is a distinctive sign. To elicit it, the fingers of one hand are to be laid on one side of the tumour, whilst a sharp percussion stroke is given with two fingers of the other hand to the opposite side of the tumour. The fremitus may also be distinguished by the stethoscope when the tumour is sharply struck. It is said that the note is only obtained when the cyst contains many vesicles, but is often absent even in this condition. If any doubt exist as to the nature of the contents it can be solved by the introduction of the aspirating needle and the examination of the fluid withdrawn. This is clear, usually alkaline, sometimes neutral, never acid, nor urinous. The specific gravity is about 1·009, never below 1·006 (Bartels); never contains albumin unless the cyst has become inflamed; hooklets and vesicles are generally to be found in the fluid, but may be absent.

When the tumour bursts and discharges into the urinary passages, the contents are evacuated by the urine. In the majority of cases, vesicles and hooklets will be passed, in others only an opalescent looking fluid in which a few scattered hooklets will be observed on carefully examining the deposit. The passage of the vesicles occurs at irregular intervals, and usually occasions much pain, whilst the urine for the time often becomes bloody and purulent, in fact giving rise to all the symptoms of renal colic. The vesicles may be sufficiently numerous to block the urethra, and so give rise to retention of urine; or a vesicle may become impacted in the ureter and so

cause for a time a condition of hydro-nephrosis. After a discharge of vesicles the tumour usually diminishes, unless the above accident happens, and recovery may take place at once, or after a few more discharges. In some rare cases a fresh discharge has occurred after the lapse of two or three years, probably due to a secondary formation. Sometimes, however, the cyst suppurates and this condition is attended with fever, which is always absent in uncomplicated cases. Rupture of the cyst often occurs suddenly, after a blow, a strain, or prolonged exertion. Sometimes it is preceded for some days, by an increase of pain, and discharge of blood. The duration of the disease is very variable, but it usually runs a favourable course, far more so than in other organs. About fifty per cent. of the cases recover, after spontaneous discharge of the contents of the cyst by the urinary passages. About twenty-six per cent. recover after tapping or other surgical operations; whilst about thirteen per cent. of the cases are fatal. These are caused either by the suppuration of the sac, the most frequent cause of death; or by rupture of the cyst internally into the abdomen or cavity of the thorax. In some rare cases calcification of the cyst may occur. Lastly, in about eleven per cent. of the cases no statement is made with regard to the ultimate issue. Dr. Roberts records a unique case, comprising a series of misadventures—the patient had only one kidney, that kidney became the seat of an hydatid cyst, the cyst burst and was discharging itself through the pelvis of the kidney, when unfortunately a calculus blocked the way and prevented the vesicles from passing, fatal retention of urine ensuing in consequence.

126. **Diagnosis.**—Hydro-nephrosis is the disease of the kidney most commonly taken for a renal hydatid cyst. The previous history of the case, in the majority of in-

stances, will enable us to distinguish between the two affections, otherwise in the absence of distinct "hydatid fremitus" a differential diagnosis cannot be made without withdrawing some of the contents of the tumour, when an analysis of the fluid (p. 321) will declare its nature. Hydatid tumour of the kidney is distinguished from other enlargements of the abdominal and pelvic viscera by the same principles as regulate the diagnosis of all renal enlargements (p. 8). It may be taken for an ovarian tumour, especially when the hydatid tumour developes downwards into the pelvis. By bearing in mind, however, the relation of the bowel to the anterior surface of the tumour, and by an examination by the rectum, and also by compression of the ureters, this error ought to be avoided.

The discharge of echinococcus vesicles and hooklets (figs. 31, 32, 33) into the urine, especially if a well-defined renal tumour is present, and the discharge is attended with symptoms of renal colic, is an undoubted proof of the existence of hydatid disease of the kidney. In some rare cases, however, hydatids of the abdominal viscera may open into the urinary passage, and discharge hooklets and vesicles, without there being hydatid disease in the kidney. According to Murchison, however, no case of hydatid tumour of the liver, has ever taken this direction.

127. **Morbid Anatomy.**—The parasite, that gives rise to echinococci cysts, is a small tri-segmented cestoid worm *(tænia echinococcus)*, which infests the intestines of dogs and wolves. They do not exceed a quarter of an inch in length, and the last joint alone contains ova. These ova received into the intestines develop embryos, which at the time of emergence from the egg, are minute ovoid bodies, about the size of the red corpuscle of the frog's blood. The embryo penetrates the tissues and organs, and forms cysts. This cyst when developed consists of a firm

fibrous capsule, about $\frac{1}{10}$ inch thick, intimately connected with the tissue of the organ, and highly vascular. Within this is a jelly-like translucent membrane, of laminated hyaline structure—this is the so-called "mother vesicle." This membrane apparently consists of a body yielding collagen, for on boiling, a peptone-like body is formed and which has a slight reducing action on alkaline solutions of cupric sulphate. This sac holds the clear limpid fluid, and unless the cyst is barren contains numerous "daughter vesicles," these develop from the walls of the mother cyst but soon separate, so that in examining the contents of an hydatid tumour we meet with some vesicles still attached (fig. 30, No. 1), whilst others are found floating free

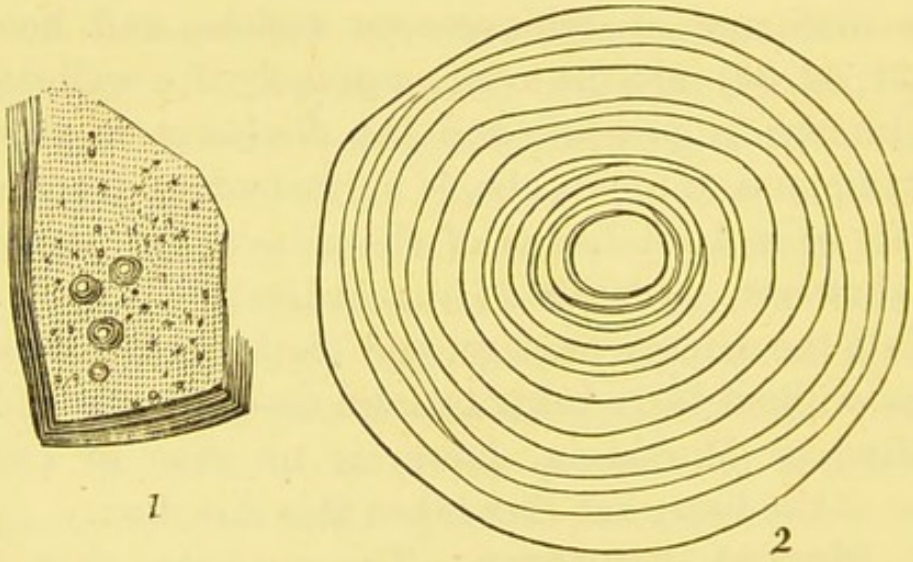


FIG. 30.—Hydatid found in man. 1. A fragment of the natural size; at its edges are shown the layers of which it is composed; on the external surface are several hydatid germs of different periods of development. 2. One of the germs flattened and magnified forty times, showing the stratified layers.

(figs. 31, 32). Some of these daughters attain a considerable size, they may range from a pin's head to a goose's egg; the largest, however, contain smaller vesicles and these again others, so that one sac may contain four genera-

tions. These vesicles being discharged from the body either of man or cattle, for oxen and especially sheep are subject to hydatid disease as well as man, find their way into the intestines of the dog, usually by eating the offal of

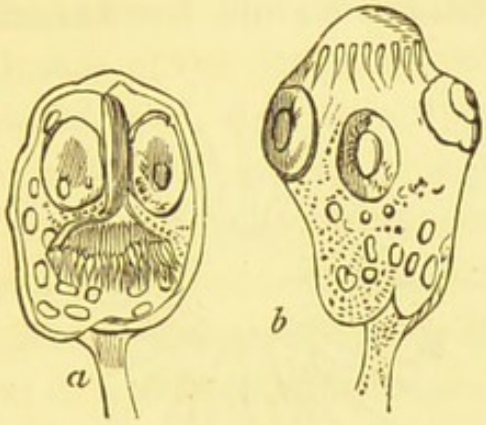


FIG. 31.—*Echinococci* or "daughter vesicles" from a hydatid tumour. The one (*a*) has the head retracted within the vesicle; the other (*b*) has the head extruded.

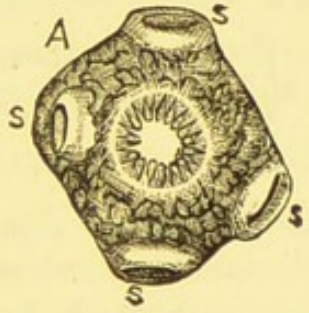


FIG. 32.—(A.) An *Echinococcus* viewed transversely, the head being directed towards the observer; s, s, suctorial discs.

slaughtered cattle, and there develop into the fully formed tænia. The proglottis or terminal segment which alone contains the ova, is discharged from their intestines this finds its way to the food of man, or on to the herbage in the case of cattle, again passes through the encysted state as a hydatid and so the circuit is constantly being renewed.

128. **Treatment.**—When the cyst has ruptured, and the vesicles are being freely discharged from the bladder, there remains little for us to do but to watch the progress of the case. The abdomen should be firmly bandaged, and gentle friction employed over the tumour to aid their escape. The patient should be warned against undue

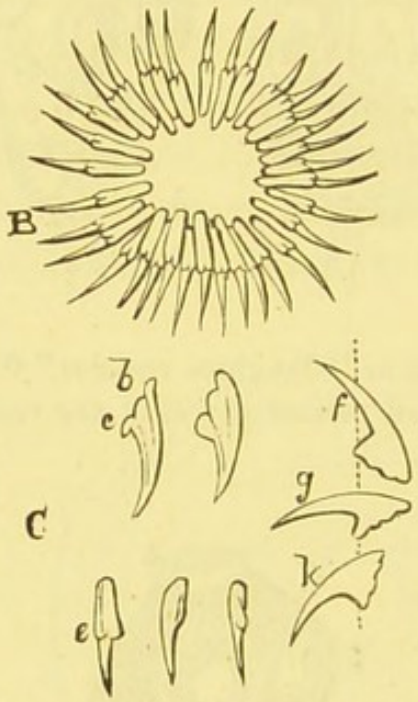


FIG. 33.—(B.) The circle of hooklets seen upon its under surface; thirty-four in number, seventeen long and seventeen short. (C.) *b*, *c*, Lateral views of the separate hooklets—*b*, the base; *c*, the central extremity or bifid process of the base; *e*, hooklets viewed upon the concave or inferior border; *f*, *g*, *k*, a diagram illustrating the movements and position of the hooklets.

exertion, or engaging himself in any occupation, likely to cause strain during their discharge, in case suppurative action be excited, or even rupture of the discharging cyst caused. As diuretics have been found to assist the discharge of the vesicles, these remedies may be administered, and if there is much pain from colic during their passage sedatives should be combined with them, indeed a small

quantity of opium, by relieving spasm, not only soothes the the irritation, but facilitates their discharge. When the cyst is intact, or if after it has burst, the escape of the vesicles is prevented either by the presence of a renal calculus, or impaction of the vesicles themselves in the ureter, the contents should be evacuated without delay. For though the chance of the cyst ultimately bursting into the urinary passages, and thus effecting a spontaneous cure is very great, still it is not fair to expose the patient to the chance of rupture in some untoward direction, and which may be unexpectedly occasioned by some unlooked for accident. It is generally sufficient to tap the tumour in the positions indicated at p. 323, with a large aspirator needle, and then to evacuate the contents. If there be many large "daughter vesicles" containing other daughter vesicles these may not escape, but usually puncture of the mother cyst is followed by their death and absorption. Galvano-puncture has been advised and many successful cases published, but it presents no advantages over aspiration, and if by-chance the needles are not sufficiently insulated, suppuration may be excited. Should the sac become inflammed and suppurate recourse must be had to free incision and drainage tubes.

To prevent the extension of the disease in districts where it has become rife, the following rules laid down by Murchison should be followed.

a. To prevent dogs feeding on the offal of sheep and of other animals infested with hydatids. Dogs ought to be rigidly excluded from all slaughter-houses or knackeries, and "dog's meat" ought always to be thoroughly boiled.

b. To destroy, as far as possible, the tape-worms generated in the dog, for which purpose it would be well that all dogs were periodically physicked, and their excreta buried in the ground or burnt.

Vermifuge medicines have, however, but little effect; but it is said, allowing cattle the free use of rock salt is prophylatic and powerfully checks the extension of the disease among flocks. It probably acts on the newly introduced ova, by hardening their envelopes, just in the same way that injections of common salt destroy thread-worms in the lower bowel.

Bilharzia Hæmatobia (Endemic Hæmaturia).

129. **Etiology.** — The Distoma Hæmatobium, now named Bilharzia, in honour of its discoverer Bilharz, was first found in the urinary passages of some Egyptians, whose diseases Griesinger was investigating. So common is it in that country, that Griesinger found it to exist in 32 per cent. of all the post-mortems he made. Since then it has been found to be prevalent among the residents of the Cape of Good Hope, South-East Africa, the Mauritius and in some other hot countries. Owing to our increased intercourse with these countries, and the tendency of Europeans to return home when invalided, instances of this disease in England are by no means infrequent. Besides inhabiting the urinary organs, especially the bladder and prostate, it is also found in the intestines and portal veins.

The Hæmatobium is a small trematode bisexual entozoon. The male, which rarely exceeds $\frac{1}{3}$ inch in length, is shorter and broader than the female which is more filiform, and may attain to nearly $\frac{3}{4}$ inch. They bear two suckers. The male possesses a long canal in its upper half in which the female is partially inserted during copulation. The ova, which are diagnostic of the disease, are oval shaped, being about $\frac{1}{200}$ inch long and $\frac{1}{600}$ inch in width, and

prolonged into a peak or spine at the anterior end of the capsule; according to Dr. Zincarol (*Path. Soc. Trans.*, 1882) the ova from the intestines have a lateral instead of an an-

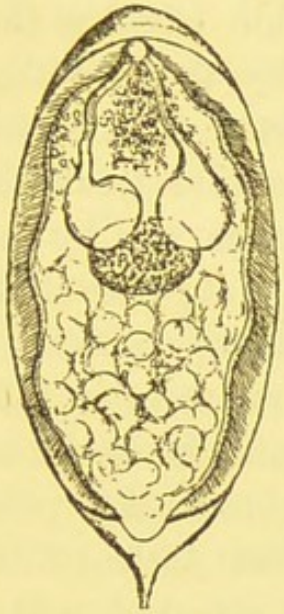


FIG. 34.—Ripe egg containing embryo (Harley).

terior spine. The enclosed embryo (fig. 34) escapes by a kind of dehiscence, and at once commences very active

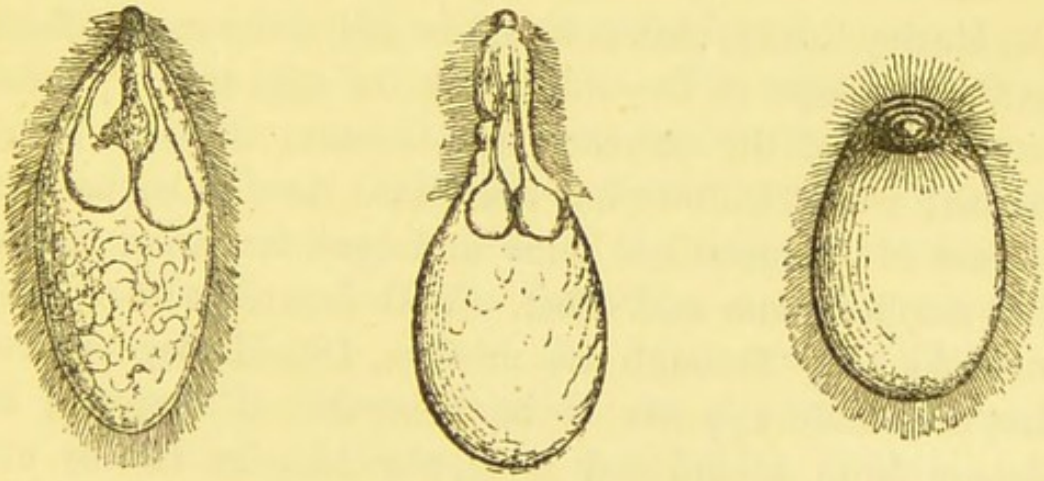


FIG. 35.—Various forms assumed by ciliated embryo (Harley).

rotatory and vermicular movements, assuming various shapes (fig. 35) cylindrical, elliptical, flask-shape, etc.

Dr. J. Harley, who has succeeded in hatching the embryos from eggs, observed that after swimming actively about for two or three hours the motions gradually ceased and the animal died, and that after death the cilia were rarely visible. It is a question whether the parasite reaches the body by the skin, by the mouth, or by the urethra. Dr. Harley is in favour of the first two suppositions, and thinks that a minute leech-like animal fixes itself on the skin of a bather, and by means of an ovipositor implants the ova in a superficial vein, during the hatching process, the irritation attending the movements of the free embryos would result in an indolent form of ulceration, and the little animals would be carried by the circulation from the ankle to the pelvis. As a matter of fact, residents in South Africa, during the first year or two, are liable to be attacked with large indolent sores, leaving scars like syphilitic ulcers. This applies to the rural population who are obliged to use river water, or water from pools and marshes; the townspeople who use stored rain or well water being rarely affected by the disease. If such a mode of infection be possible, it may be assumed, Dr. Harley thinks, that it would be still more easily affected by the passage of the animal or its eggs to the mucous membrane of the stomach and rectum directly by the mouth; whilst Bilharz has associated the similar parasitic disease of the intestinal veins and dysentery in a manner that implies cause and effect. With regard to its entrance into the body through the urethra, Dr. Harley observes that a female appears to be incapable of receiving the disease from an infected male, nor has Dr. Harley ever observed the liberation of a living embryo from the egg, when immersed in urine, or even an active living embryo. It is therefore probable that the propagation of the parasite takes place in the mucus of the urinary passages, and that

the ova which escape into the urine are retarded in their development, and ultimately perish.

130. **Symptoms.**—The parasite invades the intestines and the branches of the portal system, where it gives rise to a peculiar form of dysentery; also the mucous surface and minute vessels of the bladder, ureter, and kidney. The mischief occasioned in the genito-urinary organs is, however, far greater than when the intestinal tract alone is affected. The urine in these cases has been thus described by Harley. Pale amber coloured, sp. gr. 1·017, depositing a layer of dirtyish-white flocculent matter, containing short filaments of $\frac{1}{35}$ of an inch in diameter, of brownish colour and soft consistence, shorter and wider fragments of the same substance, a little reddish mass like a little clot of blood, and numerous white specks. This deposit, examined microscopically, contained pus corpuscles; and the filamentous bodies contained, imbedded in them, great numbers of bright highly refractive bodies, which were identified as the ova of the Bilharzia. The urine also generally contains traces of albumin, uric acid, urates, and oxalate of lime. In addition to the reddish-white deposit, pure blood is sometimes voided with the last drops of urine. The patient becomes anæmic and thin, and the general health rapidly fails if the disease is long continued. Severe cystitis, pyelitis, and disseminated suppuration of the kidneys, sooner or later supervene, and if the intestines are also affected dysenteric discharges add to the exhaustion. The ova not infrequently, when imbedded in a plug of mucus, form the nucleus of a stone in the bladder, and the frequency of stone among the natives of Egypt is no doubt attributable to this circumstance.

131. **Morbid Anatomy.**—The Bilharzia chiefly affects the bladder, and in many cases the disease is fortu-

nately limited to it, when it extends to the kidneys the condition of the patient becomes very serious. On examining a bladder that has been the seat of the disease, we find it hypertrophied with thick hard walls, patches of ecchymosed swollen mucous membrane, studded with small branched mucoid vegetations, and incrusted often with phosphatic deposits. Under the microscope, sections show the ova of the Bilharzia in the deeper layers of the mucous membrane, and also, but in smaller numbers, in the submucous tissue, and in the fibrous tracts between the muscular bundles. When the ureters and the pelvis of the kidney are attacked, their diameter becomes narrowed at the point affected, and may thus give rise to hydro-nephrosis or pyo-nephrosis, whilst the kidneys are hyperæmic and may become the seat of disseminated suppuration.

132. **Treatment.**—When the disease is limited to the bladder, good results have been obtained by Dr. Harley by injecting the bladder by means of a solution of potassium iodide, commencing with three up to five grains to the fluid ounce; this injection is to be retained for three hours. Beyond the nasal and catarrhal symptoms, and the iodine taste, the drug never produces the slightest urethral or vesical irritation. The first effect is to bring away branched mucous casts of the tunnels formed by the parasite, with hosts of imbedded eggs. Attached to these casts certain so-called "colloid corpuscles" are often observed, sometimes singly, sometimes in groups. The largest of these resemble minute grains of tapioca, possessing a jelly-like transparency and faint amber tinge. Dr. Harley thinks these corpuscles are derived from the prostate. These casts after a time lose their cylindrical character and are replaced by long skin-like membranes almost destitute of ova, whilst at the same time the ova dis-

appeared from the urine. When Dr. Harley's patient left England he still passed a few ova, not however in masses of mucus but in soft blood clots. When, however, the disease extends to the ureters and pelvis of the kidneys, this local treatment, though it should be directed against the parasite in the bladder, is of no avail, and internal remedies must be employed, of these quassia, extract of male fern, and turpentine, have been tried, and under their administration, quantities of ova have been brought away. To these I would suggest the continued use of biborate of soda, solutions of which have a poisonous influence on the ova of most parasites, whilst as a medicine it can be given without any disturbance to the patient's general health, and is one of the few remedies that pass unchanged through the system into the urine. It has also another advantage, in relieving the cystitis and pyelitis if present, and by dissolving deposits of uric acid on the ova, diminishes the chance of the secondary formation of calculous deposits. The following draught administered three times will be found very useful as an adjunct to the topical treatment. Biborate of soda, gr. xv., Chian turpentine, gr. x., acacia mixture, ʒ ii., and chloroform water, ℥ i., to which opium in some form may be added, if there be much pain or irritability of the urinary passages.

The prophylactic recommendations consist in ordering all water used for drinking in the countries liable to the disease, to be boiled and filtered, and raw salads and molluscous animals to be avoided. Dr. Harley also rightly insists on the drinking water being conveyed in covered channels and kept distinct of all sewage communication, so that the urinary and fæcal products of those infected with the disease may not be accidentally mixed with it.

Filaria Sanguinis Hominis.

133. **Etiology.**—The small worms which are so often found in the blood of patients suffering from tropical diseases, were first discovered by Lewis in 1872, and named by him filaria sanguinis hominis, are the embryo of a nematode worm discovered four years later by Bancroft, and which has been named after him *filaria Bancrofti*. As these parasites are supposed to have a special relation in the causation of tropical hæmato-chyluria, and as they appear in the urine in these cases, they are entitled to a full description under the head of renal parasites, and both they and chyluria may well be described together. The parent worms according to Dr. Manson (*Path. Soc. Trans.*, 1881) inhabit the lymphatics of the body, the two sexes probably living together. Only a small part of the male worm has hitherto been found, it is considerably smaller than the female. The latter is a long, slender, hair-like animal, quite three inches in length, but only $\frac{1}{100}$ in breadth, of an opaline appearance, looking as it lies in the tissues "like a piece of catgut animated and wriggling." A narrow alimentary canal runs from the simple club-like head to within a short distance of the tail, the remainder of the body being entirely occupied with the reproductive organs. As fully formed embryos can be seen under the microscope escaping from the vagina, it is supposed that under ordinary circumstances the animal is viviparous. The parent filaria thus lying in a lymphatic channel emits her embryos into the lymph stream. The embryo is a long, slender, snake-like animal, averaging from $\frac{1}{75}$ to $\frac{1}{92}$ of an inch in length, and $\frac{1}{3153}$ of an inch in breadth, perfectly transparent and apparently structureless (fig. 36). The anterior part of the body

tapers slightly, and at its extremity a pouting movement as if of breathing is to be noticed; posteriorly the body tapers down to a fine point. It is covered by a delicate sheath about one-third longer than the body, so that it is never fully occupied by the animal, and forms a lash-like projection (fig. 36, *c*) at the head or tail or both,

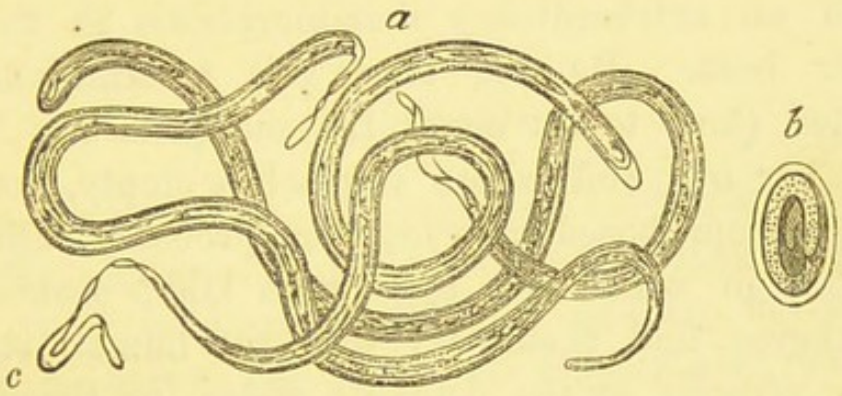


FIG. 36.—*a*. Filaria Sanguinis Hominis. × 250. (After Lewis).
b. Ovum. × 250. (After Cobbold).

according to the movements of the animal—the lash always trailing behind. One of the most remarkable phenomena connected with the disease, is that the embryos disappear from the blood stream and reappear at certain periods of the day. Thus they are absent during the day and are present at night, the greatest number being observed at midnight, whilst by 3 a.m. a sensible decline is observed, and by 9 a.m. they have quite disappeared except an occasionally belated straggler. At 6 p.m. they again begin to appear and increase as before up to midnight. Dr. S. Mackenzie (*Path. Soc. Trans.*, 1882) by turning night into day, induced the filaria, in the case under observation, to change their nocturnal into diurnal habits, thus making it clear that the periodicity of filarial migration is dependent on the moving and resting conditions of the patient, and independent of the time when the chyle reaches the circulation.

Dr. Manson (*Path. Soc. Trans.*, 1881) has described how these embryos developed in the blood, require the aid of an "intermediary host" to enable them to attain maturity. The host, he has shown, is the female of a certain species of mosquito. This animal piercing the skin of a filaria-infected subject, becomes infested with embryos; some are ejected, some perish, but a few undergo an extraordinary metamorphosis in the body of their host. By the time this metamorphosis is completed (four to six days), the mosquito who has deposited her ova and whose stomach is empty, except for these metamorphosed embryos, dies, probably falling into the water in which her eggs were laid; from thence the embryos find their way into the human stomach, whether directly by the drinking water, or through the channel of another host is a disputed point, but once in the stomach it bores its way to the lymphatics, and working up stream pierces the glands and finally arrives at its permanent abode in some distant lymphatic vessel. Here it is followed by one of the opposite sex and they may live and grow together comfortably for years, breeding a numerous progeny, and without necessarily giving annoyance to their human host. But unfortunately the female worm is liable to occasional miscarriages with her numerous offspring, that is to say the immature embryo instead of being born in its free and elongated state, escapes in an unstretched condition enclosed as an ovum (fig. 36, *b*); and as in this state in its smallest diameter it is five times greater than that of the fully outstretched embryo, we can readily understand that when carried into the lymph stream it should plug the smaller vessels, when they break up into smaller channels. There will thus be complete stasis of lymph along the line of this particular vessel, as far back as the first anastomosing lymphatic. As more

immature embryos pass, this process of obstruction of the lymphatic vessels and stasis of lymph will go on increasing till eventually a rupture of a lymphatic vessel occurs. Should the parent worm inhabit a lymphatic trunk in the pelvic or lumbar region, the stasis caused by the immature embryos may involve the lymphatics of the kidney, ureter, or bladder, and chyluria result.

Chyluria.

134. **Symptoms.**—In this disorder the urine assumes a milky appearance, and is usually slightly tinged with blood, and yields on standing a delicate fibrinous clot, which possesses the power of decomposing peroxide of hydrogen. Beyond the addition of the finely divided fatty matter, the blood, and the fibrinous clot, the urine is but little altered in its general characters. After separating these abnormal elements, I have found the amount of urea excreted in the twenty-four hours to be generally normal, though the amount of water excreted daily is usually increased. An analysis of the fatty material shows it to be composed of saponifiable fatty matters, cholesterin and lecithin. The albumins consist of serum albumin and fibrin, the latter may amount to as much as ·18 per cent.; peptones are invariably to be found, as also traces of indican. The amounts of these abnormal constituents vary considerably; in a very milky-looking urine yielding a considerable amount of clot, the total fatty matter amounted to 0·75, and the albumins to ·80 per cent. On the other hand, in a lymphous looking urine, yielding a yellow gelatinous clot, the fat only amounted to 0·06 per cent., whilst the albumins were not so greatly diminished, being 0·61 per cent.

The discharge of chyle or lymph by the urine is not always uniform. In some cases it is intermittent, days or even months elapsing between the discharge. In some rare cases it never returns after its first appearance. Even when the discharge is permanent considerable variations occur in the amount discharged from day to day. Intermittent chyluria is generally observed in the tropical cases, which are generally supposed to be caused by the rupture of the renal lymphatics by the pressure of the immature filarial embryos, and the intermittency is the result of the same cause. For a communication having been made with the renal passages through the lymphatics, by means of these immature embryos, the passage may also become occluded whenever the parent happens to abort, and the discharge of chyle will be arrested till the obstruction is overcome. On the other hand, the permanent discharge of chyle is most generally noticed in the European cases, in which the communication of the lymphatics with the urinary passages is brought about by traumatic agency, though in these cases an occasional intermittency may occur, if the passage happens to be temporarily obstructed by a fibrinous clot. The diurnal variations in amount passed in these cases, however, depend on the pressure of the lymph in the lymphatic vessels, and the amount of chyle is decidedly increased after meals and after exercise. The amount of blood varies considerably, it is rarely entirely absent giving a pink tinge to the bottom of the vessel, and to the clot on standing; it is, however, much more abundant, in the intermittent cases, no doubt from the rupture of small vessels from the increased pressure in the lymphatics. Chyluria may exist without giving rise to any other symptoms except the milky appearance of the urine, and the general health of the patient may not be affected by it. In many cases, however, dragging

pains across the loins are complained of, especially in intermitting cases just before the discharge occurs. If the coagulation of the fibrin occurs within the pelvis of the kidney, there may be renal colic; if in the bladder, strangury with obstruction to the passage of urine.

The exact point at which the chyle reaches the urinary tract has yet to be determined, it may as Dr. Stephen Mackenzie has suggested (*Path. Soc. Trans.*, 1882) take place either (1) between the vascular and lymphatic systems at their entrance into the kidney, or (2) between the renal lymphatics and uriniferous tubes of the kidney, or (3) as Dr. Roberts has suggested in some cases by the bladder. In Dr. Mackenzie's case, the thoracic duct was found to be impervious, one and a half inch above the aortic opening of the diaphragm, whilst the iliac, lumbar and renal lymphatics were very much enlarged, especially the left, whilst the left renal lymphatics contained numerous hard round masses, apparently calculous. As already stated, the malady does not necessarily affect the general health, and the patient may live for many years. Roberts cites a case in which the disease commenced at twenty-five, and continued to seventy-eight years of age, when the patient was still alive, and I occasionally see a patient who has had the disease in an intermittent form for fifteen years, and whose general health is excellent, and who the last few years has gained rather than lost weight. Still the continued drain of nutritive material must tell, and though so long as they are not exposed to vicissitudes or severe illness, and they are able to balance the loss, they may live, yet they are liable to succumb to intercurrent disease, especially pulmonary affections. For this reason it is necessary to attend carefully to their diet and shield them from cold winds, damp soils, and malarious influences. The diet should be abundantly

fatty, milk, cream, butter, bacon, and during inclement weather, cod-liver oil. The under clothing should be of flannel in all seasons, with chamois leather vests for winter use. Care should be exercised in selecting their residence, if in England the sub-soil should be carefully drained if not naturally dry, and the house sheltered from the east winds, whilst those who can afford it, should winter in the South of France or Italy. With a view to diminishing the discharge through the lymphatics, abdominal pressure has been resorted to, and a horse-shoe tourniquet applied to the abdomen, which has certainly had the effect of temporarily arresting the discharge of chyle into the urine. But the principle is wrong, for we ought to encourage rather than obstruct the flow if it has been established, for by damming it up we only increase the pressure in the lymphatic vessels, and lead to their further dilatation, whilst powerful compression of the abdomen must have an injurious influence if long-continued, on the general health of the patient. If attempted at all, it should be in cases that evidently are of traumatic origin, in which we may hope that an arrest of the passage of lymph through the lesion in the walls, may permit its occlusion, though the impossibility of determining the exact point where the communication takes place, renders such a probability a matter of extreme chance. When the disease, however, is undoubtedly due to filarial abortion, only harm can result from its employment. Our chief efforts must be directed in these cases to secure the death and removal of the parent worm. For this purpose, many remedies have been suggested, gallic acid, mangrove bark, benzoate of soda, and direct anthelmintics, are the ones most employed. Dr. Simpson of Assam (*Lancet*, Nov. 24th, 1883) records four cases of chyluria; in two of which the urine became natural after five grains of gallic

acid, followed by ℥xv-doses of perchloride of iron, three times a day, had been administered for ten days. In two others perchloride of iron was given, with twenty-grain-doses of quinine every morning, when the urine became natural in fourteen days; of these cases, only one recurred a second time. Dr. Acton of Winnipeg (*Lancet*, Oct. 20th, 1883) reports favourably of salicylate of iron in large doses. A patient of mine who has been under treatment in various parts of the world (for the disease at different times), has experienced most relief from terebinthine remedies. It is probable that these remedies, even if they do not cause the expulsion of the worm, may prevent the tendency to the premature expulsion of the embryos, and thus keep the disease in abeyance. In Dr. Mackenzie's case, the accession of febrile symptoms put a stop at once to the appearance of filariæ in the blood, by, he supposes, causing the death of the parent worm, but this event most likely sealed the death warrant of the patient, for the post-mortem examination showed that the double pleurisy of which the patient was the victim, was due to inflammation originating in the thoracic duct, probably excited in the first instance by the disturbed parent worms. On the other hand, many cases recover spontaneously, the parent worms being discharged, apparently without any unpleasant symptoms being occasioned during the process of removal. In others, the discharge of chyle by the urinary passages ceases, whilst filariæ are still found in the blood. In these cases which unfortunately are of very rare occurrence, the lesion in the lymphatic vessels probably becomes closed, whilst the parent worm ceases to abort. The prophylactic treatment is the same as recommended for the prevention of endemic hæmaturia, viz., avoidance of suspected drinking water. As the female mosquito lays her eggs in stagnant pools, the water from these should

be scrupulously avoided, both for drinking purposes, and for washing fruit and uncooked vegetables, salads, etc. When circumstances absolutely compel its use, it should be subjected to prolonged boiling, and careful filtration.

Rare Renal Parasites.

136. **Strongylus Gigas** is a large nematoid worm, which is occasionally found in the renal pelvis of dogs, wolves, weasels, and other carnivorous beasts of prey, rarely in the ox and horse, and still more rarely in man. It resembles in appearance a large ascaris lumbricoides, but is distinguished from it by its huge size, and by having six oral papillæ instead of three. The female is larger than the male, the former may attain the length of thirty inches, whilst the latter rarely exceeds twelve to fourteen inches. So rare is this parasite among human beings, that only seven authentic cases are recorded. Nothing is known with regard to the life-history of the parasite, or how it is introduced into the body. The symptoms it gives rise to, are the same as those caused by any foreign body in the renal passages, viz., colic, hæmaturia, and pyuria. Long clots of blood from the urethra, or lumbrici which have been discharged into the chamber vessel containing urine, have sometimes been hastily taken for a "gigas," but a very slight examination is sufficient to correct the error. So rarely are these animals observed in man, that no case has now been recorded for some years, and the only specimen I am acquainted with is that in the Royal College of Surgeons. *Pentastoma Denticulatum*, a minute parasite which occasionally is found under the capsule of the liver of herbivorous animals, and sometimes (in Germany) in man. It has only once been found under the capsule of

the kidney of a patient who died from Bright's disease. In its larval state it is boat-shaped, having at its fore part four hooklets or anchors, at its side spines said to resemble oars. In this state it is found in the viscera. In the adult form it developes into a small maggot found in the nasal cavities of dogs and wolves, introduced whilst the animals were devouring the offal of cattle infested with the larvæ.

136. *Extra-renal parasites.* — When a communication exists between the intestines and the urinary passages, lumbrici ascarides, or the joints of tape-worms may be voided per urethram, or they may simply escape from the bowel into the chamber vessel. So also, the parasites of other animals may accidentally or intentionally find their way to the urine, an interesting account of such deception is given in Beale's *Archives of Medicine*, vol. i., p. 290. Dr. Curgenven (*Brit. Med. Jour.*, June 14th, 1884) relates an interesting case in which the mucous membrane of the whole urinary tract was invaded with a fungus growth, the spores probably coming in contact in the first instance with the orifice of the urethra and parts adjacent, and giving rise to the growth of *mycelium*, which spread up the urethra to the bladder and ureters.

CHAPTER VIII.

Abnormalities of the Kidneys, including Moveable Kidney.

Under this head we shall consider 1. *Abnormalities of Position*, and 2. *Abnormalities of Form and Number*, the former being clinically much the more important.

I. *ABNORMALITIES OF POSITION.*

137. The normal position of the kidneys has already been laid down in Chap. I., p. 7, and while the positions there assigned to them, are to be regarded as merely the average of a number of instances, still the variations are for practical purposes not great. Assuming then, that the kidneys are situated in the upper and back part of the abdominal cavity, the hilum of each on a level with the first lumbar spine, two and a half inches from the middle line, we may say that if the hilum is displaced from this point by an inch and a half, the case comes already within the abnormal or the morbid.

Such displacements from the normal position, fall under two categories. 1. *Fixed Malpositions of the Kidney*, and 2. *Moveable Kidney*, and under each of these heads we shall have to consider the congenital and the acquired varieties.

1. Fixed Malpositions of the Kidney.

138. In these cases the kidney is fixed in an abnormal position, which may be congenital, or acquired subsequently.

The displacement in *congenital* cases is most frequently downwards, and in the majority of instances affects the *left* kidney. Of twenty-one cases collected by Dr. William Roberts, in every instance only one kidney was involved, in fifteen cases the left, in six the right. Weisbach (*Wien. Med. Wochenschrift*, 1867) makes the disproportion much more marked, viz., thirty-five to eight. He also states that of twenty-nine cases, twenty were men, only nine women. In other words, while mobility of the kidney as we shall see, occurs more frequently on the right side, and in the female sex, fixed malpositions occur more frequently on the left side, and in the male sex. The displaced organ lies usually in the region of the sacro-iliac joint on the brim of the true pelvis, and frequently as in a case recorded and sketched by Dr. MacWilliam (*Brit. Med. Jour.*, 7th Oct., 1882) in front of the great vessels. Its shape is rarely reniform, more generally oval and flattened with persistent fœtal lobulation. The ureter leaves it on its anterior aspect, its vascular supply is derived usually from the neighbouring vessels, and it is interesting to note that the corresponding supra-renal capsule is not displaced with it.

Such a congenitally displaced kidney has been mistaken for a tumour, and energetically treated in accordance with the diagnosis. It has also presented before the descending fœtal head, causing considerable difficulty in delivery. As a rule, however, the condition, giving rise to no symptoms, is not recognised during life. If the possibility of such a condition is present to the mind of the examining

physician (and this proviso is the most important element in the diagnosis of all abnormal conditions of the kidney), then a mistake will be avoided if attention is paid to the smooth, rounded, elastic character of the mass, to the feeling of faintness and nausea caused by pressure upon it, and to the flattening and tympanitic resonance occasionally present in the usual position of the kidney. In case of doubt, a rectal examination should not be neglected.

Of the *acquired* malpositions of the kidney, the most important is that due to inflammation in the tissue surrounding a moveable kidney with subsequent fixation. This condition we shall discuss under the head of moveable kidney. The displacement due to enlargement or malignant growth in neighbouring organs, will be simply an incident in the more serious disease, important only if such displacement causes pressure on the ureter or on the renal vessels.

2. Moveable Kidney.

139. The kidney is normally a retro-peritoneal organ, lying in the position already defined, largely within the bony thorax. It is provided with two capsules, the *fibrous* — thin but strong, and closely adherent to the organ, the *fatty*—of very variable thickness in different individuals, and in the same individual at different times. The fatty capsule is connected by loose areolar tissue, both with the fibrous capsule on the one hand, and with the peritoneum and abdominal wall on the other. It forms, therefore, as will readily be understood, a most important element in the etiology and pathology of moveable kidney. Landau in his admirable clinical monograph (*Die Wanderniere der Frauen*, 1881, p. 9)

describes the sub-peritoneal areolar tissue of the child as dividing into two layers, one of which remains immediately sub-peritoneal, while the other passing behind the kidney and its vessels, forms a sort of suspensory ligament for the kidney (Englisch) connecting it closely with the peritoneum, and loosely also with the abdominal wall. Only after the tenth year does the areolar coat thus formed develop in its meshes the fat which constitutes the fatty capsule of the kidney.

The kidneys are in close relation anteriorly, with the hepatic and splenic flexures of the colon, and it is to be noted as Landau points out, that the splenic flexure of the colon is much more firmly fixed in its position than is the hepatic. The difference is due principally to the strong membranous band, termed the pleuro-colic fold which connects the splenic flexure with the inner wall of the thorax, and supports the spleen on its upper surface. We shall revert to this point again in discussing the greater frequency of right moveable kidney than of left. But by far the most important of the structures retaining the kidneys in position, are the renal vessels, and more especially the renal arteries. These being connected with the practically immovable aorta and vena cava, act as a tether to the kidney, allowing even in case of mobility, only a limited range downward, forward, and inward, upward displacement being rendered practically impossible by the presence of the liver and spleen.

Such displacement of the kidney behind the peritoneum, constituting moveable kidney, does in fact occur, and that too not unfrequently. Rollet states (*Pathologie und Therapie der beweglichen Niere*, 1866, p. 13) from the examination of five thousand five hundred patients, that moveable kidney occurs once in two hundred and fifty cases, adding, however, that this proportion is but a rough

approximation. As bearing on this point, it may be stated on the one hand that in only a very small proportion of the cases in which it occurs, do symptoms present themselves, drawing attention to the condition, while on the other hand in the majority of instances where such symptoms do occur, the cause will be overlooked, not being present to the mind of the physician.

As a very rare condition the kidney may be more or less completely surrounded by peritoneum, being then connected with the spine by a double fold of membrane termed a *meso-nephron*. This abnormality is invariably congenital, and will usually be found associated with other abnormalities of the peritoneum. The kidney in such cases is moveable, and we have no means of diagnosing the condition from that above described. Sir William Jenner proposed to reserve the term floating kidney, for this form of moveable kidney, in which case floating and moveable kidney would be synonymous with congenital and acquired mobility of the kidney. The former conditions will undoubtedly even more rarely than the latter give rise to symptoms, and what we are about to say will have almost exclusive reference to moveable kidney of the acquired variety.

140. **Causes.**—In any enquiry as to the causes of moveable kidney, certain statistical facts must be borne in mind. In the first place it occurs with very much greater frequency among women, than among men. Of 290 cases collected by Newman (*Malpositions of the Kidney*, 1883, p. 13) 252 were women, and 38 were men, *i.e.*, about one male case for seven female. Again as to age, by far the greater portion of cases occur between the ages of 25 and 40 years, that is as Dr. William Roberts states, roughly within the childbearing period in women. Lastly, the condition occurs much more frequently on the right than

on the left side. Among 178 cases cited by Landau (*loc. cit.*, p. 14) the right kidney was moveable in 151, the left in 13 and both kidneys in 14. It is impossible to avoid the conclusions suggested by these statistics, that women are specially liable to moveable kidney, and that more particularly during the period of childbearing. In support of this we find from a table compiled by Landau (*loc. cit.*, p. 103) that a very considerable proportion of the cases have born a large number of children in rapid succession. The result of *repeated pregnancies* is in the first place to produce great relaxation of the abdominal walls and of the pelvic floor, and in the second place by the alternating upward pressure, and sudden subsidence of the kidneys to cause a greater mobility of these organs. This relaxation with the consequent pendulous abdomen, and diminished intra-abdominal pressure, occurs most markedly in women of the lower classes, who are frequently engaged in hard manual labour within a few days after delivery. Accordingly we find prolapsed uterus and moveable kidney, very frequently co-existent, so commonly indeed that the first has been alleged as a cause of the second, the intermediate link being hydro-nephrosis due to urinary obstruction by the prolapsed uterus. *Tight-lacing* has received the blame, and deservedly too, of a considerable proportion of female ailments, among others of that we are now considering. Notwithstanding the arguments of Landau, and more recently of Newman, there can be little doubt that there is truth in the opinion expressed by Cruveilhier, and supported by Dr. William Roberts, that tight-lacing is competent to produce downward displacement of the kidney, as it is competent to produce vertical elongation of the liver, and downward displacement of the pylorus. But acquired downward displacement of the kidney practically means a moveable kidney, for once displaced from its

nest the kidney goes adrift. In connection with the greater frequency of moveable kidney in women, Becquet has put forward a theory. He states that at each *menstruation* there is a marked increase in the size and vascularity of the kidneys, due probably to the close association of the renal and ovarian nerve plexuses. This periodic enlargement he believes to be a cause of moveable kidney, as well as of the lumbar aching, so frequently complained of during menstruation. Ebstein (*op. cit.*) considers the statement unsupported by fact, but Dr. William Roberts has recently recorded an interesting case, where in a girl, aged seventeen, a displaced kidney increased by fully one half, and was also more sensitive during the two menstrual periods that she was under observation. Also it is a fact that the symptoms produced by moveable kidney are usually more marked, indeed are sometimes present only during menstruation.

Why should the right kidney be so much more frequently moveable than the left? Most probably for a double reason, positive and negative. First, the right kidney lies below and behind the massive liver, while the left is in the same relation, only to the lighter spleen and more yielding stomach. Second, the attachments of the left kidney, as we have already seen, are firmer than those of the right. The left renal artery is shorter than the right, and the splenic flexure of the colon with which the left kidney is closely connected, is kept firmly in place by the pleuro-colic fold.

Considering that the kidney is imbedded in fat, it is *à priori* probable that *rapid emaciation* would tend to produce mobility of the kidney, not only indirectly by reducing intra-abdominal pressure, but directly by loosening the fatty bed of the kidney. This conclusion is fully justified by facts, for example thirteen per cent. of Landau's

cases suffered from carcinoma. Any condition which increases the weight of the kidney will tend to produce mobility, such for example as malignant tumours of the kidney, hydro-nephrosis, calculi, etc. Traumatic causes again, such as falls and blows, have undoubtedly displaced the kidney, although in the great majority of such cases, some of the predisposing causes above mentioned have been present.

141. **Symptoms.**—We have already remarked that in many cases of undoubted moveable kidney, no inconvenience has been felt, and the condition has been discovered only accidentally either by patient, or by physician. Having been discovered, it is often the source of great anxiety to the patient, more especially if the physician gives an indefinite opinion as to its nature or pronounces it to be a malignant tumour. And this anxiety as Landau points out is greater than it would be with almost any tumour, for every movement makes the patient conscious of something unusual in the abdomen, and so keeps the condition constantly in mind. In a proportion of cases, however, there are most definite symptoms, and Ebstein believes that to this condition are due many vague feelings of abdominal discomfort for which no cause is discovered simply because no thorough physical examination of the abdomen is made.

The symptom most frequently complained of is the "*feeling of something loose*" in that region of the abdomen, which moves for example on turning over in bed, with a sense of *dragging* or gnawing at the spot, sometimes amounting to sharp pain. Along with the dull aching localised pain there may be distinct *neuralgic pain* in the course of the lumbar nerves, shooting round the abdomen to the hypogastrium, and down the thighs. These uneasy feelings and pains are as a rule much increased during the

period of menstruation, indeed, as already stated, may be present only during these periods. They are undoubtedly due to the dragging upon the renal plexus of nerves and its connections. Owing to the mobility of the displaced organ, it is rare to meet with pressure symptoms, but Landau quotes a case of floating kidney recorded by Girard, and one of moveable kidney observed by himself, in which *œdema of the lower limbs* was caused by pressure on the veins, there being in Girard's case an actual thrombosis of the inferior cava. Rollet (*loc. cit.*, p. 20) quotes a case in which the inferior cava was obliterated by the pressure of a dislocated kidney. Cases of obstinate constipation due to pressure on the colon have been recorded, *e.g.*, by Rollet, but such cases must certainly be extremely rare, and ought to be received with caution. As regards *disturbances of the digestive organs* due to moveable kidney, Dr. William Roberts relates a very instructive case. It is that of a gentleman who from the date of a fall on the ice, suffered from a dragging sensation in the right loin, paroxysmal diarrhœa, and progressive emaciation. Examination showed a moveable right kidney. He was advised to wear a belt and pad to keep the organ in position. This he did, with the result that his symptoms were completely relieved so long as he persisted, but returned as soon as he left off the belt and pad. Some evidence has been brought to show that moveable kidney may be a cause of *recurrent icterus* by pressing on the common bile duct, and it seems to be a fact that recurrent icterus is common in cases of moveable kidney, but the condition is more probably due to the chronic gastro-intestinal catarrh so frequently concomitant with moveable kidney.

By far the most important and most serious of the symptoms due to moveable kidney, are those of what has

been termed *strangulation* of the kidney. Usually after some sudden exertion, but occasionally while at perfect rest the patient is attacked with severe abdominal pain, and great tenderness in the neighbourhood of the kidney, frequently accompanied by rigors, nausea, and vomiting. If palpation can be exercised, the swollen and immovable kidney may be felt displaced downward and forward. After a few days, which may extend to two weeks, the condition invariably ends in recovery, the first sign of this being a copious discharge of urine, which may contain pus, and is in marked contrast with the urine passed during the attack, which is generally dark and scanty. The cause of these attacks which occur repeatedly, is not clear, but according to Rollet it is due either to torsion and compression of the ureter with consequent hydro-nephrosis, or to inflammation and exudation in the tissues surrounding the kidney.

142. **Diagnosis.**—Apart from the symptoms mentioned, most of which will serve merely as suggestions, we must depend for our diagnosis of moveable kidney upon the bimanual palpation of the organ practised, and recommended many years ago by Sir William Jenner. It may be doubted if ever in the normal subject we can make certain of actually palpating the kidney, but as stated above, those suffering from moveable kidney are as a rule the subjects both of emaciation and muscular relaxation. In such cases it is possible by pressing one hand well into the loin, to detect with the other through the abdominal wall a reniform tumour, which glides to and fro between the hands. If we are successful in making out the reniform shape, and can also produce the peculiar nausea and faintness resulting from its compression, there can be no possibility of mistake. If not, however, it may be confounded with enlargements of, or tumours connected with,

the liver, gall-bladder, stomach, spleen, or omentum. The surface and shape of these will generally enable us to decide, as also the fact, that the displaced kidney almost invariably lies behind some coils of intestine. Impacted fæces, especially in the right colon, may simulate displaced kidney, but their position, shape, and consistency, will assist in diagnosis, and the action of a brisk purge will dissipate any doubt that may remain. Any difficulty regarding ovarian and uterine tumours will as a rule be decided by careful vaginal and rectal examination.

Jenner would diagnose floating from moveable kidney by the greater mobility of the former, due to its mesonephron. Experience does not seem to confirm this criterion, and accordingly, although the difference is both anatomically, and as Newman has shown, (*loc. cit.*, p. 11) operatively important, we cannot clinically distinguish them.

143. **Prognosis.**—Opinions differ widely as to the importance and dangers of moveable kidney, and as fairly typical, we may take those of Keppler, Newman, and Landau. The first considers the condition fraught with so much danger, not only to the comfort, but even to the life of the patient, that he would on its producing any symptom whatever, at once, and notwithstanding the absence of any complication, extirpate the organ by an abdominal incision. Landau on the other hand denies that moveable kidney has ever caused death, nay he says in a fair proportion of cases it tends to a spontaneous cure, and that in no case is operative interference, much less extirpation, justifiable. Newman takes his place between these two extremes, and the cases adduced by him, although few in number, go far to justify his position. In many cases the condition produces no symptoms, and therefore requires no treatment, in a considerable propor-

tion of the remainder, the symptoms can be relieved by simple means to be discussed presently, in a few cases severe symptoms occur which can be relieved only by operative measures, and even as a last resort by nephrectomy.

144. **Treatment.**—Our first object in the treatment of moveable kidney, is to replace the organ in position; our second to keep it there. Replacement is as a rule easy, even where adhesions have formed, gentle manipulation with the patient in the horizontal position being generally quite sufficient. On resumption of the erect posture, however, the organ at once drops into its abnormal position. In cases of traumatic displacement, the patient should be kept for a prolonged period in the supine position, but in these and other cases, it will be necessary to adopt means for keeping the kidney in position. We should in the first place enjoin the avoidance as far as possible of those habits and conditions which tend to produce mobility of the kidney. All violent exercise such as leaping or dancing, and riding, should be strictly interdicted, more especially in a female during the period of menstruation. Tight-lacing should also be forbidden, and the bowels ought to be regulated, so as to prevent straining at stool. Prolonged rest in the recumbent position after delivery has in some cases actually cured a previous existing mobility of the kidney. Good food and tonic treatment, including the well directed application of massage and electricity, may in some measure correct the effects of emaciation and muscular relaxation. When the symptoms above described as strangulation of the kidney set in, the patient should at once be put in the horizontal position, and an attempt made to replace the kidney. If the diagnosis is certain, Rollet holds that this attempt should be made even energetically if necessary. Should the attempt fail, the patient

may be put in a warm bath, and then a second attempt made. Poultices and leeches or cupping may be applied to relieve the pain and congestion, and a full dose of morphia should be administered. Replacement of the kidney will certainly be possible within a few days, when the symptoms will subside.

To keep the kidney in position when the patient gets up, is an extremely difficult matter, but in many cases the symptoms will be relieved if we can keep it still. Many complicated mechanisms have been devised for this purpose, the success of which is in direct proportion to the degree in which they supply an artificial abdominal wall. Landau recommends a well-applied abdominal bandage made of drill or flannel, elastic at the sides, and provided with shoulder straps to prevent its slipping down. Better than this, however, he considers, is a peculiar form of 'corset,' the principle of which is precisely the opposite of that usually worn. It must not constrict the lower thoracic region, and it should reach in the middle line to the pubes (the middle steels being jointed if necessary), and at the sides to Poupart's ligament. Over the region of the kidney in place of the usual pad should be placed a concave tin plate.

In those cases where for some reason mechanical support cannot be borne, or fails to relieve, and where the symptoms are so severe as to incapacitate for the ordinary duties of life, *operative interference* is necessary and justifiable. This will take the form of nephroraphy, or even as a last resort nephrectomy. For a full account of the first operation which consists in making an incision over the kidney in the loin, and stitching it into the wound, we must refer the reader to Dr. Newman's monograph on malpositions of the kidney, where also will be found a discussion of the circumstances in which nephrectomy is or is not justifiable for moveable kidney.

II. *ABNORMALITIES IN FORM AND NUMBER.*

145. These abnormalities are almost without exception congenital, and accordingly the same remark applies to them as to the fixed malpositions of the kidney, that they are more of anatomical curiosities than conditions clinically important.

1. Abnormalities in Form.—The two principal conditions of the kidney falling under this head, are the lobulated and the horse-shoe kidney. The *lobulated kidney* is the result of the persistence of the fœtal lobulation which we see permanent in many animals, and which is the external indication of what is evident internally, that the kidney consists not of one gland, but of a cluster opening into a common duct. The *horse-shoe kidney* is produced by the union of the two kidneys by means of a transverse portion lying in front of the vertebræ. The concavity of the horse-shoe lies in the great majority of instances upwards, the transverse portion joining the inferior extremities of the vertical portions, and having in front of it the two ureters, behind it the aorta and inferior vena cava. Such malformed kidneys are not unfrequently also misplaced, and as a rule downwards. The principal danger connected with them is, as in the case of fixed malposition, mistaken diagnosis, and the anxiety and active treatment the patient may in consequence have to undergo. Cases are, however, quoted by Ebstein, which show that the possession of a horse-shoe kidney is not quite an indifferent matter. In one case, thrombosis of the great veins was caused by a congested horse-shoe kidney, in another compression of the ureters during pregnancy caused pyelitis and death.

2. Abnormalities in Number.—From what has been

already stated as to the kidney being really an agglomeration of many glands, it is not to be wondered at that we occasionally meet with small *supernumerary kidneys* having separate ducts. A far more important variety is the *solitary kidney*, which in the majority of instances is a congenital, but may be an acquired condition. Of twenty-nine cases of solitary kidney collected by Dr. W. Roberts, twenty-two occurred in males, six in females, and in one the sex was not stated. In sixteen the solitary kidney was on the right side, in twelve on the left, in one the side was not stated. In nineteen cases the condition was congenital, in three it was acquired, that is resulted from destruction of the other kidney, and in seven it was doubtful. It will be seen, therefore, that solitary kidney is much more frequent in males than in females, and that the left kidney is more frequently absent than the right, agreeing in both respects with fixed congenital malposition of the kidney. In congenital absence of a kidney, it is usual to find no trace of its ureter or vessels, but Buchhammer's cases (*Arch. für Anat. und Physiol.*, 1879) show that it is common for the solitary kidney to possess two ureters and two sets of vessels, the ureters crossing each other to open normally at the base of the bladder. Where owing to disease, one kidney has been destroyed, we usually find its ureter remaining, and frequently some trace of the organ itself. In both cases the single kidney is hypertrophied, and so long as matters go smoothly, seems perfectly competent to carry on the double duty laid upon it. The danger of the condition, however, and this is to be borne in mind in considering nephrectomy, is shown by the fact that in twenty-four cases, death was in ten cases directly due to there being but one kidney, a renal calculus having developed, while in two other cases death was caused by the pressure of a cancerous tumour

on the single ureter. Nephrotomy and nephrectomy have now mainly through the results of Knowsley Thornton, Henry Morris, Beck and others in this country, become not only recognized but highly successful operations. In both operations, however, it is well for operators to remember that rare as the condition is, any given case may be one of solitary kidney. By careful physical examination, and by compression of one ureter, with Davy's Rectal Lever, some assurance will be acquired as to the presence, and also the secreting powers, of a second kidney.

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CHAPTER IX.

Diabetes Insipidus. Diabetes Mellitus. Anuria.

Diabetes Insipidus.

146. Under the terms diuresis, diabetes insipidus, polyuria, and polydipsia, writers have described a certain morbid condition of the system characterised by the excessive and persistent discharge of urine of low specific gravity—containing, however, neither sugar nor albumin. Most authors apply either of the above terms to denote this urinary superflux, without reference to the quantitative relationship that may exist in individual cases between the urinary water and solids. Others, of whom Willis seems to have been the first, have attempted to form a classification on this basis. Thus Willis divided cases of diabetes insipidus into three groups:—(1) those attended with excessive discharge of aqueous urine, in which the solid matters are deficient—*hydruria;* (2) those attended with a copious discharge of urine characterised by a deficiency of urea—*anazoturia;* and (3) those in which the excessive discharge of urine was attended with a superabundance of urea—*azoturia.* Parkes also supported the view that diabetes insipidus was to be found existing under three different conditions:—(1) in cases where there is no increase or decrease of tissue metamorphosis; (2) in cases where there is a decided decrease of tissue metamorphosis; (3) cases where there is evidence of increased tissue metamorphosis, as shown by the increase of some of the urinary solids. For this latter class

of cases Professor Parkes thinks the term polyuria preferable to that of azoturia, which only expresses the fact of the urea being increased; whereas in the cases quoted by him the fixed salts, as chlorides, sulphates, and phosphates, were also present in abnormal quantities. Lastly, Dr. Tessier of Lyons has recently recorded a series of cases closely resembling saccharine diabetes, in the increased discharge of urine, the thirst, the neuralgic and rheumatic pains, the wasting, and the secondary lung complications, only that no trace of sugar could be found in the urine, and that the constant phenomenon was a very considerable increase in the quantity of phosphoric acid excreted (fifteen to twenty grammes of earthy phosphates in twenty-four hours). For the purpose of convenience it is better at present to construct a classification which has reference, first to the excessive excretion of water by the kidneys, and secondly to the increase of solid matter by the same channel. For this purpose the terms suggested by Willis and Parkes can both be utilized, the former, *Hydruria*, referring to cases attended with excessive discharge of aqueous urine, with or without decrease in the amount of the solid constituents of the urine. *Polyuria*, as relating to cases in which the urea, singly, or else together with the other urinary constituents, is excreted in abnormal quantities.

147. **Symptoms.**—1. *Hydruria* is characterised by a copious and persistent discharge of pale limpid urine of low specific gravity. The amount of water discharged in the twenty-four hours is enormously increased, taking two-and-a-half pints as the normal daily excretion of a healthy adult. Trousseau (*op. cit.*, p. 530) records a case in which the urine discharged amounted to fifty-six pints. This, of course, is exceptional, and as a general average the quantity ranges between ten and fifteen pints. Owing

to the difficulty of collecting the urine in children, it is difficult to form an appreciable idea of the amount they pass when subject to the disease; but to judge from the constant diuresis going on it must be very great. The older writers thought that the amount of water discharged by the kidneys in this disease was in excess of that ingested. They, however, overlooked the fact that a considerable amount of water is taken into the body with the solid constituents of the food. The specific gravity is extremely low. In severe cases, it has been noticed as low as 1·0005, the general range, however, is between 1·003 and 1·004. The solid matter discharged does not, however, show any marked reduction; indeed, if the appetite is good, there is usually some increase, especially when much fluid nourishment such as beef tea, milk, etc., is taken, to support the patient and relieve thirst. Thus a patient passing 9000 c.c. of urine in the twenty-four hours having a specific gravity of 1·003, would, according to Trapp's formula, be eliminating by the kidneys 54 grammes of solid matter, an amount closely approximating to the normal. In a patient of my own who, however, took considerable quantities of beef tea and milk, the figures were—amount of urine 9500 c.c., specific gravity 1·004, solids 76 grammes, or about 20 grammes more than the normal, showing that the eliminating powers of the kidneys are not diminished in this disorder. The urea is not diminished, though stated by Willis to be so, in the hydruria of young children.

Sir Andrew Clark has recently drawn attention to some cases in which, with a urine of very low specific gravity, there was a very considerable decrease in the amount of urea excreted; there is, however, no superflux of urinary water, in fact the amount of urine may be decreased. Such a urine as that described by Sir Andrew

Clark, is also passed by patients suffering from myxœdema. Sir Andrew Clark believes in these cases the kidneys fail in their eliminating function (renal inadequacy), whilst I have suggested that the deficiency of the urea is due to defective tissue metabolism generally. They cannot, however, be regarded as in any way allied to diabetes insipidus. Uric acid is said to be decreased in hydruric urines. This I doubt; the apparent deficiency being caused, I believe, by the fact, that the urine is too dilute to allow of uric acid crystallizing out, when acidulated; by concentrating these urines to a specific gravity of 1·020, and then adding acid, an abundant yield of crystals will generally be obtained. Phosphoric acid, especially that in combination with the earthy salts, is generally, but not invariably, increased. When an increase is noted, it may be attributed, I think, to increased ingestion, as from beef tea and milk, and to the washing out of the tissues by the drainage going on through the body. In cases directly the result of intra-cranial disease, the increase of the earthy phosphates may be due to metabolism of the nervous centres. The chlorides and sulphates may also be increased, both from increased ingestion, and from washing out of the tissues. The reaction of the urine is usually neutral, or feebly acid, rarely alkaline, and then only temporarily so. The colour when viewed by transmitted light, is of a pale green with a bluish tint (sea-green). The urine often contains inosite, sometimes albumin, which occasionally becomes abundant, and often traces of sugar. Beyond the profuse discharge of aqueous urine and the thirst it occasions, there may be no other symptoms, and it may be compatible with fair bodily health, and even long life. Thus cases are recorded of the continuance of the disease for twenty-four, thirty-seven and thirty-nine years, in persons who during that

time remained in fairly good health. As a rule, however, hydruric patients, though suffering from no definite disease, have only poor health. They are chilly, and sudden changes from temperate weather to cold increase their diuretic tendencies. Though the bowels are usually constipated, diarrhœa is easily provoked. The appetite is capricious, a sinking, gnawing sensation being complained of rather than the ravenous hunger of saccharine diabetes. As a rule the ingestion of alcohol is followed by an increase of the urinary flux, and small quantities act on the nervous system; on the other hand cases have been recorded in which enormous quantities of alcohol have been swallowed; Trousseau mentions twenty bottles of wine at a sitting, without producing any effect.

2. *Polyuria* is characterised by the discharge of urine increased as to the quantity of its aqueous and solid constituents. The amount of water passed in the twenty-four hours, however, never approaches the enormous quantity discharged in hydruric cases, though the solid matters may be increased twice or even three times in amount. The quantity of urine passed in the twenty-four hours averages about 2500 to 3500 c.c., and the specific gravity ranges from 1·010 to 1·025. The following table will show the chief characters of the urine in polyuria, as compared with the normal secretion.

	Age.	Weight.	Quantity.	Specific Gravity.	Solids.	Phospho-ric Acid.	Urea.
Normal	35	11 st.	1400 c.c.	1·020	58 grms.	2·8 grms.	33 grms.
Case 1	16	9 st.	3900 c.c.	1·010	76 grms.	5·2 grms.	51 grms.
Case 2	25	9 st.	2300 ,,	1·015	69 ,,	7·8 ,,	33 ,,
Case 3	27	8st. 7lb.	1500 ,,	1·022	66 ,,	5·2 ,,	41 ,,
Case 4	37	12st. 7lb.	2300 ,,	1·018	83 ,,	4·6 ,,	69 ,,
Case 5	20	9 st.	3825 ,,	1·016	122 ,,	6·7 ,,	87 ,,

In all these cases the amount of solid matter excreted is

in excess of the normal, and in some considerably so. In cases two and three, however, the increase is in the amount of phosphoric acid excreted, the urea in Case 2 being normal, and in Case 3 only slightly increased. These two cases, therefore, resemble very closely those described by Tessier under the term "phosphatic diabetes." In the others, however, the urea as well as the phosphoric acid are both considerably increased, and resemble the cases of azoturia, related by Prout and Willis, and those of Vogel, quoted by Parkes (*op. cit.*, p. 365). The urines passed by these patients are usually acid in reaction, and are free from albumin and sugar, traces of the latter, however, may occasionally appear. Although the amount of urine is generally in excess of the normal, still in some cases no such increase is noted, in these cases, however, the specific gravity is enormously increased, thus I recently saw an instance in which the urine averaged daily about 1300 c.c., with a specific gravity of 1·034, making the solid matters excreted about 88 grms.

The symptoms attendant on polyuria are debility and languor, loss of weight, neuralgic and rheumatic pains, chiefly in the loins and down the thighs, and a moderate degree of thirst. Tessier observes that in those cases marked by an excessive elimination of phosphates, cataract sometimes ensues. I have, however, never seen an instance, though I have seen patients suffering from boils, a circumstance that Tessier also insists on, as showing the relationship of the disorder to saccharine diabetes into which it sometimes merges.

148. **Etiology.**—*Hydruria.*—According to Lancereaux and Roberts the disease occurs twice as frequently in men as in women. It is slightly more prevalent in the first twenty years of life than in the second, whilst after middle age it is comparatively rare for the disease to originate.

The following are the chief causes to which the disease has been attributed, in cases which are not distinctly of cerebral origin. Hereditary influences, sudden chilling of the body when heated, sunstroke, alcoholic excesses, especially in persons already suffering from alcoholism. Insipid diabetes in young children has in some instances been traced to the parents allowing them to drink spirits, a practice not uncommon among some of the drunken mothers of the lower orders. Violent mental emotions, and hysterical conditions, violent muscular exertions, severe illness, especially after fevers, malarial cachexia, have all been assigned as causes, though as Dickinson very fitly remarks, these supposed causes may be no more than chance antecedents. When the disease can be distinctly referred to the nervous system, the exciting cause is then usually traced with greater positiveness. Thus injuries of the head; tubercular, and epidemic cerebro-spinal meningitis; intra-cranial growths, syphilitic or tubercular; pressure on the renal nerves by abdominal tumours; irritation of the pneumogastric by growth of intra-thoracic aneurisms, etc. (see cases in *Lancet*, Feb. 26, 1876, by author), have been found to give rise to hydruria. Temporary hydruria may occur during pregnancy, especially in the later months, and disappears after delivery. It often occurs as a fleeting symptom in hysterical and emotional women.

Polyuria.—The etiological conditions which give rise to this form of insipid diabetes are still to be elucidated. They depend no doubt upon some profound disturbance of the nervous system, the result of which is to cause increased tissue metabolism (p. 78). When both urea and phosphoric acid are increased, then the increased metabolism probably affects the system generally; when, however, the phosphoric acid is relatively in excess of the urea, it

points undoubtedly to disintegration of nervous matter. Of Dr. Tessier's cases, the majority were males between the ages of 20 and 40. In eight cases that have been under my observation all were males, the oldest was 48 years of age, the youngest 16, the average age being 22 years. In five of the eight cases the disease came on insidiously, and no definite cause could be assigned for it, whilst three were decidedly tubercular, and one developed phthisis whilst under observation.

149. **Pathology.**—*Hydruria.*—Experimentally it has been proved that puncture of the floor of the fourth ventricle, a little above the orifices of the pneumogastric and auditory nerves, gives rise to a superabundant flow of urine, which is sometimes albuminous. Irritation of the middle lobe of the cerebellum has also the same effect; whilst section of the splanchnics, and irritation of the pneumogastric, are both followed by a copious secretion of aqueous urine. Consequently pathologists have sought for lesions in these regions, in order to explain the phenomena of diabetes insipidus, and as a matter of fact, such lesions have been discovered in connection with the disease. With regard to the intra-cranial lesions it is not necessary for the primary pathological change to occur exactly at the floor of the fourth ventricle, their effect, no doubt, may be propagated to it. Thus in the case of a patient who died with marked cerebral symptoms, and had profuse hydruria for some weeks before his death, at the post-mortem examination, a small syphilitic gumma about half the size of a small hazel nut, was found situated in the middle line, under the floor of the third ventricle, obstructing some of the vessels at the base, whilst there was some softening of the brain substance in that region. So also with injuries to the head, since the effect of a blow may be transmitted to the basal and posterior por-

tion of the brain either directly or by contre-coup. The kidneys have been found but little changed structurally. They are usually somewhat enlarged, and Dickinson has observed punctiform injection of the cortical tissue. Saccular dilatation of the kidneys has been described as a post-mortem condition, but these cases were probably ones of ordinary hydro-nephrosis. Other renal changes have also been described; but in these some other morbid conditions co-existed in the urinary passages sufficient to account for them.

Polyuria.—No post-mortem examination has ever, as far as I have been able to ascertain, been made on one of these cases. In a patient under my care the only positive pathological lesion that could be discovered during life, was pulmonary consumption, and which might probably account for the increase of phosphoric acid in the urine; since Marcet has shown from analysis of pulmonary tissue in consumption, that a considerable reduction of phosphoric acid and potash takes place, both in the insoluble tissue and nutritive material, as compared with healthy lung. Those cases, however, in which both urea and phosphoric acid are increased, are probably the result of an increased intra-molecular action of the cells throughout the body, whereby they make use of the oxygen stored up in them, and so give rise to increased tissue metabolism. This condition may be transient, and produced by excess of food, especially when highly nitrogenized, nervous influences, or temporary disturbance of function.

150. **Diagnosis.**—In hydro-nephrosis considerable discharge of a highly aqueous urine takes place. This disease, however, can be distinguished from insipid diabetes by the fact that, in hydro-nephrosis, the diuresis is more or less intermittent. In sacculated kidney, the urine is

abundant, and of low specific gravity, but the amount never approaches to anything like what we meet with in hydruria. Nor is it possible in the ordinary run of cases to confound diabetes insipidus, even when the urine contains albumin, with the diuresis of granular kidney; for putting aside the absence of cardio-vascular changes in the former condition, the urine of chronic Bright's disease falls short of that passed in hydruria, nor does the specific gravity ever fall so low. But there are some anomalous cases in which the diagnosis is at first difficult; thus a hospital patient who had slight albuminuria and some degree of diuresis, and had suffered from repeated attacks of ague, after treatment with large doses of quinine the albuminuria ceased, but at the same time the diuresis enormously increased, and the disorder assumed the form of insipid diabetes, and which was subsequently reduced by the administration of ergot, given with quinine. The absence of sugar both in hydruric and polyuric cases distinguishes them from saccharine diabetes. The great increase of the urinary solids in polyuria, and the absence of albumin prevents confusion with regard to any form of chronic renal disease. Temporary albuminuria (see functional albuminuria), however, is not infrequently attended with an increased excretion of urea, resembling what is noticed in polyuria; both conditions being probably allied and due to the same cause, viz., a disturbance of the nitrogenous equilibrium, from increased metabolism, caused probably by over-stimulation—by a too highly nitrogenized diet.

151. **Prognosis, Course, etc.**—*Hydruria.* It has been already stated that the prolonged discharge of a highly aqueous urine in excessive amounts, may not affect the bodily health, and is not incompatible with length of days. Even in the most unfavourable cases, as those dependent upon lesions of the encephalon, improvement often takes

place under treatment. Absolute cure of the disease is, however, rare, though the diuresis may be controlled. In some instances the disease has been arrested by the onset of some acute disease. Death when it occurs is usually by some intercurrent affection, but in some instances uræmic coma supervenes, as if the function of the kidney had undergone suspension.

Polyuria.—The long-continued discharge of the urinary solids in excessive amounts must always be regarded as a grave circumstance, and is often the prelude of some serious constitutional disturbance, of cancer, tubercle and constitutional syphilis. In the more pronounced form they may run a distinct course, resembling saccharine diabetes, but without sugar, and terminate either with marked nervous disorder, or in phthisis; or after a while sugar may appear in the urine, and the case becomes one of true saccharine diabetes.

152. **Treatment.**—Since *Hydruria* depends on the interruption of innervation by the vaso-motor tracts leading to dilation of the renal arteries, and consequently giving rise to increased capillary pressure, it has been sought to restore the arterial tonicity by means of special remedies. Of these ergot of late years has been chiefly used, and several instances of its successful employment have been recorded. In some cases its administration is said to have been followed by a cure. I have never seen myself such a favourable result, but there can be no doubt that in some cases it does diminish the hydruria, both during the time the drug is taken, and some time after. In some cases it has failed to do good, whilst in some it has done positive harm. Valerian too is a remedy that has been largely employed for the treatment of insipid diabetes, and in cases where the hydruria is a fleeting symptom, rather than an established disease, it undoubtedly does good when

given in large doses, such as half an ounce of the tincture three times a day, valerianate of zinc in three grain doses may be given advantageously at the same time. Nux vomica or its alkaloid, strychnia, is also a useful adjuvant, perhaps helping to restore the arterial tonicity. Belladonna has been given with the view of causing contraction of the vessels, but it should be administered with caution, as instances have been recorded in which hydruric patients have shown a marked susceptibility to its influence. In no case, however, should the indications for special treatment be overlooked, that is to say, if there is any definite evidence that the disorder has originated from or is connected with any special cause, such as traumatic lesion of the brain substance, intra-cranial growths, constitutional taints, such as scrofula, syphilis or malaria, alcoholism, etc. In these cases we must apply special remedies before we can hope to restrain the diuresis by medicines like ergot, valerian, etc. Thus, in the case already alluded to of profuse hydruria, following on albuminuria, in a malarial subject, quinine was given in large doses before and during the administration of ergot, and the relief of the diuresis was, I am convinced, as much due to the one as the other. And in children improvement often follows the administration of cod-liver oil and syrup of the iodide of iron. With regard to the dietetic and hygienic treatment. Food should be liberally given, three substantial meals daily, whilst any craving and sinking between meals should be promptly relieved by some minor meal. The diet should be a mixed one, with a liberal supply of fatty food. The patient should be allowed to relieve his thirst at pleasure. When undue restraint has been practised on patients in this respect, serious disturbance of the bodily functions results. In cold weather the fluids should be warmed, the ingestion of

large quantities of water at a temperature little above freezing point must abstract a large amount of heat from the body, and as these patients suffer much from depressed temperature it is a point worth paying attention to, since the patients themselves prefer cold drinks because they are more grateful to the parched tongue and palate. The drink too should be thickened, either with barley or better still with oatmeal. A handful of raw oatmeal stirred into a quart of boiling water with one lemon sliced into it forms a most grateful and thirst-quenching drink. The clothing should be warm, the vests, drawers or stockings being all of wool. When it is possible, sufferers from this disorder should select a locality, with a dry sub-soil, with a South or South-west aspect, to reside in, whilst if they are in a position to afford it, they should pass their winters in Southern latitudes. The employment of the Russian vapour bath, and sea-water douches, either natural or artificial, give great relief in the majority of these cases, and are nearly always followed by a temporary diminution of the diuresis.

With regard to the treatment of *Polyuria*, the main indications are rest and an endeavour to promote nutrition generally. To attain this end opium or codeia should be given in full doses, when the patient first comes under observation. As soon, however, as the nervous system is quieted, and the rheumatic and neuralgic pains are less severe, it should be discontinued, lest it interfere with digestion. General tonics, such as iron, phosphorus, quinine, nux vomica, hydrochloric acid, and cod-liver oil, should be persevered with. When there is a history of syphilis, iodide of potassium should be combined with these remedies. Vapour baths, followed by tepid douches, sea-water or sea-salt, give great relief to the neuralgic pains, and also soothe the nervous system. The soluble phosphates may be administered; but their utility in these

cases is questionable. There appears to be no lack of these constituents in the system; the difficulty seems rather to lie in the want of power of the tissues to retain them. The food should be light and nutritious, and if urea be greatly in excess, the nitrogenous articles of diet should be reduced to a minimum. Alcohol should be avoided; it invariably, even in small quantities, increases the diuresis. The same may be said of coffee. Change to dry bracing air should be obtained if possible. The residence should face South or South-west, with a dry subsoil. The patient should clothe warmly, keep early hours, and avoid all excitement and fatigue.

Diabetes Mellitus and Glycosuria.

153. **Varieties.**—Sugar occurs pathologically in urine under a variety of conditions. There are, however, two forms in which it presents itself, viz., a form in which the discharge of sugar is persistent, or is only held in check by the adoption of a strict dietary; the other, which is of a temporary character. The first is usually spoken of as *diabetes mellitus* or true diabetes, signifying the drain of sugar taking place from the body; whilst the more transitory form is generally designated as *glycosuria*, indicating that the chief clinical significance lies in the appearance of the sugar in the urine. Although the adoption of the terms diabetes mellitus and glycosuria to distinguish between the persistent and temporary forms of the disease respectively, may be considered fanciful and somewhat arbitrary, still some such classification is necessary, if we wish to avoid confusion, and rigidly distinguish between saccharine urine, the result of profound and permanent disorder of the vaso-motor centre, that regulates

the glycogenic function, and a mere fleeting disturbance of the same. Further, "diabetes mellitus" may be divided conveniently into two forms. One severe, characterized by an excessive discharge of sugar, in which although the amount of sugar is materially reduced by a strict avoidance of saccharine and amylaceous articles of diet, yet it does not actually disappear; and a mild form, in which on the assumption of a rigorous diet the sugar disappears entirely from the urine, to return again, however, when a mixed diet is resumed. No very rigid line can, however, be drawn between the two classes, the severe form may gradually become milder, whilst the mild form may suddenly increase in severity. So also in "glycosuria" the derangement of the glycogenic function, may be so great as to cause the appearance of large amounts of sugar in the urine, so that in many respects the case resembles the confirmed form of diabetes mellitus; whilst on the other hand the sugar may be present in only small quantities, and, what is so especially characteristic of glycosuria, in amounts that fluctuate considerably from day to day.

154. **Etiology.**—One of the most important predisposing causes of non-traumatic diabetes is undoubtedly that of *hereditary* influence. In a considerable number of cases that have come under my observation, particularly among private patients, in which the disease has been attributed to some other cause, a close examination of the family history has revealed a morbid taint, predisposing to this affection by rendering the possessors more liable to the influence of exciting causes. In most the transmission is direct, passing from parent to child, in some cases even to the third or fourth generation. Thus, in one instance, the disease was brought into the family by the great grandmother; of her children, who were numerous,

and lived to marry, only one had children, and this one was known to have had diabetes. Of his children, two died of diabetes, one suffered from rheumatoid arthritis; whilst another who was killed early in life, left a son who is diabetic, and at the age of forty is the sole survivor of what promised at the beginning of the century to be a numerous family. In some instances the transmission affects one line of descent. A diabetic patient informs me, that two of his brothers died of diabetes, and a third has the disease in a mild form, whilst his sisters have escaped. In this case the disease came into the family through the mother. In other cases the hereditary influence is not direct, the parents or grand-parents never having suffered from the disease, but from what may be considered allied diathetic conditions; of these, gout and rheumatoid arthritis seem to have most influence. But whilst hereditary tendency either direct or indirect can be traced in most cases of confirmed diabetes, still there are many in which no such relationship can be proved. This is no doubt owing to the little attention hitherto paid to the important bearing of hereditary influence upon disease. Besides, we must not overlook the fact that many cases of acute diabetic coma would, had they occurred twenty or even ten years ago, have been put down as either due to heart disease or serous apoplexy, and in this way the records have become confused. *Mental disturbances.*—"Sadness and long sorrow" since the time of Willis (1645) has been recognized as one of the causes of diabetes, to which may be added strong mental emotion of all kinds, such as business anxieties, protracted intellectual toil, shock, fear, etc. I have been struck with the considerable number of diabetic patients I see in the out-patient department of the London Hospital who attribute the disease to vicissitude and want. *Cold.*—Exposure to cold and

drinking cold fluids whilst heated have been said to cause diabetes. The evidence on this point is negative. Supposing, however, the predisposition exists, there can be little doubt that cold may act as an exciting cause. Two sailors both referred their illness to cold and exposure, and a gentleman told me that he became diabetic after riding home, one December night, on the outside of an omnibus. On arriving home he had several rigors and was roused several times to pass water. Alarmed at the diuresis he consulted his medical man, who found he was diabetic. In the case of a lad aged 15, the only cause the parents could assign, was his having drunk cold water when heated; in this case, however, I have suspicions, that some latent tubercular disease of the brain existed.

Constitutional disorders.—Gout and rheumatoid arthritis have been already mentioned as allied diathetic conditions predisposing to diabetes. The relationship to gout has long been recognized by the profession and needs no further comment; but the connection between rheumatoid arthritis and diabetes is not so well established. Dr. Garrod (*op. cit.*) was the first, I believe, to draw attention to this point, and I have met with four instances in which the relationship was well marked. Diabetes is said to supervene upon attacks of malaria, and that residents in a malarious district are very liable to the disease. During the seven years I was connected with the Dreadnought Seamen's Hospital, where a very considerable number of patients suffering from malarial affections are admitted every year, I failed to find a single case in which the disease was attributable to that cause. Indeed, among sailors, diabetes seems very rare, for during the seven years I acted as physician to that institution only three cases of saccharine diabetes came under my observation, two of these, as already stated, referred the disease to

exposure to cold, neither had ever had ague; in the other, the disease followed after a blow on the skull. However, although I never noticed a decided case of diabetes associated with ague, still sugar was by no means infrequently found on testing the urines, sometimes in considerable amount, but which generally passed off when arsenic or quinine was given. This glycosuria is what one would naturally expect, since malaria, by inducing a catarrhal condition of the digestive organs, intefreres materially with saccharine assimilation. A fact pointed out many years ago by Prout. Malarial glycosuria assumes importance with regard to the question of surgical operations; Professor Verneuil (*L'Union Médicale*, No. 142) having shown very conclusively that during its continuance wounds do not close. Diabetes sometimes supervenes on the subsidence of acute affections, such as pneumonia, acute rheumatism, typhoid fever, scarlet fever, etc.; in cases of this kind that have come under my observation, I have found on enquiry, either a family predisposition to the disease, or else reason to suspect that the disease had previously existed in a mild form. Dr. Dickinson (*op. cit.*, p. 62) has drawn attention to the frequency of glycosuria in insanity. Dr. Hales White (*Path. Soc. Trans.*, 1883) has, however, questioned the accuracy of this assertion.

Food.—Excess of starchy and saccharine food undoubtedly induces glycosuria in some persons till the effect of the meal passes off, but whether habitual excess will eventually cause true diabetes is very doubtful. During the "lentil" craze, some five years ago, I saw two patients who had reduced the amount of animal food to a minimum, taking hominy for breakfast, lentil soup for lunch and dinner, with rice and other farinaceous puddings, both became glycosuric, but on resuming an ordinary mixed diet they speedily recovered. These were probably

instances of individuals extremely susceptible to the influence of sugar, and probably the tendency was aggravated by the sudden change in their mode of living. Confirmed vegetarians, or West Indian negroes, who largely consume the sugar cane, however, do not appear to be particularly liable to diabetes. Excessive indulgence in alcohol has, by some writers, been said to cause diabetes. Dr. Dickinson (*Med. Chir. Trans.*, vol. lvi.) with his usual industry has exposed the fallacy of this statement. There is, however, probably some truth in the statement that the immoderate use of acid wines and cider have sometimes occasioned the disease. *Injuries to the head* or blows and falls likely to affect the brain by indirect violence, are not infrequently followed by the appearance of sugar in the urine, which in some rare cases has become persistent. Blows over the abdominal region have been said to have sometimes had the same effect, but in these cases it is difficult to exclude the possibility of some remote injury to the head. The existence of intra-cranial tumours, or of softening in the neighbourhood of the fourth ventricle, may cause transitory or permanent diabetes; but such instances are not so common as with insipid diabetes.

General Etiology.—Saccharine diabetes is essentially a disease of adult life. Dr. Dawson Williams (*Path. Soc. Trans.*, 1883) has compiled, from the returns of the Registrar-General, a table showing the age at which death from diabetes most commonly occurs, and the proportion of males to females, which makes this very plain. According to this table, the proportion of male cases to female is as 3 to 1·7. This, however, I am convinced is too high, since I believe in females, that many deaths from diabetes occur in connection with the puerperal state, without the disease having been recognized. In Dr. Matthews Duncan's (*Trans. Obst. Soc.*, vol. xxiv.)

interesting collection of cases of puerperal diabetes, we see in how many instances the saccharine condition of the urine was discovered accidentally.

Deaths from Diabetes during Decenium, 1871-1880.

	Males.	Females.	Total.
Total under 5 years . . .	23	25	48
From 5 to 10 years . . .	65	54	119
,, 10 ,, 15 ,, . . .	134	133	267
,, 15 ,, 20 ,, . . .	284	171	455
,, 20 ,, 25 ,, . . .	348	201	549
,, 25 ,, 35 ,, . . .	816	502	1318
,, 35 ,, 45 ,, . . .	906	494	1400
,, 45 ,, 55 ,, . . .	954	547	1501
,, 55 ,, 65 ,, . . .	1236	660	1896
,, 65 ,, 75 ,, . . .	922	464	1386
,, 75 ,, 85 ,, . . .	229	121	350
,, 85 ,, 95 ,, . . .	12	2	14
Totals . .	5929	3374	9303

Dr. Dawson Williams has also drawn up an instructive table showing that diabetes is becoming year by year more common, and also that urinary diseases are increasing proportionately more than nervous diseases.

Mean Annual Rate of Mortality in England. Annual Deaths to 1,000,000 Living.

Years	1850 to 1854.	1855 to 1859.	1860 to 1864.	1865 to 1869.	1870 to 1874.	1875 to 1879.	Average. 1850 to 1879.
Deaths from all causes .	22,299	22,052	22,248	22,760	22,019	21,250	22,105
,, ,, Nervous Diseases .	2,777	2,758	2,823	2,859	2,817	2,812	2,808
,, ,, Urinary Diseases .	190·6	227·	270·6	320·2	352·2	420·	296·9
,, ,, Diabetes .	23·	24·8	28·4	32·2	35·2	40·6	30·7
,, ,, Gout . .	12·4	13·2	13·4	18·2	20·8	25·6	17·3

Persons of sanguine temperament and fair hair are said to be more prone to the disease than the melancholic and dark haired, but I imagine the distinction is fanciful. There is one point, however, I can affirm, that diabetics are generally individuals of superior intelligence. Hufeland observes he never saw a stupid man affected with diabetes. Dr. Dickinson, from statistics collected with amazing industry, has arrived at the conclusion that diabetes is more abundant in agricultural districts than in manufacturing and mining, and that it is more common in the colder than warmer countries. Dr. Roberts, however, is of opinion that the disease is more frequent in urban than in rural districts, and this I think is in accord with general experience, though Dr. Dickinson's statistics are indeed strongly against such a supposition. Can the fact, that diabetics improve in country air—and many leave the towns to reside in the country for the purpose of maintaining health—and that the imported factory hand or miner probably goes back to die in the workhouse of the rural district from which he was drawn, account for the greater number of deaths from diabetes that undoubtedly are recorded in rural districts? Dr. Dickinson's theory, that cold and exposure are the causes predisposing to this excess of mortality from diabetes, can hardly be accepted, since if this were so, then the disease ought to be common among the sailors of our mercantile marine; whereas, as the experience of the Seamen's Hospital shows it is far from being frequently met with. Dr. Dickinson's statistics also show that the disease is more prevalent in the colder and bleaker Eastern counties than in the Western. Yet here, again, we are confronted with the fact, that the disease is tolerably frequent in inter-tropical countries, as Ceylon for instance, whilst it is comparatively rare in Russia.

So far we have considered the causes that may give rise either to permanent or temporary forms of the disease, we must now briefly refer more especially to those that concern the latter form. This is chiefly induced by the passing action of certain toxic agents, either introduced from without, or from some altered condition of the blood itself. *Glycosuria* has been found, experimentally, to follow the administration of carbonic oxide, chloroform, alcohol, ether, when given in large doses; strychnine and morphia have the same effect. The ingestion of large quantities of acid is sometimes followed by glycosuria, according to Pavy, phosphoric acid has a special irritating effect upon the liver; an increase or an accumulation of uric acid in the blood has also been regarded as a cause of "gouty glycosuria." It has also been shown, when the red blood corpuscles are extensively destroyed, that sugar appears in the urine. To these morbid conditions of the blood may be added those of rheumatism, malaria, and cholera, lactation, etc. Abnormal conditions of the alimentary tract leading to malassimilation of the amylaceous and saccharine elements of the food, play, although their nature is not yet determined, an important part in the production of glycosuria. The frequent association of organic disease of the pancreas with permanent diabetes, makes it not improbable that a temporary functional derangement of this organ, by causing an arrest of the highly alkaline secretion, may, by lowering the alkalescence of the blood in the portal vessels, disturb the hepatic circulation, and thus induce glycosuria. Sugar not infrequently makes its appearance during states of debility, thus the urine may become saccharine during convalescence from influenza, or after blood-poisoning from sewer gas, etc. Overwork, care, anxiety, or even simple debility, will frequently be attended with saccharine urine.

I have noticed that women at "the change" often pass considerable quantities of urine containing sugar. The glycosuria, or rather the mild form of diabetes, that elderly persons so frequently exhibit, is the result of exhaustion and debility. Claude Bernard looked upon the appearance of sugar in these cases as a salutary effort of nature to repair, by an over-production of glycogen, the exhaustion of the organism; but it is more probable that it is due to a general nervous exhaustion bringing about vaso-motor paralysis.

155. **Symptoms.**—When the amount of sugar passing out of the body is considerable, it is usually attended with marked symptoms. These are, great bodily weakness, thirst, excessive micturition and saccharine urine. Some cases, although there may a considerable amount of sugar in the urine, complain neither of weakness, thirst, or excessive micturition; these, however, are exceptional instances, and generally occur in glycosuric and not truly diabetic cases. The symptoms usually come on insidiously, and the disease gradually developes; in some instances the invasion is sudden, the patient being able to refer to the very day on which the disease began. These cases generally run an acute course. The symptoms vary very much in individual cases, being more pronounced in some cases than in others. Bodily debility is generally the first symptom complained of, and on being questioned, the patient also complains of thirst and a frequent desire to pass water. Sometimes if we examine the trousers or stockings, we may find whitish sticky stains caused by drops of saccharine urine falling on them. The loss of strength is also generally attended in severe cases with emaciation, though in mild forms of the disease; the patient though complaining of feeling tired and weak, maintains his usual bulk. The

temperature is subnormal, unless some secondary lung complication exists, it has been recorded as low as 93° F.; the more usual range is 95·5° F. to 97° F. The thirst is always aggravated by the ingestion of saccharine and starchy food; it differs from that of diabetes insipidus, in that the desire seems to be rather to alleviate the sensation of thirst, than to swallow enormous quantities of water. A patient with hydruria will seize a water-jug and empty it at a draught, whilst the patient with melliturıa prefers oft repeated sips.

The URINE at quite an early period acquires a peculiar character. It loses its amber tint, and becomes a greenish-yellow, and if exposed to the air for a few days, often becomes deeply red, probably from oxidation changes of the indican, which is always in excess in diabetic urines. Its reaction is nearly always highly acid, and the acidity increases by exposure to air, and long resists alkaline fermentation. The quantity of urine is usually very greatly increased, and generally bears a fairly definite proportion to the amount of sugar excreted. This is not always the case, however, and I have met with two instances in which with a very considerable excretion of sugar the amount of urine hardly exceeded the normal. Both cases ran an acute course, and died of diabetic coma. The amount of urine, however, passed in ordinary cases of diabetes, ranges from 4000 to 8000 c.c., six to twelve pints, though exceptionally it has been known to reach the prodigious quantity of more than thirty pints. The *specific gravity*, owing to the increase of solid matter caused by the sugar, is always raised, and in cases of ordinary severity ranges from 1·028 to 1·045. It may, however, rise considerably higher, and a degree of 1·070 has been recorded. On the other hand, in exceptional instances it may fall below 1·020; these, however, are usually cases of

glycosuria, in which the saccharine state of the urine is purely symptomatic of some other morbid condition. The specific gravity of diabetic urine diminishes when it is kept some time, owing to the transformation of the sugar by vinous fermentation and the disengagement of alcohol. The elimination of *Urea* is always increased, and this increase is usually proportionate to the severity of the disease. Thus in mild cases in which the amount of sugar excreted is readily checked by the adoption of a restricted dietary, the increase is not considerable; whereas, in severe instances of the disease the increase in the proportion of the urea to the sugar excreted, is often as one to five, or even one to three. In making the calculation, the normal amount of urea excretion must be deducted. Thus a patient who in the twenty-four hours excreted 69 grms. of urea, and 148 grms. of sugar, was calculated from his normal body weight to have a normal excretion of 36 grms. of urea, consequently the morbid excess of urea over the physiological excretion, amounted to 33 grms., or as 1 to 4·5 in proportion to the amount of sugar discharged. This excess of urea, however, must not be considered to be entirely pathological, since a considerable proportion is due undoubtedly to the increased ingestion of nitrogenous food. It is, however, so difficult to discriminate between the two, that it is more convenient to make the calculation with only the deduction of the normal excretion of urea, without attempting to subtract that caused by the additional ingestion of nitrogenous food. It has been stated by some writers that *Uric Acid* is diminished in diabetes, I have never observed a diminution, but always a slight excess of the normal. Owing, however, to the abundant aqueous discharge by the kidneys, it is rarely deposited in a crystalline state, a fact which probably ac-

counts for the idea that it was actually diminished in quantity, and for another erroneous statement, that saccharine diabetes alternates with manifestations of the "uric acid diathesis." The truth being that uric acid, if anything is increased in diabetes, and that its deposition from the urine when the amount of sugar excreted is diminished, or entirely checked, by diet, really means that the diuresis being less, the urine is more concentrated, and consequently the tendency to throw down uric acid and urates is increased; and this condition is no doubt heightened by the continuation of a highly animal diet for sometime after sugar has disappeared, a diet which keeps the urine above its normal degree of acidity. *Hippuric Acid* is often found in excess in diabetic urine. Those writers who suppose that the excretion of uric acid is decreased in diabetes, hold that it is replaced by hippuric acid. A careful examination of the urine, however, will prove that both are usually increased. The amount of *Phosphoric Acid* excreted is in most cases above the normal, this is perhaps due in some measure to diet, but when the increase is very great not wholly so, since the phosphates of an increased meat allowance hardly counter-balance the phosphates of the bread withdrawn. Some portion of the excess is also caused by the drain of water going on through the body, washing out the tissues, but the main increase is undoubtedly due to increased metabolism going on in the nervous system. It has also been shown that in addition to the increased elimination of phosphorus, as phosphoric acid, a considerable amount of unoxidized phosphorus is passed into the urine in diabetes (see p. 98). *Chlorine* and *Sulphuric Acid* are generally found increased but not to such amounts as cannot be accounted for by the highly animalized diet adopted. According to Dr. Dickinson, *lime* salts are in some cases

of diabetes eliminated in excess. Dr. Dickinson accounts for this by assuming that phosphoric acid being in excess in the blood withdraws lime from the tissues; but this is not probable, since the phosphoric acid, as separated, would be already combined with some base; it is more likely for oxalic acid, formed by the oxidation of some of the sugar in the tissues or blood, to act in this way, forming oxalate of lime, of which a considerable quantity is usually met with in diabetic urine. Or lime may be withdrawn owing to the peculiar physico-chemical affinity that seems to exist between it and sugar. *Glucose* is of course the most important constituent of diabetic urine. The amount may vary from a mere trace, to, in exceptional cases, several pounds per diem. The average range, however, of most diabetic cases is from about three ounces to ½lb. in the twenty-four hours. But cutting off all saccharine and starchy food, the quantity of sugar in the urine is diminished, and in some cases it entirely disappears. If the amount of sugar be frequently estimated, it will be found to fluctuate considerably from day to day. It is often difficult to account for these diurnal variations, except on the supposition that the patient has surreptitiously transgressed. But in spite of the closest supervision, such variations do occur that recourse must be had to some other supposition. A medical friend who is diabetic, and who carefully watches the turns of his disease, tells me these variations depend very much on the state of his bodily health. Whenever, he says, his liver gets out of order, and he has a bilious attack, or if he sits up late writing, or is in any way worried, the sugar increases without being referred to any relaxation of his dietetic precautions. The amount of sugar is always decreased by fasting, and increased after food; the period when the greatest amount of sugar passes out of the body, being

about three hours after a meal. When the case is about to terminate fatally, there is generally a considerable diminution in the amount of sugar excreted, though that it completely disappears is doubtful, since there is usually no difficulty in determining the presence of sugar in urine taken from the bladder after death. Pyrexial complications also temporarily diminish the amount of sugar excreted.

Many substances besides those above enumerated, may be casually present in diabetic urine. *Albumin.*—Traces of albumin are usually met with in the urine of cases of confirmed diabetes, it is probably caused by the irritation produced by the constant passage of saccharine urine through the urinary tubules. No renal changes, beyond increase of, and fatty changes in, the epithelium, have been noticed. Besides this, diabetes has no connection with albuminuria or renal disease of any kind. There are, however, certain cases of albuminuria in which the urine is intermittingly saccharine, but these are not cases of diabetes but only of transient glycosuria. They occur generally in persons whose health has been broken by habits of dissipation, and who are victims of chronic alcoholism, syphilitic cachexia, etc. The urine is usually of low specific gravity (1·010-1·015), and the amount of sugar present is never very great, rarely exceeding three per cent. *Acetone.*—Saccharine urine usually contains acetone, or a body that yields acetone when the urine is distilled with hydrochloric acid. Acetone is a limpid, colourless liquid, specific gravity 0·7921, having a peculiar etherial odour. Its solution gives a mahogany-red coloration with ferric chloride. Heated with iodide of potassium and caustic potash, iodoform is formed. A solution of nitroprusside of sodium and ammonia added to a fluid containing acetone, and the mixture well shaken, gives

rise to rose-violet colour. As already stated (p. 32) the antecedent of acetone in the blood is aceto-acetic acid. It has been objected by Le Nobel, however, that aceto-acetic acid is so volatile, that it cannot be kept even a few hours in a stoppered bottle, and yet the substance that gives rise to acetone can be extracted from the urine with ether. It is probable, however, that aceto-acetic acid does not exist in a free state, but in combination with some base, or is derived from a more stable compound. Thus Minkowski has recently discovered the presence of an acid (β- or pseudo-oxybutyric acid) in diabetic urine, which is capable of breaking up into aceto-acetic acid. Acetone, or acetone yielding bodies, however, is not alone found in diabetic urines, since it has been met with in the urines of many acute diseases, scarlet fever, pneumonia and the like, also in anæmia, dyspepsia, cancer of the stomach, etc.

Inosite may be present in diabetic urine, and is of no special significance; not infrequently it appears unaccompanied by glucose, giving rise to a condition known as inosituria (see also p. 126). *Lævulose* is also sometimes present in diabetic urine, it can be distinguished from glucose by its left-handed polarisation (p. 128). When glucose or lævulose are both present in sufficient quantities, as is sometimes the case, the evidence drawn from the polariscope will be negative, the left-handed rotation of one sugar, interfering with the right-handed rotation of the other.

In addition to such special symptoms, as emaciation, thirst, diuresis and saccharine urine, there are others of more general character which may be present in some cases and absent in others. Anomalous nervous symptoms are frequent, such as cramps in the legs, and the peculiar neuralgic pains, coming on especially after food,

which chiefly attack the epigastric, lumbar, sciatic and brachial nerves (see also p. 33). Cutaneous hyperæsthesia, usually localized. Sudden sweats, frequently unilateral, or affecting only the palms of the hands or the soles of the feet. Also sensations of great internal bodily heat. Failure of vision, due to premature presbyopia, glycosuric amaurosis, cataract, or to actual changes in the fundus oculi (see p. 37), often occur. The intellectual faculties are not affected in diabetes, and many distinguished men, who have suffered from the disease, have performed their professional duties, provided they did not entail much bodily exertion, with clearness and vigour up to the very last. They, however, as a rule suffer much from nervous irritability, hypochondriasis, and are disinclined for social pursuits. The sexual instinct is lost at a very early period of the disease, though an amelioration of the symptoms is generally marked by its return. The breath has a peculiar odour, like that of decaying apples, and the mouth is dry, with usually a sweetish-acid taste, and the tongue covered with a thick sticky saliva, which forms streaks over the organ which is often bright-red. The gums are usually tender and spongy, and have a tendency to recede, leaving the roots of the teeth bare and loosened. The appetite may continue ravenous till the end, but usually in the later stage declines, and there may then be a disgust for food though the craving, sinking sensation remains. Diabetic patients suffer much from flatulence, causing painful distension of the abdomen, eructations and sometimes retching. The bowels are constipated, the motions when passed being dry and scybalous, this state sometimes gives place to a troublesome diarrhœa, especially in a late stage of the disease. The skin is usually harsh, dry, and, owing to the disappearance of the subcutaneous fat, wrinkled, the surface is generally pallid or of unhealthy yellowish

tinge, but the cutaneous vessels of the face are often injected, giving a deep reddish tinge to the checks, so that the patient's face looks like a withered winter apple. This dry state of the skin is often succeeded by sweats of longer or shorter duration, sometimes these sweats are unilateral, sometimes they only affect the extremities. In an advanced stage of the disease, boils, small carbuncles, and impetiginous eruptions often occur, whilst the contact of the saccharine urine produces a troublesome eczema of the vulva in females, and of the prepuce and glans penis in men. Patches of eczema, lichen, or psoriasis, in different parts of the body, may appear during the course of the disease. Spontaneous gangrene sometimes occurs in protracted cases of the disease, it may invade the chin, the nose, the lungs, or other parts of the body, but most frequently attacks the feet. Œdema of the lower extremities occasionally sets in towards the close of the disease, and is apparently due to the existing anæmia. Such are the main features exhibited by cases of typical diabetes, though the disease may exist in a mild form for many years without causing the patient much discomfort, indeed without in any way affecting his general health, or interfering with the nutrition of the body.

The question of diabetic coma is best reserved till we consider the course and pathology of the disease.

156. **Diagnosis.**—A typical case of diabetes cannot be taken for anything else, and our difficulty is to determine between true diabetes and mere glycosuria. In the majority of cases, when the patient first comes under observation, it is impossible at once, to come to a definite conclusion, though we may be helped by the following considerations. Glycosuria, as a rule, is not always attended with the ordinary symptoms of diabetes, and the saccharine condition of the urine is only detected

by chance, owing to a routine examination of the urine. It also usually runs an anomalous course, and there are greater fluctuations in the amount of sugar, than is noticeable in confirmed diabetics; moreover, the amount of sugar excreted hardly ever reaches so high a grade. Cases of glycosuria, however, may occur, which in their onset resemble true diabetes, both with regard to the amount of sugar excreted, the profuse diuresis and other symptoms; these acute cases usually speedily recover, and are often quoted as recoveries from diabetes. A good case of this kind is related by Dr. Weber, and quoted by Dickinson, of a merchant who during the commercial crisis of 1857 became glycosuric, passing about eight pints of urine, specific gravity 1·036-1·044, who recovered in three weeks, remained free from all symptoms till 1866 when during another crisis, again became glycosuric and again recovered. Glycosuria is also generally attended with some other morbid condition, such as functional derangement of the liver, the result of plethora; gouty proclivities; or conditions of debility, such as follow on diphtheria, blood-poisoning, prolonged lactation and the like; or after severe bodily and mental exhaustion, or the weakness of old age. It is rare for glycosuria to be long persistent, and it generally yields to treatment, and though like diabetes the sugar in the urine is diminished when starchy and saccharine food is cut off, still the influence of diet is not usually so marked, as it is in the case of diabetes. That is to say, we frequently meet with cases of glycosuria in which the sugar is scarcely controlled in spite of dietetic restrictions, whilst those, in which it is not increased by permitting a mixed diet, recover when the cause which brought about the increased glycogenetic activity of the hepatic cells has passed away. The great distinction, however, between glycosuria and diabetes lies in the fact

that the former is curable, whereas the latter relapses whenever the dietetic restrictions are relaxed. It is also important for us to bear in mind, in expressing an opinion with regard to any given case, that a transient or intermitting glycosuria may at any time pass into confirmed diabetes. Sugar may be added to the urine for the purpose of deception, impostors, however, not being educated in pathological chemistry usually employ cane sugar, so the fraud is easy of detection.

157. **Course.**—As a rule saccharine diabetes runs a chronic course, but the progress varies greatly in individual cases. In some the disease commences insidiously, and progresses slowly and mildly for years, and then suddenly becomes aggravated and speedily carries off the patient. In others the disease at first assumes a severe type, and then under treatment becomes milder and so remains stationary for a considerable period, neither advancing nor declining. Again there are cases, as Dr. Pavy (*op. cit.*) has pointed out, that progress as it were by a series of short bounds or leaps, very much like cases of progressive muscular atrophy or locomotor ataxy. Thus, when they first come under observation the disease is checked by diet, then there is another exacerbation which is again checked, but this time opium is required in addition to dietetic restrictions, and which has to be repeatedly increased as each fresh downward step is taken, till finally a stage is reached in which neither diet nor opium avails to control the advance of the disease. Lastly, there are cases of a "foudroyant" type in which the disease sets in suddenly with great severity, and rapidly proves fatal through diabetic coma. These cases, however, are quite exceptional, and most that have been recorded, probably belong to the first class of cases mentioned, viz., a mild form of diabetes suddenly assuming an intense form, since

a close enquiry into the patient's antecedents generally reveals the fact that for some time previously the patient has been passing more water than usual, or has been more thirsty than usual, as in a case related by Professor Paget and quoted by Dickinson (*op. cit.*, p. 107). Or as in another case in which the housemaid remembered that for some time previously the water-jugs in the patient's room were always empty of a morning, and she could only account for the disappearance of the water by his having drunk it. In the case already mentioned (p. 40), if Dr. Duncan had not previously found traces of sugar in the patient's urine, we might have been led to suspect that the disease was recent.

Owing to the irregular progress of the disease, and the long periods during which it may remain stationary, and be fairly controlled by treatment, we are unable to assign a possible duration to any given case, since a mild form may become aggravated any day, whilst an apparently severe case may prove more amenable to treatment than expected. In fact a diabetic patient may be aptly compared to some tower undermined, its downfall is assured, but none can tell when the catastrophe will occur. Cases of patients whose urine has been continuously saccharine for more than twenty years are on record, and instances of the disease lasting twelve, fourteen or sixteen years are by no means infrequent. The prompt recognition of the disease, owing to the more routine employment of urinary tests than was customary formerly, and the possibility of thus detecting it at an early stage before it assumes an aggravated form, gives us better hopes of controlling its progress, and giving the patient a better expectation than was previously possible. When, however, a case of diabetes has entered on a steadily downward course, and in spite of dietetic restrictions and full doses of opium the

disease is not controlled, our prognosis must assume a more gloomy form, for when the disease assumes a permanently aggravated character, the patient usually dies within two years of the exacerbation, frequently much within this period.

Diabetes may terminate fatally by exhaustion. Owing to the continued drain on the system, the patient becomes reduced to a state of extreme weakness; whilst owing to the anæmia the lower extremities become œdematous. The tongue becomes red, raw and glazed, and the mouth and throat covered with apthous patches, an incontrollable diarrhœa may set in, which itself is sufficient to carry off the patient in his already weakened state, but the end usually comes through some acute inflammatory affection of the lung, accompanied with pulmonary œdema. Or the patient may succumb at an earlier stage of the disease from the development of chronic pneumonia, which at first may run an insidious course, but at length causes a breaking down of the lung tissue, and the formation of phthisical cavities, though rarely associated with the deposition of tubercle. Contrasted with this comparatively lingering termination is the somewhat sudden death that occurs by what is known as acute diabetic coma (Küssmaul's coma). Many writers have described this sudden death as if due to one and the same cause, though in reality two forms at least are clinically recognizable.

In the first form the coma follows closely upon an attack very much resembling collapse or syncope, the patient becomes suddenly faint, often after some complaint of oppression over the region of the heart, the extremities are cold, the pulse extremely weak but often very rapid (130-140) at first, but soon rapidly falling, often great restlessness but no delirium, there is no panting respiration, and the patient quietly sinks from exhaustion.

In the other form, of which a description has already been given (p. 30), the onset is ushered in with gastric disturbance, a peculiar panting dyspnœa, followed by a delirium of a noisy character which is succeeded by profound coma; occasionally convulsions of an extremely violent character occur, in which the patient may die without becoming comatose; when this happens the kidneys are usually found diseased as well.

In both forms the quantity of urine is considerably diminished at the onset of the attack, in the latter it may be entirely suppressed. In one case I saw, no urine was passed from the onset of the symptoms till death, a period of fifteen hours, when an ounce or two was found in the bladder; whilst the excretion the previous day had amounted to 120 ounces. In this case the odour of acetone which had been noticeable in the breath and urine for some time previously, disappeared during the two last days.

Such are the modes by which diabetes proves fatal. The first is undoubtedly the natural termination, the others are rather accidents by the way. Death by exhaustion more usually results in those cases which have run a uniform course; the syncopal form generally occurs in those cases in which emaciation is a marked feature from the commencement; whilst diabetic coma is a characteristic termination of acute cases of diabetes, or of cases previously existing in a mild form that have suddenly become acute. According to Dr. Frederick Taylor (*Path. Soc. Trans.*, 1883) the deaths from coma are fully one-third more numerous than deaths through pneumonia and phthisis, and mostly occur in young persons. Dr. Saundby (*op. cit.*), who has recently ably reviewed the whole of our knowledge concerning diabetic coma, has pointed out, that not only is acetone frequently

found in the urines of patients who are not diabetic, a fact which Windle and others had previously determined; but also relates a case of a female patient, who died with symptoms of "acetonæmia," death taking place after a convulsion of uræmic character, but whose urine was not saccharine, and whose kidneys were extensively disorganised. With regard to the conditions which tend to induce this peculiar comatose condition in diabetes, fatigue, mental emotion, or some inter-current illness often of a trivial nature, are usually the chief exciting causes. Constipation seems especially to predispose to the condition. In one of my cases, it followed closely after the administration of a dose of castor oil, given for the relief of obstinately confined bowels; in another constipation throughout had been a prominent symptom. A high degree of acidity of the urine is often noticed prior to the onset of diabetic coma. As already stated death from coma is more frequent among young persons than those of more advanced years, and according to my experience occurs more frequently in the irregular and anomalous forms of diabetes, than in cases that have run a regular, and somewhat a protracted, course.

To sum up, therefore, the present state of our knowledge, concerning "acetonæmia" or "Küssmaul's coma," we may say:—

1. That acetone, or an acid body yielding acetone, is frequently present in diabetic urine, though also noticed in some other conditions.
2. That acetone, etc., may be present in the urine of diabetes without coma necessarily ensuing, and may be absent from the urine when that event occurs. More commonly, however, it is noticed to be more abundant just before the onset, and to decline, or altogether disappear, when the comatose symptoms develop.

3. The urine, often, for some time immediately preceding an attack may become extremely acid; and in some cases when the comatose symptoms set in, the quantity of urine secreted may be considerably diminished, and the amount of sugar in it considerably reduced.
4. The symptoms of "acetonæmia" or Küssmaul's coma are very similar to those produced in animals, when attempts are made to reduce the alkalescence of the blood, by the injection of acids.
5. A toxic condition resembling "acetonæmia," but accompanied with convulsions, and somewhat partaking of the character of uræmia has been noticed, when both kidneys are extensively diseased.

158. **Pathology.**—Of the numerous explanations that have been offered to account for the abnormal presence of sugar in urine, the two most important are those of Claude Bernard and Dr. Pavy; the others, being more or less modifications or refinements of these views. Thus Claude Bernard has taught that whilst in health, the hepatic glycogen is converted into sugar, which passes into the circulation, and is consumed either in the lungs, or utilized in the nutrition of the tissues; in diabetes, owing to an increased production of glycogen, more sugar is formed than can be destroyed in the organism, and the overplus is discharged with the urine. Or else without any increased activity of the glycogenic function, the normal amount of sugar is not consumed in the organism, and is consequently excreted. Dr. Pavy, on the contrary, considers that in the normal condition, little or no sugar passes from the liver into the circulation, and that instead of being a sugar forming organ, the liver is a sugar assimilating organ, and it is only when this function of assimilating sugar (converting it into fat most probably) is interrupted, that

sugar appears in the urine. I believe Dr. Pavy's explanation to be the one nearest the truth. The strongest objection that has been raised against it is, that if sugar be injected continuously into the blood, in small quantities so that the percentage present does not much exceed 0·2, the urine does not become saccharine. But in answer to this objection I think it sufficient to observe, that if the experiment is performed in a healthy animal, the conditions are not the same as those that are claimed to exist in diabetes, in which the power of assimilating sugar is lost. For we must not suppose that the power of assimilating sugar is limited to the hepatic cells, since undoubtedly all tissues whose cells contain glycogen (and this is especially the case with muscular tissue) would possess the same power. Therefore, if sugar pass into the circulation of a healthy animal, it would be assimilated by the tissues and liver. That this is so, may fairly be assumed by the fact that a small quantity of sugar passes daily from the intestines, by the lacteals and thoracic duct, directly into the circulation without first having gone round by the liver, as this sugar does not appear in the urine, we may reasonably infer that it is assimilated by the organism. Another objection raised by the opponents of Dr. Pavy's theory is, that the amount of sugar found in the hepatic vein, is greater than in other vessels of the body, and they have argued from this that sugar is normally formed by the liver, and passes into the circulation, but Dr. Pavy (*op. cit.*) has, I think, conclusively answered this objection, by showing that the original experiments on which the objection is founded were faulty, and that when the experiment is performed with care, the blood of the hepatic vein is not sensibly richer than that of the other vessels of the body. These objections being disposed of, I think we may assume that the

primary cause of saccharine diabetes *lies in the disturbance of the glycogenic function, by which the sugar assimilating powers of the liver, and probably also of all glycogen-yielding tissues, are interrupted, and that sugar, instead of being utilized by the organism, is passed out of the body by the kidneys.*

The next question that arises is, what causes this interruption of the glycogenic function? Most authorities are agreed that it depends upon some alteration of the circulation in the liver brought about through the influence of the nervous system. The divergence of opinion is whether this alteration consists in an active or passive congestion; whilst Dr. Pavy (*op. cit.*) believes that mere congestion of the liver is not an efficient cause, and that there must also be an afflux of blood not properly venous. Dr. Pavy has brought forward many facts to show that venous blood is favourable, and oxygenated blood is unfavourable, for the accumulation of glycogen, and since there is no organ in the body supplied with venous blood to such an extent as the liver, nowhere does glycogen exist to a like extent. Now in diabetes, Dr. Pavy maintains, the blood is imperfectly venous owing to the dilatation of the arteries of the chylopoietic viscera brought about by vaso-motor paralysis; just as in the well-known experiment on the rabbit's ear, when section of the sympathetic shows such a modification in the circulation, that the blood when it reaches the veins has still an arterial character. The bright red appearance of the tongue so often noticed in diabetes, also suggests that the blood is flowing through the organ, without being properly deprived of its arterial character.

Dr. Pavy (*Path. Soc. Trans.*, 1883) has also recently adduced another interesting fact, to prove that diabetes is caused by the afflux of blood not properly venous. He

has shown that while all the ferments of the body can only bring starch into the condition of *maltose*, or a dextrin of low cupric oxide reducing power, yet the principle found in diabetic urine is *glucose*. Now under ordinary circumstances when the blood of the portal vein was thoroughly venous it contained maltose and dextrin, which were in turn converted into glycogen, which accumulated and was assimilated in the liver; but when the blood was experimentally rendered imperfectly venous glucose, and not maltose, was the result. Accordingly Dr. Pavy thinks that the interruption of the glycogenic function is induced by a *vaso-motor paralysis which causes dilatation of the arteries of the chylo-poietic viscera, by which means the liver is supplied with blood imperfectly venous.*

This brings us to the nature of the nervous lesion in diabetes. Owing to the fact, first pointed out by Claude Bernard, that puncture of the medulla oblongata at the diabetic centre,* was followed by discharge of saccharine urine, pathologists have sought for lesions in that neighbourhood to explain the phenomena of diabetes. Dr. Dickinson has been foremost in this field of investigation and has described and exhibited microscopical specimens showing chiefly the following morbid changes in the brain in diabetes, viz., dilatation of the blood vessels, extravasation of blood in small amount, enlargement of perivascular spaces, and alterations in the perivascular sheaths and nervous matter bounding the cavities. It was upon the nature of these lesions that the Debate in 1882 at the Pathological Society, "On the Morbid Anatomy of Diabetes," chiefly turned; when the Committee, appointed to

* This, according to Eckhard, in the rabbit, is 4 or 5 mm. above the point of the calamus scriptorius for the lower limit, and 1 or 2 mm. below the corpora quadrigemina for the higher (Foster's *Physiology*).

investigate the changes exhibited by specimens of the nervous centres in cases of diabetes, submitted by various exhibitors, reported that they failed to find in the specimens "any changes which could be regarded as exclusively or constantly associated with diabetes." The same may be said with regard to gross lesions, such as intra-cranial growths, aneurisms, etc., involving the nervous centres. It has also been suggested that it is not necessary for the vaso-motor centre itself to be the seat of lesion; since the vaso-motor nerves may be morbidly affected at some point between the centre and the liver, or there may be reflex irritation like the glycosuria induced by acting on the sciatic nerve, or by irritation of the liver-tissue itself. Experimentally it has been shown, that glycosuria can be induced by acting through the vaso-motor sympathetic system; whilst specimens showing changes, usually of a chronic inflammatory nature, affecting the sympathetic ganglia, in diabetes, have been frequently brought forward. The best description of these changes will be found in the *Pathological Society's Transactions* for the current year, in a paper read December 16th, 1884, by Dr. Hales White, describing the microscopical examination of the sympathetic in diabetes. These changes, however, are certainly not constant, nor exclusively met with in diabetes.

Our present knowledge, therefore, with regard to the action of the nervous system in diabetes amounts to this. That whilst no constant or exclusive pathological changes of the nervous system are found post-mortem in diabetes, yet everything points to a disturbance acting through the vaso-motor nervous system. This may originate in the vaso-motor centre itself, or it may be induced in a reflex manner, or through the sympathetic vaso-motor nerves. Nor need the disturbance necessarily

arise from a demonstrable lesion, since in many cases it is probable that the circulation of blood charged with some morbid agent may cause the disturbance, either by irritating the vaso-motor system at the centre, or at their peripheral terminations on the hepatic vessels.

The *blood* in diabetes often contains as much as 0·5 per cent. of sugar. In most cases there is a demonstrable increase in the amount of fatty matter present, whilst in some cases the increase is so great as to give the blood a lactescent appearance (*lipæmia*); it is in these cases that the fat emboli originally discovered by Hamilton and Saunders (*Edin. Med. Jour.*, July, 1879) in the vessels of the lungs and brain are found. Professor Gamgee (*op. cit.*, p. 172) has given an analysis of the blood in this lactescent condition, which shows that the total fatty matters were 13·55 per 1000, of which 9·86 parts were neutral fats, 1·55 lecithin, and 2·14 cholesterin. The nature of this fatty increase is not well understood, many have thought it was due to admixture of acetone with the blood, but shaking up blood with acetone will not give the appearance; moreover, it is doubtful whether acetone exists at all as acetone in the blood, but is derived from a fatty acid. The fat emboli, moreover, are probably not formed during life, but are caused by the coalescence of the fatty matters in the blood after death. I have advanced the explanation (*Path. Soc. Trans.*, 1883) that the increase of fatty matter so often observed in diabetes, not only in the blood, but in the muscles, the liver cells, and renal epithelium, is allied to similar changes produced by phosphorus poisoning, or poisoning by the injection of mineral acids, bile acids, or oxalic and tartaric acids, into the blood of animals, both as regards the clinical symptoms as well as the pathological changes, and that the condition in diabetes is not brought about by

the presence of acetone, but by aceto-acetic acid, from which the acetone in urine is probably derived. The discovery by Minkowski (*op. cit.*) of pseudo- or β-oxy-butyric acid which is capable of breaking up into aceto-acetic acid in the urine of diabetic patients, strengthens this view; whilst Henry (*op. cit.*) has shown, by injecting acids into the blood of herbivorous animals, that my statement, made at the debate at the Pathological Society in 1882, with regard to the similarity of the symptoms of acute diabetic coma and that of acid poisoning, was quite correct. It has been urged, however, against this view, as well as that of Professor Hamilton's, who believes that the symptoms of diabetic coma are occasioned by the fat emboli, that many cases of diabetic coma occur in which no increase of fat in the blood takes place, nor any fat emboli can be discovered. But this objection is fairly met by pointing out that there are at least two forms of sudden death in diabetes, both spoken of as by coma; but one, and that which in my experience is the most frequent, is rather due to collapse from cardiac syncope than to a toxic condition brought about by changes in the blood; and in this form neither an increase of fat in the blood nor fat emboli would probably be observed. Moreover, if the toxic condition of the blood is the cause of the coma and of the fatty changes, it may happen in some cases when the development or accumulation of the toxic agent occurs suddenly, and the poison is present in large quantity, that death may occur before the fatty changes have time to develop.

With regard to the changes in the other organs, the *liver* has been described by the older writers as somewhat enlarged, dark coloured, and of tough consistence. Dr. Dickinson has described overgrowth and crowding of the epithelium as often seen, along with frequent evidence of

hyperæmia. In the majority of cases, however, no special changes can be observed, and the liver instead of being enlarged and tough, may be small and soft; in some rare cases, as in the one described by Professor Gamgee in his work on Animal Chemistry, the liver cells had undergone changes analogous to those of acute yellow atrophy.

The *pancreas* has been so frequently found in a morbid state in diabetes, that some relationship has been supposed to exist between derangements of that organ and the disorder; but disease of the pancreas is not a constant phenomenon, and is also often found to exist without diabetes. The changes that have been observed, are fibrosis with atrophy of the glandular parenchyma; cancer; atrophy following occlusion by concretions; fatty changes, an interesting account of a case of which is given by Dr. Frederick Taylor (*Path. Soc. Trans.*, 1883) in which the pancreas seemed reduced to a mere lump of fat.

The *lungs*.—The most frequent morbid conditions observed are pneumonic and phthisical. According to Dr. Stephen Mackenzie (*Path. Soc. Trans.*, 1883) the process appears to begin as a (in a sense) croupous pneumonia, with some thickening of the alveolar walls; the exuded and proliferated contents of the air vesicles and the alveolar walls then undergo a necrotic process, the vessels become obliterated, and the necrosed part crumbles away. The "obliterative arteritis" of Friedländer can be well seen in many of the alveolar blood vessels. The occurrence of giant cells is rare. Tubercular phthisis is, however, not at all common in diabetes.

In the *heart*, the microscopic changes usually resemble those met with in persons dying from chronic disease, though in some instances, in cases in which the death was sudden, fatty degeneration and accumulation had occurred in the muscular tissue.

The *kidneys* are generally enlarged and hyperæmic, and the epithelium somewhat granular. In the majority of cases the peculiar "dropsical degeneration" of the epithelium first mentioned by Cantani can be observed. This change which is confined to the collecting tubes, consists in a vesicular condition of the cells which become swollen and translucent, and look as if they had been washed out, only the framework being left; a good representation of this condition is given by Mackenzie in plate xxiv., *Path. Soc. Trans.*, 1883. Frerichs (*Zeit. für Klinische Medicin.*, Bd. vi., 1883) by hardening sections in absolute alcohol, and then keeping them for a short time in a dilute solution of potassium iodide and iodine, has been able to demonstrate by means of the dark mahogany stain, the presence of glycogen in the renal epithelium; this seems most abundant in Henle's loops, and to be present in mild as well as in severe cases of diabetes.

159. **Treatment.**—The treatment of diabetes is almost a matter of restricted diet, the principle question in any given case being whether the withdrawal of starchy or saccharine food should be absolute or partial. For twenty-four hours after sugar has been first detected in the urine the patient should be allowed to continue his usual diet, whilst the whole of the urine passed during that period should be collected, carefully measured, and the amount of sugar and urea excreted exactly determined. The patient should then be placed upon a diet from which every article containing the slightest trace of starch or sugar must be rigidly excluded (see Appendix II.). After a fortnight of this diet the urine must be again collected and the amount of sugar and urea determined. In mild cases it will usually be found that the sugar has either disappeared or at all events is greatly reduced in quantity.

In more severe cases the reduction though marked will not be so considerable. Supposing the sugar to have altogether disappeared, then no other treatment will be required, but a continuance of the diet for at least two months, after which time if the urine continues free from sugar a very gradual return to the ordinary diet may be attempted. If, however, the sugar does not entirely disappear from the urine under dietetic restriction, then recourse must be had to opium. This drug has long been employed in the treatment of diabetes. It is generally supposed that Dr. Pelham Warren first recommended it for the treatment of diabetes, but to Paracelsus (1527) undoubtedly belongs the credit, for he gives the following prescription for the treatment of the disease: "℞ de liquoribus papaveris ℥ ss, lolii ʒ j, camphoræ ʒ j, rosarum plantaginis solatii ℈ iss; reduc in formam liquidam." Under its administration the amount of sugar is sensibly diminished, and in mild cases the excretion may be altogether arrested, even though saccharine articles are taken. Diabetic patients are exceedingly tolerant of the drug, and large quantities can be taken by them without inducing any of the unpleasant symptoms usually attendant on its administration, nor do they seem to acquire a craving for the drug, so noticeable when employed for the relief of other diseases. Under its influence the urinary excretion is considerably diminished, the appetite and thirst restrained, the neuralgic pains disappear, and the patient gains in weight and strength. Objections have been raised to its use, that it enhances the tendency to diabetic coma, but a reference to published cases does not bear this out, and my own experience is contrary to it; since in the instances of diabetic coma I have seen, in the majority opium had never been administered, as they were cases of disease running a mild course, not requiring opium treatment, but

which had suddenly become aggravated. The opium treatment of diabetes is chiefly called for, when, after a fair trial of restricted diet, sugar still continues to be excreted in the urine. In these cases the opium should be given in gradually increasing doses till the sugar entirely disappears, or till in spite of an increased quantity of opium being given, no further reduction in the amount of sugar excreted takes place; before this is effected, however, very considerable quantities of the drug have often to be employed. Thus, I have a patient at present under my care who for the past two years has taken every night a quantity of opium equivalent to half an ounce of liquor opii sedativus. Except in controlling the disease this quantity of opium seems to have no effect on his general health, his weight and strength are well maintained, he conducts his business with energy and vigour, he digests his food well, which is restricted, except as regards a daily allowance of four ounces of bread. By means of this dose of opium the amount of sugar in his urine is reduced to a mere trace, but whenever an attempt is made to reduce the quantity of opium, then the sugar is at once increased, and that too out of all proportion to the reduction made. It is interesting to record that though he has taken this quantity of opium for two years, he has not had further to increase the amount.

Opium may also be used in diabetes, either when, in a mild form after the continuous employment of restricted diet the sugar has disappeared, an experimental return is made to ordinary food; or in cases when owing to the state of the patient's general health, or his disgust at a diet almost entirely animal, it is impossible to enforce absolute restriction as regards starchy and saccharine articles of food, and a relaxation must be permitted. When the administration of opium is determined on,

questions arise as regards the quantity and the frequency of administration. Some give opium in small and often repeated doses. I prefer, however, the administration of one large and sufficient dose taken at bedtime. As regards the amount of the dose the requirement varies with the individual, and experience has taught me that each diabetic has his own capacity for opium which we have to find out. We should therefore begin with a moderate dose, say a grain, and increase this till a point is reached at which the sugar either disappears, or is no longer reduced by increasing the quantity of the drug; when this point is reached I have often found that no further increase is required for a long time. Various preparations of opium have been recommended instead of the crude drug, or its tincture. Of these, *codeia*, introduced by Dr. Pavy is the chief; but the solution of *bi-meconate of morphia* (Squire), and *nepenthe* (Ferris and Co.), are also very efficient. These preparations are said to have the advantage of not disordering digestion, nor causing headache or constipation, like the preparations of crude opium.

When it is determined to allow a slight relaxation in the matter of diet, we have to consider what article we shall commence with. And undoubtedly bread is what diabetics most crave for, besides which bread is not wholly farinaceous. To begin with I usually allow 2 oz. of bread for breakfast, and another 2 oz. with the last meal of the day, so that twelve full hours intervene between each introduction of starchy food. With regard to bread a medical friend who suffers from diabetes, tells me that whereas a small quantity of stale bread always renders his urine saccharine, the same quantity of new bread does not; he explains this by saying that stale bread being more easy of digestion, the starch is more quickly converted into sugar, and reaches the liver more rapidly,

whereas new bread is not so quickly acted on, and the sugar is presented more slowly, so that the glycogenic function is not stimulated to the same degree. The hard chippy fragments of dry toast seem to act in the same way. The relaxation of diet, however, must be carefully watched, since in some cases the most trivial transgression will bring back the disease in full force. Rollo says, he has known "half a biscuit, such as are sold three for a penny," to bring back the disease in full force, though previously sugar had been sometime absent from the urine. Of all articles of food potatoes are the most injurious, not only from their containing more starch, but from its being cooked, and is therefore in an easily assimilable form; for this reason, they should never under any circumstances be permitted to either diabetic or glycosuric patients. Some diabetics are more tolerant than others of saccharine food, especially of fruit sugars. An eminent chemist who has suffered for some years from diabetes has observed, that he may take in moderation, jam, marmalade, or any of the red fruits, without greatly increasing the sugar in his urine, but the slightest particle of starch taken at once aggravates the tendency. With regard to the insistance of a continuance of a restricted diet in those cases, in which after all starchy and saccharine food has been cut off, sugar still appears in considerable quantities in the urine, I have found that after no further reduction is possible, it is advisable in order to maintain the patient's general health to permit a relaxation, such as a small quantity of bread, and the use of such vegetables that contain only but little sugar or starch (these are marked with an asterisk in the diet list in the appendix), always however, excluding potatoes. When this relaxation is made it is necessary, however, generally to administer opium in some form, or increase the dose if it has already been given.

There is only one condition under which saccharine urine is passed, which is not benefitted by an animal diet, and that is the so-called "gouty glycosuria." Patients suffering from this condition are usually corpulent and plethoric, have a tendency to piles, and to uric acid gravel, and although their urine is saccharine they rarely show any of the ordinary symptoms of diabetes. These are the cases, and they are tolerably numerous, in which the skim milk diet usually agrees so well, not because there is any special merit in skim milk, which contains at least 3·5 per cent. of sugar, but simply because whilst on it, habits of gross feeding are checked, and the patients are kept in a state of semi-starvation. Even in cases of diabetes, in which meat forms the chief staple of diet, the amount should be restricted within moderate limits. Diabetics too often think that as they are restricted in other articles of food, they are bound to make up the deficiency by eating enormous quantities of animal food (see also Appendix II.).

Ought diabetic cases to be allowed alcohol; the answer to this question must be that it depends upon the individual case. Some diabetics are singularly tolerant of alcohol, and it seems to have little or no influence in the excretion of sugar; others again complain that it increases the diuresis, adds to their thirst and makes them feel generally uncomfortable. If permitted it should be in as a dilute a form as possible, and only taken with meals, for this purpose the light Bavarian or Vienna beers now so popular, brût champagne, dry sherry, or a little whisky and water may be permitted. Burgundy and dry port may be given if there is great debility.

Next to diet and opium, the diabetic patient will receive the most benefit from the constant use of the *vapour bath*. Willis (*op. cit.*) pointed this out years ago, and quoted

several cases in which undoubted benefit resulted. It not only relieves the diabetic pains and the weariness, but diminishes for a time the amount of sugar as much as 20, 30 or even 50 per cent. It is strange that such an efficacious aid to our treatment should have been persistently overlooked by recent English writers on the subject. M. Campardon (*Progrès Médicale*, April, 1884) also reports favourably of air douches. In one case after eighteen douches, the sugar fell from 77·4 to 36·65 grms., and in another from 102 to 68 grms. The douche is applied for five or ten minutes over the cervical and upper dorsal region, when it causes pallor of the skin, and a considerable fall of temperature. When neither the vapour bath nor air douche is available, then the cold pack may be tried with advantage.

Alkalies often prove serviceable in diabetes, probably from their oxidizing influence and diminishing acidity in the intestinal canal. For this purpose, I usually prescribe about twenty grains of bicarbonate of soda, ten grains of phosphate of soda, five grains of carbonate of ammonia, in a draught, to be taken two hours after food. Their use is specially indicated in "gouty glycosuria."

Acids with or without pepsin are useful in aiding digestion. Dr. Wilks (*Medical Times and Gazette*, March, 1884) recommends the use of mineral acids with nux vomica, which he thinks beneficial, not merely by their action on digestion, but also from a positive effect on the glycogenic functions. Half a drachm of diluted hydrochloric acid in half a tumbler of water, flavoured with tincture of orange-peel taken immediately after a meal, often proves an excellent digestive.

With regard to other remedies *iodoform* has been recommended by Moleschott (*Wien. Med. Wochenschrift*, Nov.

1882) and other physicians, it undoubtedly checks the excretion of sugar, but is inferior in its action to opium, whilst owing to the accumulative properties of the drug, its administration should not be ventured on ; not even if we follow Post's suggestion (*Archives of Medicine*, New York, April, 1884), and systematically interrupt the administration, since even in small doses there are cases in which it may produce anæmia and fatty degeneration. *Arsenic*, *bromide of arsenic*, *phosphorus*, the *salicylates*, *calcium sulphide*, and numerous other drugs have been recommended for the treatment of diabetes, and instances of their beneficial action have been recorded, on looking through the cases, however, I have come to the conclusion that the good results depend either on strict dietetic regulation, having been employed as well, or that the cases were not ones of true diabetes, but only temporary glycosuria. Thus arsenic or the salicylates would be found serviceable in malarial glycosuria, and phosphorus in conditions of exhaustion and weakness.

The *hygienic* treatment of diabetes is fulfilled by the careful regulation of the diet; by keeping the patient warmly clad, and sheltered from cold damp winds; by encouraging moderate exercise and cheerful employment, but avoiding all fatigue bodily or mental, and the avoidance of all long railway journeys; by change of air, especially, to the sea-side. Great benefit, especially in mild cases, is often experienced by the use of Carlsbad and Vichy waters, but owing to the long railway journeys I advise patients to take these at home, or else use the mineral waters of the Hot Wells Clifton, or Bethesda, in England. Finally, with regard to the so-called modes of cure. The "*skim milk* system of diet is only useful in cases of gouty glycosuria," in other forms of saccharine diabetes it does undoubted harm. The "*sugar*" treatment is altogether

fallacious and has been universally condemned. The *rennet* or *pepsine* cure can only be obtained when the observance of a most rigid abstention of starch and sugar in any form is enforced as well. The *lactic acid* treatment as recommended by Cantani has been given a fair trial by numerous physicians, but the results obtained have been far from satisfactory, so that it has been practically abandoned; though in some cases of glycosuria, dependent apparently on malassimilation in the intestinal canal, it has done good.

With regard to the treatment of diabetic coma many suggestions have been made, but as yet all means have proved useless. Some temporary improvement seems to have followed the injections of a weak solution of sodium phosphate and sodium chloride into the veins in a case reported by Dr. Frederick Taylor, but it has never proved successful. Perhaps more encouraging results might be obtained by combining venesection with intravenous saline injection, and I should feel disposed to try a saline solution composed of 0·1 per cent. of sodium carbonate, and 0·5 per cent. of neutral sodium phosphate. When seen at an early stage before the symptoms are fully developed, a vapour bath given in bed, and the administration of powerful stimulants such as ether, ammonia, musk, valerian and camphor might stave off the fatal attack. By means of the hot bath, promptly administered, I believe I rescued a patient from the danger of a threatened attack. When I saw her she was drowsy, her face dusky, her breathing irregular, the quantity of urine very much diminished, and she complained of severe abdominal pain. After the bath she was much relieved, and went on comfortably again for some weeks longer. When, however, death is threatened by syncope, rather than by coma, neither venesection, nor the vapour bath, can be em-

ployed, and we must place our reliance entirely on stimulants. As both death by coma, and death by syncope, may come on at any time during the progress of a case of diabetes, and as the onset is usually sudden, we must be on the watch, and also instruct our patient to watch, for threatening premonitory symptoms. Before the onset of diabetic coma, a decided increase in the acidity of the urine, or a sudden and unaccountable diminution in the amount of urine and sugar excreted, or increasing lividity of the cheeks and lips, often give timely notice of the approaching danger, and give us an opportunity of warding it off for a time. For this purpose alkalies should be freely administered with the view of diminishing the acidity, or to speak more correctly of restoring the alkalescence of the blood to its normal point; whilst the elimination of any retained acid products, such as oxybutyric acid, aceto-acetic acid and the like, should be promoted by acting on the skin with vapour baths, and the bowels with gentle purgatives. The syncopal form of death in diabetes is generally preceded by symptoms of great exhaustion and debility, for some weeks emaciation has been more marked than previously, the muscles not only have wasted rapidly, but are extremely soft and flaccid, the anæmia becomes profound, whilst after any exertion slight œdema of the lower extremities occurs. From such a state of prostration it may be possible to rescue the patient by care and attention. He should be kept in bed, and his diet carefully attended to, should his digestive powers fail which is often the case, and is the cause of the profound exhaustion, it will be necessary to give peptonized food by the bowels in addition to what can be taken by the stomach. This should be given in as concentrated a form as possible, raw meat rubbed up with cream, egg and brandy mixture, essence of beef, jugged chicken,

and the digestion of this highly proteid diet assisted by means of an acid solution of pepsin, taken after each ingestion of food. Good brandy or dry port wine, must be given according to the tolerance of the patient for alcohol. Large doses, twenty to thirty drops of tincture of perchloride of iron, should be given three or four times a day; whilst a draught containing carbonate of ammonia, musk, etc., should always be on readiness in case of his becoming faint, or the heart's action irregular. Gentle massage will be found useful in promoting the nutrition of the muscles, and in restoring their lost tonicity.

Anuria.

160. **Suppression of Urine.**—Heidenhain (*Pflüger's Archiv*, vol. ix., 1874) has made the interesting observation, that after injecting a certain quantity of excretory material, and allowing such a time to elapse as he knew from previous experiments would suffice for its passage through the renal epithelium to be pretty well completed, he found, if he injected a second quantity, that "the excretion of this second quantity was most incomplete and imperfect; it seemed as if the cells were *exhausted by their previous efforts*, just as a muscle which has been severely tetanized will not respond to a renewed stimulation." That peculiar condition to which Sir Andrew Clark has given the name "renal inadequacy" in which the amount of urinary solids, and often times the quantity of urine itself, are considerably diminished, may probably originate from such an exhausted condition of the epithelium; since the disorder chiefly occurs in those who have indulged in the pleasures of the table, whilst the most satisfactory treatment of the

condition, as Sir Andrew Clark has pointed out, consists in adopting a dietary, chiefly of farinaceous articles of food. If this is continued, the exhausted epithelium seems to recover itself, for after a time, though the amount of nitrogen ingested is reduced to its lowest limit, the quantity of urea excreted begins again to increase.

In the early stage of acute Bright's disease, the urine may be completely suppressed for many hours or even days. Three or four days have been recorded. It is a question, however, whether the arrested or diminished flow of urine in acute nephritis, is due to suppressed secretion; Prof. Hamilton (*op. cit.*) would not be surprised if the quantity of urine actually excreted by the glomeruli was increased in these cases, but that being unable to make its way down the obstructed tubules it is reabsorbed; and he points out the important histological fact that the lymphatic interspaces are all widened, both in the glomeruli and between the tubules. On the other hand, Klein favours the view that the anuria in acute nephritis, when not directly referred to inter-tubular changes, is caused by changes in the arterioles; and Klebs holds that the suppression is due to compression of the vessels of the glomeruli by the pressure of the nuclear germinations (see p. 195). Suppression of urine occurs especially in connection with the acute nephritis of scarlet fever, though it may occur in any of the etiological varieties, and may arise as Dr. W. Roberts has pointed out, in scarlet fever dropsy, unaccompanied with albuminuria. Cases of complete suppression also sometimes occur in children after "cold catching," an interesting case of which is recorded by Dr. H. E. Paxon (*Lancet*, Sept. 29, 1883), and others have also been recorded. Indeed, anything that tends to induce renal hyperæmia may lead to this condition. Thus in poisoning by cantharides, turpentine, lead, mineral

acids, and other irritants, renal hyperæmia is excited, and the flow of urine suppressed or considerably diminished.

Mr. Beck (*op. cit.*) has insisted on the intimate nervous relation that exists between the kidneys, and the urethral orifice of the bladder, trigone, etc., and believes that any irritation of that part is followed by sympathetic hyperæmia of the renal organs. This hyperæmia no doubt accounts for the acute suppression of urine that often follows after the passage of a catheter, especially for the first time, and to which Sir Andrew Clark has drawn attention in his paper read before the Medical Society of London, 1883. The suppression of urine in these cases is only temporary, for if the patient recover, the secretion of urine again goes on as before, whilst even if *pyelo-nephrosis* result, neither the urine nor the urea excreted is notably diminished, as has been already stated (p. 289). The suppression of urine, therefore, in these cases is manifestly due to nervous influences.

When acute inflammatory affections, especially in typhus, small-pox, yellow fever, and typhoid fever, are about to terminate fatally, the secretion of urine is often suppressed for some hours before death; what is known as the "typhoid state" is a good example of this condition. Care must be taken, however, in these cases not to mistake suppression of urine for retention; for urine may be secreted by the kidney but be retained in the bladder, owing to that organ having lost its extrusive power.

The secretion of urine is more or less arrested in what is known as the state of shock or collapse. Thus it occurs after severe injuries to the abdominal viscera. The suppression of urine that takes place in the algide state of cholera is due chiefly to the state of collapse, though the drain of water from the system by the bowels, also might in some cases account for it; whilst if Dr. George

Johnson's theory is correct, of spasm of the arterioles producing the collapse, we need seek no further for an explanation of the anuria of the collapsed stage of cholera.

In hysterical females the tendency is rather towards the prodigious discharge of large quantities of pallid urine, than diminution or suppression of the secretion, still occasionally it happens. In these cases, however, it is usually retention in the bladder and not suppressed secretion. But in a few rare cases true suppression does occur. I had a case of this kind once under observation in the Doncaster Workhouse, the girl aged nineteen used to get trance-like seizures, often lasting two or three days, during which time, very little, and on some occasions, no urine as far as could be ascertained, would be secreted; during the continuance of the attack, she used to be troubled with hiccough and occasionally vomited. I regret now that I did not examine the vomit to see if it contained urea, it certainly had not a urinous odour, nor was it profuse. These attacks used to come on two or three times a year, but occasionally the hysterical manifestations would take other forms.

The treatment of suppression of urine must generally be conducted on the principles indicated for its management when it occurs in acute nephritis (see p. 252). When due to shock, and there is no reason to suspect that the kidneys are diseased, opium should be administered. In the suppression of urine in cholera, the means taken to restore the patient from his collapsed condition will, if successful, be followed by restoration of the secretion, the first samples passed being bloody and highly albuminous. Hysterical suppression is best disregarded, as far as our conduct towards the patient is concerned; the administration, however, of valerian, valerianate of zinc, bromide of potassium may help us to overcome more speedily the

neurotic element in the affection. If troublesome vomiting should arise during suppression, from any cause, it is best combated by the administration of drop doses of hydrocyanic acid in a teaspoonful of water, mustard plasters to the epigastrium, and injections of chloral hydrate by the rectum.

161. **Retention of urine** may be conveniently considered here, though it cannot be regarded in any way as a functional derangement, but merely as a symptom of some mechanical impediment to the discharge of urine already secreted. Obstruction to the flow of urine may occur at any point of the urinary tract; in the urethra, from stricture, vascular growths, or pressure from a perinæal abscess; at the neck of the bladder, from an enlarged prostate; in the bladder, from abnormal growths obstructing the orifice of the ureters; or the bladder may be compressed by a tumour from without, as occurred in a case at the Seamen's Hospital, in which a cystic growth of the right vesicula seminalis increased to such a size, that making its way upwards between the bladder and rectum, it compressed and flattened the bladder, and completely obstructed the lower portion of both ureters, causing during the last few days of life complete retention. Or the ureters may be occluded, by stricture, by the impaction of calculi; or obstructed by cancerous or tubercular masses, or by blood clots; or by the formation of valvular folds, or thickened condition of the mucous membrane; or compressed by tumours from without.

The retention may be complete or partial. When the former is the case, the obstruction is situated either in the urethra, or at the neck of the bladder, or both ureters are compressed, or else the patient has only one kidney available for secretion, the other being congenitally absent or destroyed by previous disease. When the retention is

partial, then either the obstruction does not absolutely impede the flow of urine as is the case with many strictures of the urethra, or else it is so situated, as when only one ureter is obstructed, as to allow the discharge of urine by the unaffected channel.

Retention may be produced suddenly, as when for instance a renal calculus suddenly obstructs the ureter in a patient, who has only one kidney that secretes urine. Thus in the case of a sailor admitted into the Seamen's Hospital with suppression of urine, and who the previous day had received a severe blow across the loins, it was found, post-mortem, that the left kidney was absolutely destroyed by the pressure of a large branched calculus, whilst the right was fairly healthy, but in the upper part of whose ureter was found impacted a small calculus. This had been dislodged by the blow, from its position in the pelvis of the kidney, and had entered the ureter, but being unable to pass had caused the fatal obstruction. In the majority of cases, however, the onset of retention is gradual, there may be some difficulty in passing water, but a little more extrusive force overcomes the resistance, as is often seen in cases of stricture of the urethra. Or the bladder may become distended, and instead of the urine coming in a full stream it dribbles away, as in enlarged prostate, or in paraplegia. Or the urine accumulates behind the obstacle, till at length the *vis à tergo* is sufficient to overcome the resistance, and the accumulated urine is discharged; this occurs chiefly in those cases in which the obstruction is seated in the ureter. Here we have periods of complete retention alternating with a discharge of somewhat aqueous urine (see also hydro-nephrosis, p. 319).

The effects of long-continued obstruction are observable in the dilated and distended condition of the urinary pas-

sages behind the obstruction. Rupture does not, however, occur, because when the pressure in the distended urinary passages rises to the degree of the blood pressure in the renal vessels, the further secretion of urine is arrested, so that long-continued retention leads at last to suppression of urinary secretion. When, however, the obstruction is long-continued, the distension leads to considerable changes in the urinary organs. The walls of the ureters become thickened, both from hypertrophy of the muscular wall and from swelling of the mucous membrane, whilst the cavity is dilated so as to resemble a piece of small intestine; the pelvis of the kidney becomes distended and its calices dilated; then commences absorption of the pyramidal portion of the kidney commencing at the papillæ. The whole of the pyramidal portion may eventually disappear leaving only hollow depressions formed by expanded calyces. Finally, the cortex dwindles, and becomes stretched and thinned, and the kidney becomes converted into a cyst (see also pyo-nephrosis, p. 278, and hydro-nephrosis, p. 320). This absorption of the renal tissue would proceed more rapidly were it not accompanied by chronic interstitial nephritis, which causes an overgrowth of the connective tissue. This overgrowth, as Beck (*op. cit.*) has pointed out, may be regarded as mainly conservative, rendering the kidney more capable of withstanding the stretching to which it is exposed. Again, as we have seen, when the pressure in the urinary passages equals the pressure in the renal vessels, secretion of urine is arrested. Now the effect of this growth of connective tissue, as Beck observes, prevents this setting in at an early period, for the new growth between the tubules causes some degree of obstruction to the venous circulation and so increases the pressure in the Malpighian tufts. The result being, so far from secretion being di-

minished, it is increased, especially as regards the amount of water, and thus for a time suppression of urine is averted.

Complete retention ends, as already stated, ultimately in suppression of the secretion of urine. The period that intervenes between the commencement of the retention and the fatal termination varies considerably, and depends very much on the nature of the obstruction and state of the urinary passages. When these are healthy, and the obstruction sudden, as for instance, when a calculus blocks the ureter of a solitary kidney, the patient may survive several days, as many as twenty-one days have been recorded (*Trans. Clin. Soc.*, vol. ii.). In cases, however, in which the obstruction is brought about by previous disease of the urinary passages, and there has been long-standing pyelitis or cystitis, a fatal termination will probably occur much earlier, owing to the supervention of suppurative nephritis, though even in these cases the patient may survive even five or six days. The fatal termination is ushered in by uræmic symptoms, though these are not generally of a violent character, convulsions and coma being rare, muscular twitchings and a heavy dreamy state being the main features. The pupils are often contracted, the tongue dry and brown, the temperature, when the uræmic state is pronounced, often becomes subnormal. Vomiting and diarrhœa sometimes occur, and are usually provoked rather than spontaneous; but hiccough is common. The skin is moist, sometimes drenched with cold sweat.

When the retention is partial, as for instance in the case of enlarged prostate, the case may run a protracted course before the ultimate destruction of all renal secretion tissue by pressure. Owing to the increased pressure in the Malpighian vessels by the obstruction caused by the growth of the connective tissue, the amount of urine

secreted is increased, though it is deficient in solid matter. When the retention affects one kidney only, and the other remains healthy, the sound organ in time takes on the work of the one whose function is suppressed, and no further ill consequences may result.

The treatment of retention of urine is mainly a surgical question. When the obstruction is due to impaction of a calculus in the urinary passages, we may endeavour to promote its onward passage by the means suggested in the ensuing chapter, but should it obstinately resist our efforts the propriety of surgical interference must be discussed. This becomes imperative, if from the fact of the urinary secretion being entirely arrested, we are lead to the conclusion that the kidney obstructed was the only one available for use, and that the other is either congenitally absent, or else incapacitated by previous disease. Happily owing to the advances of renal surgery, operative procedures are attended with abundant success in a large proportion of these cases. When the obstruction occurs in the lower urinary passages from stricture or enlarged prostate, no time should be lost in affording instrumental relief, before hypertrophy of the muscular walls of the bladder occurs, and thus prevents compression of the orifices of the ureters by the thickened muscular bundles. This cannot be too much insisted on, since I fear it is too often the practice to defer catheterism, so long as the patient can pass urine without apparent difficulty. For a similar reason vesical calculus should be removed as soon as detected, and cystitis treated with vigour.

LEEDS & WEST-RIDING
MEDICO-CHIRURGICAL SOCIETY

CHAPTER X.

Stone and Gravel.

162. **Origin of Stone.**—The older writers distinguished between gravel and urinary deposits, by the fact that the former was separated from the urine in the urinary passages and discharged with the urine, whilst the latter was only deposited after the urine had left the bladder. If gravel were retained in the urinary passages, and it became concreted, then a stone was formed. This concretion according to their view might take place, either in consequence of the heat and dryness of the urinary organs drying the slime, just as a portion of soft clay may by external heat be turned into brick or tile (Hippocrates), in which case the calculus would be reddish; or by coldness or humidity of the parts, as marble is formed (M. Sanctus), when the calculus would be of a whitish colour. These speculations of the ancient physicians point to an entirely local origin for stone. The chemical doctrines of Paracelsus, Van Helmont, and the iatro-chemists of the sixteenth and seventeenth centuries threw this view into the background. Calculous matter, according to Paracelsus, was of the nature of *tartar*, and caused by the union of a nutritive principle with a saline spirit, which coagulated the earthy matter of the urine. We have here the first indication of the chemical origin of stone, and in the doctrine of the *archæus* a foreshadowing of the idea of constitutional diatheses, which for many years dominated urinary pathology. When, however, the iatro-chemical school fell into discredit, physicians reverted to the old

views, and stone once more was considered as of local origin, as was ably set forth by Dr. Austin in the Gulstonian Lecture of 1790. But a new school of chemistry was arising, based upon actual analytical fact and not hypothesis. In 1776, Scheele discovered uric acid, which from being found in the majority of calculi was termed *lithic* acid, whilst the discovery of calcium oxalate, ammonio-magnesium phosphate and calcium phosphate, as constituents of some stones, was made soon after. It was first supposed that these substances were formed in the body, and eliminated in such quantities as to be precipitated in the urinary passages, where by their aggregation they formed a stone, and hence the application of the doctrine of "diatheses" to urinary pathology. The next advance, however, was to show that excessive production and elimination was not essential for the formation of calculus, and that alterations in the reaction of the urine was an important element to be taken into account, since many of the substances entering into the composition of a stone, when present only in their normal proportions, may be precipitated when there is a marked change in the reaction of the urine. Still, however, the formation of stone could not be satisfactorily attributed altogether to these chemical variations in the composition of the urine, since undoubtedly urinary matters were frequently precipitated without its occurrence. At this point the important researches of Rainey on molecular coalescence, again drew attention to the part played by local conditions in the formation of stone, by indicating that the mucus of the urinary passages furnished the medium requisite for the aggregation of the precipitated urinary matters. Professor Rainey's observations have been followed up by Vandyke Carter (*op. cit.*) and Ord (*op. cit.*), and it has been clearly demonstrated that in the presence of a suitable colloid medium,

precipitated urinary matters lose their crystalline form and become *sub-morphous*, that is become more or less spheroidal. The nature of this colloid medium is, however, at present not determined. It can hardly be the ordinary mucus furnished by the urinary passages under catarrhal and inflammatory conditions, since if that were the case, calculous formations would be infinitely more common than they are, though no doubt when stone is once originated both renal and vesical catarrh furnishes the medium for its increase in growth. In order to overcome this difficulty many have suggested the existence of some special form of mucus as furnishing the colloid medium. Thus, the Germans speak of a stone-forming catarrh (stein bildenden catarrh), in which the mucus undergoing acid fermentation leads to the precipitation of uric acid, or the formation of oxalate of lime. Dr. Owen Rees (*op. cit.*) thinks that in gout the urinary passages furnish a mucus secretion, which has a special tendency to agglutinate and form masses. Whilst others have imagined that stone is the result of some chronic inflammatory condition.

In considering, however, the origin of stone, the question must be separated from that which concerns its growth. All stones present a point round which all subsequent deposition collects, and it is to the study of this central nucleus that our attention must be directed if we wish to trace the early history of calculous formations. Now the nuclei of all urinary calculi, except in the case of foreign bodies introduced from without, have a renal origin, that is they are not formed in the pelvis of the kidney, but in the urinary tubules. This is not a mere supposition, but is supported by pathological evidence. For instance, in the small pisiform calculi (of uric acid) so common in elderly people, we sometimes have an opportunity of seeing, post-

mortem, a minute calculus separating from the mammillary processes. An instance of this kind has been described by Sir Benjamin Brodie, in his *Lectures on Diseases of the Urinary Organs*, in which the mammillary processes having been longitudinally divided, the tubuli uriniferi were seen blocked up with calculous matter; in one of them the development of the calculus being further advanced it was seen partly embedded in the apex of the mammillary process, and partly projecting into the infundibulum. The uric acid infarcts that occur in young infants is another evidence of the deposit of calculous matter in a sub-morphous form in tubules of the kidney. Those who admit the early formation of calculi in the straight portion of the renal tubule, account for it by the fact that the urine is more concentrated in this portion of the tubule; but as I have pointed out (*Clinical Chemistry*, p. 239), the degree of concentration is slight, whilst the diameter of the straight portion of the tubule being wider than the convoluted, the flow of urine through it is freer, which compensates for any degree of concentration that occurs. Moreover, concentration of urine whilst accounting for crystalline deposition does not account for the formation of sub-morphous bodies, such as compose this calculous material. It may happen that the colloid material is furnished by some special secretion of the renal cells, but of this we have no positive evidence. Whilst thinking over this matter a few years ago, I came across in Dr. Golding Bird's work on Urinary Deposits, a representation of a renal cell filled with octahedral crystals of oxalate of lime, and which had been detected in the urine by Dr. G. Johnson. Further, on referring to some lectures of Professor Quekett (*Medical Times and Gazette*), I learnt that in those animals who secrete uric acid in large quantities from the kidneys, this substance is often contained in the cells

of the renal epithelium. It therefore appeared to me that the deposition of calculous matter forming the original nucleus, might also in man occur primarily in the cells forming the wall of the renal tubules, and not in the lumen of the tube itself, and further that this deposition was caused by some *vital impairment*, so that products that normally ought to be eliminated by the renal cells are retained and deposited by them instead. Many arguments may be adduced in support of this view. Heidenhain's experiments (p. 451) have shown that with regard to one substance at least, the renal epithelium does exercise a distinct secreting activity, independent of and distinct from the relations of blood pressure, nay more, he has shown that the renal cells may even *become exhausted* by their previous efforts at elimination (Foster's *Physiology*). Again, the part of the urinary tubules in which calculous deposits are most frequent is the straight portion, especially the lower part towards the mammillary processes. This as is well known is less freely supplied with blood than any other part of the kidney tubule, and we know by analogy, that textures possessed of a feeble circulation are prone to degenerative changes, especially to deposits of this kind, as witness the tophi in the cartilages of the joints and ears in gout. Besides this, the basement membrane is absent at this part of the tubule, so that the wall consists alone of epithelium, this probably has some determining influence. Another point which I think also may fairly be taken into consideration in support of the view that calculous deposit occurs in the renal cells as the result of their vital impairment, is the fact that stone is most frequent at the extreme periods of life, viz., during childhood and old age, when either from rapidity of growth, or general decay, the vital powers undergo impairment. Stone, moreover, not infrequently occurs after disorders which have greatly

exhausted the vital powers, and this probably explains the frequent association of stone with gout, since in that disease there is always more or less a condition of impaired vitality and textural degeneration. Lastly, if Heidenhain is correct in saying that the renal cells become exhausted by over activity, the constant over elimination of uric acid, oxalic acid, etc., might lead to their deposit in the renal cells, owing to the impairment of the activity of the epithelium. The sudden onset, too, of renal colic, is in favour of the view of the tubular origin of renal calculi, since if the nucleus was moulded in the pelvis of the kidney, and gradually developed, the onset of the symptoms would be gradual, whereas colic generally sets in without warning, as if a foreign body had suddenly dropped into the pelvis of the kidney. The only objections that can be raised to the cellular origin of the nuclei of calculi, lies in the fact that no remnants of a cell wall can be found in examining the formed nuclei. But reflection must convince us that the observation of a cell wall, like that depicted by Golding Bird and seen by Dr. G. Johnson, must be of extremely rare occurrence, and only possible in the very earliest stage of formation, since the cell wall furnishing the colloid medium, must itself be incorporated with the crystalline bodies to form the sub-morphous granules that compose the calculous material. In thus claiming for the nuclei of calculi a cellular origin, I of course exclude those in which the nucleus is distinctly hæmic, as may occur after blows and injuries to the kidney, or are mere collections of altered fatty matters, as in concretions of uro-stealith.

To sum up, therefore, the views I think we may hold with regard to the origin of stone, I would say :—

1. That all urinary calculi, except those formed upon extraneous substances introduced into the bladder, have a renal origin.

2. That the nuclei of all renal calculi, except those of evidently hæmic origin, are developed in the tubules of the kidney.

3. That these nuclei probably take their origin in the renal cells, by the retention within them of uric acid, oxalate of lime or phosphate of lime, owing to some vital impairment of their function, by which their power of eliminating these substances is diminished.

4. That the nucleus, having passed into the urinary passages, grows by a gradual accretion in successive layers to its surface, the material for which is furnished by the mucus of these passages, and the substances deposited from the urine.

5. That the nature of the successive layers of a fully formed calculus, will be found to vary according to the prevailing character of the urine at the time of their formation, so that in the same calculus we may find layers of uric acid alternating with phosphate of lime, and finally incrusted with a coat of triple phosphate, or any other possible variation.

Varieties of Urinary Gravel and Concretions.

163. **Lithuria.**—Uric, or lithic, acid, as it is generally called, from the old idea that it was the essential constituent of stone, is deposited from the urine either in a free state, or combined with bases as salts, whenever the urine is highly acid, or when uric acid is either absolutely or relatively in excess. Considerable difference of opinion exists as to the mode of formation of uric acid within the human body, and its pathology. According to the generally received opinion, uric acid is one of those substances, through which every particle of proteid matter passes, be-

fore it is thrown out of the body, and therefore when oxidation is imperfectly performed in the organism, uric acid and the urates are not reduced to the form of soluble urea. The conditions that bring about this condition of imperfect oxidation are numerous, and may be referred to disturbance of the nitrogenous equilibrium, the employment of too highly animalized a diet, by nervous influences, or the disturbance of function of some important organ (the liver according to most authorities). There are difficulties, however, in the way of accepting this as a complete explanation. In the first place, uric acid is only found in very small quantities in the human body, and then, except in gout, is only found in the tissues and never in the blood. Again, it has been shown that uric acid is not a necessary antecedent of urea, and that it is more probable that the antecedents of urea in the blood are partly kreatin and partly leucin. Again, after strictly non-nitrogenous diet, uric acid is always found in the urine, and this in spite of the fact that the nitrogen is cut off, and consequently the oxygen is in relative excess; surely if the hypothesis above mentioned were correct, all the uric acid ought to have been converted into urea, but it is not so, but passes off *pari passu* with the urea, as if furnished by special cells (Parkes). Moreover it has been pointed out that the amount of uric acid excreted daily is within narrow limits comparatively constant, and the want of connexion between its changes and the variations in the amount of urea in health and disease, also seems to afford strong arguments against the supposition, that urea is largely derived from uric acid. These objections and others, which might also be advanced, have somewhat discredited the "imperfect oxidation theory," and fresh views and hypotheses are already being advanced. Professor Latham of Cambridge (*op. cit.*) believes that the abnormal

formation of uric acid in the human body, occurs just as in the case of glucose in diabetes, on the inability of the liver, or system generally, to effect the metabolism of glycocine. This glycocine, derived from the glycocholic acid of the bile, after the bile has served its purpose in digestion, is conveyed to the liver and is converted, not into urea as we would naturally expect, but into an amido-body, to which Dr. Latham gives the hypothetic formula of—

$$CO\begin{cases} NH—CO \\ NH \quad | \end{cases}$$
$$CO\begin{cases} \\ NH—CH_2 \end{cases}$$

and which passes from the liver into the circulation, and when it reaches the kidney is converted by conjugation with urea into ammonium urate, thus :—

Urea. Amido-body. Ammonium urate.

$$CO\begin{cases} NH_2 \\ NH_2 \end{cases} + \begin{matrix} CO\begin{cases} NH—CO \\ NH \quad | \end{cases} \\ CO\begin{cases} \\ NH—CH_2 \end{cases} \end{matrix} = H_2O + C_5H_3N_4O_3, NH_4$$

Uric acid according to this view depends upon a functional derangement of the liver in regard to the metabolism of glycocine, and Dr. Latham therefore advises that treatment be directed, first of all, to measures by which the formation of glycocine can be lessened, such as by proper diet, which should be chiefly farinaceous with the avoidance of all gelatinous articles. Also that the amount of glycocine be lessened in the system by exercise, and by the use of saline cathartics. Secondly, remedies are to be administered which will combine with glycocine, and so prevent the formation of uric acid, such as benzoic acid, which according to his view and that of Dr. Garrod, passes out of the system conjugated with glycocine as hippuric

acid. Iodide of potassium and chloride of ammonium are other remedies, which, Dr. Latham thinks, act by preventing the conjugation of glycocine with urea to form uric acid, since hydriodic acid and hydrochloric acid both, out of the body, decompose uric acid, hence as he suggests, the beneficial effect, that certain mineral waters, rich in chlorides, have on gouty patients. Before Dr. Latham's view can be accepted, there are several points connected with it that require further explanation and discussion. His hypothesis for instance tells us how ammonium urate may be formed, but it does not explain how it is that sodium urate is the salt deposited in the tissues, unless we have recourse to a theory of double decomposition. Again, uric acid of all urinary constituents is the one least affected by variations of diet, yet still we should expect, if the glycocine theory were true, that excessive ingestion of this substance, or food rich with it, would lead to an increase of uric acid in the urine, but is this the case? Moreover, if iodide of potassium prevents the conjugation of glycocine with urea, would not there be, if Dr. Latham's hypothesis were correct, a diminution of uric acid in the urine when this drug is administered, whereas according to most authorities, iodide of potassium increases the elimination of uric acid. Moreover, Dr. Cook (*Brit. Med. Jour.*, July, 1883) has shown that so far from benzoic acid and the benzoates diminishing the amount of uric acid, by replacing the conjugation of glycocine with urea, for a conjugation with benzoic acid, leading to the formation of hippuric acid, the formation of uric acid is not checked by the administration of these substances, but that they merely prevent uric acid from crystallizing out from solutions, and thus being presented in a ponderable form. Without accepting any special theory with regard to the formation of uric acid the following propositions may be offered as being most in accordance with ascertained facts.

1. That uric acid is only found to a slight extent in the human body. 2. That in health it is probably destroyed at the seat of its formation, viz., in the tissues or organs, since uric acid cannot be obtained from healthy blood in quantities sufficient for identification. 3. In gout alone does uric acid appear in the blood. 4. The cause of this appearance in the blood may be due (*a*) to excessive production, and that a portion so produced is not destroyed in the tissues and organs; (*b*) that owing to some failure of oxidation probably from disturbance of innervation acting through the vaso-motor nerves, the uric acid is not destroyed in the tissues or organs. 5. If the first supposition (*a*) is accepted then we must suppose that the uric acid is carried by the blood current, and deposited in regions where the circulation is feeble, as in the cartilages of the joints and ears, or in the straight portions of the urinary tubules (p. 231). If the second hypothesis (*b*) is held, then an explanation must be sought in the supposition, that the uric acid not destroyed is, in the case of the large organs, swept into the circulation where it gradually becomes oxidized, but in the case of the tissues where the circulation is feeble as in the cartilages of the joints, etc., it is simply deposited. 6. In either case, the occurrence of uratic deposit depends on the insolubility of the uric acid salt.

This view binds us to no special theory as regards the chemical antecedents of uric acid, whilst it serves to fix in our minds the points on which our treatment should be based.

First, to promote oxidation so as to ensure the destruction of uric acid, either in the organs and tissues in which it is formed, or in the blood into which it has passed. The former may be effected, perhaps, by the agency of drugs such as colchicum, salicylic acid, etc., acting through the influence of the vaso-motor nerves on the process of oxi-

dation; the latter by more general means, such as exercise in the open air, spare diet, and the use of alkalies, which, as is well known, promote oxidation in the blood current. Secondly, to prevent the ill effects of the deposited uric acid and secure its removal, by the administration of solvents. Of these, Dr. Cook has shown that the benzoates act by preventing the crystallization of uric acid and its salts, whilst iodide of potassium, salts of lithia, etc., act probably as direct solvents.

The following summary gives some of the chief pathological and clinical conditions which lead to the deposit of uric acid or urates from the urine.

A. *Deposits of uric acid or urates, not, however, necessarily eliminated in excessive quantities.*

1. Absolute increase in the acidity of the urine.

The occasional deposit of urates observed in winter arises from this cause. The action of the skin being checked the acidity of the urine increases during cold weather. Similarly in many extensive cutaneous diseases, such as eczema and psoriasis, uric acid deposits are of frequent occurrence; these disorders therefore need not be attributed to lithæmia. Also in forms of dyspepsia associated with irregular secretion of gastric juice.

2. Relative increase in the acidity of the urine.

The deposit of urates frequently noticed during the summer months originates in this way, the cutaneous transpiration being increased in hot weather, the urine is more concentrated. Similarly in pyrexia, especially rheumatic fever, and in diarrhœa. Uric acid deposits alternating with sugar are often caused in this way; since as the sugar disappears urination is not so profuse, and a relative increase of the acidity of the urine occurs. This relative increase may not only be caused by a diminution of the water excreted, but from deficiency of the alkaline phosphates; this condition is frequently met with in the urines of ill-nourished or strumous children.

B. *Uric acid eliminated in excess, but not necessarily deposited from the urine.*

1. Uric acid in excess usually attended with a diminution of the other urinary constituents (true lithæmia).	Chiefly in diseases of the liver, such as acute yellow atrophy, cirrhosis, and cancer. In scurvy an excess of uric acid is generally observed, with a diminution of urea and the alkaline phosphates.
2. Uric acid in excess attended with an increase of the other urinary constituents.	In functional derangements of the liver, especially those brought about by disturbance of the "nitrogenous equilibrium" by the ingestion of too much animal food. As a condition antecedent to the development of phthisis or cancer, and sometimes of diabetes, or preceding the outbreak of such constitutional conditions as syphilis, scrofula, and of gout in its early attacks.

1. *Uric acid calculi.*—Calculi mainly composed of uric acid are the most frequent of all urinary concretions, being present in some form or other in at least 80 per cent. of all calculi that come under observation. This frequency led the earlier observers to consider that uric acid was a necessary constituent of all stones, and they believed it to have special concreting powers, (concreting acid), in consequence of this view the term "lithic" or stone acid was given it. The discovery, however, of oxalate of lime and phosphate of lime in calculi, solely composed of these substances led to the abandonment of this error, though the term is still erroneously applied. Uric acid calculi may be large and solitary, (fig. 37), in which case they have a smooth, or a slightly granular surface, of a yellow or reddish-brown colour, oval in shape, and range in size from a pigeon's egg to that of a hen's egg, on section they are hard and brittle, and marked with concentric laminæ of often different degrees of friability, which are apparently determined by the amount of organic matter pre-

sent. Medium sized and multiple calculi are like the preceding, only smaller, ranging from that of a bean up to a pigeon's egg, their surface is often facetted from mutual pressure. Small and numerous "pisiform" calculi are small, yellowish, rounded bodies, ranging in size from a pin's point to that of a marrowfat pea, these are often discharged from the bladder in considerable quantities, especially in elderly people. The formation of these small calculi may go on continuously for some time, and no sooner has one collection passed than another forms; any one of these small stones being retained may in process of time become a large calculus,

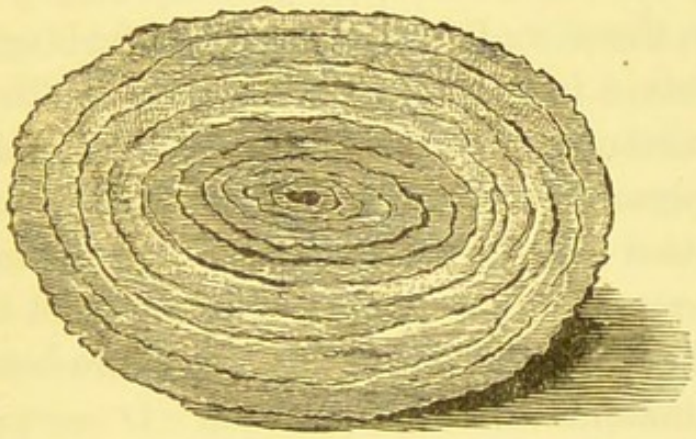


FIG. 37.—Uric acid calculus showing concentric laminæ.

but as a rule it will be found that the larger stones have a history of only one attack of colic, and if removed do not usually recur. These pisiform concretions seem to be intermediate between the usual form of calculus, and gravel, which latter consists of crystalline aggregations of uric acid. This gravel or red sand may accumulate in the pelvis of the kidney, or in the lower portions of the ureters in such abundance as to occasion considerable colic, and irritation of the urinary tract in its passage. The tendency to the formation of uric acid calculi is most marked at the extremes of life, *i.e.*, in children and elderly per-

sons, whilst gravel is more common among adults. In all cases an highly acid condition of the urine is essential for its deposition in either form, and the close relationship between it and gout has long been recognised. "We have married two sisters," writes Erasmus to a friend, "you have gout and I have gravel," and this observation is no doubt true as regards the calculous formations of uric acid in adult life. In children, however, no such relationship exists, for though the children of a gouty stock may suffer from calculous and uric acid deposits, yet in a vast majority of cases no such connection can be traced. In children calculus is more frequently the result of some debilitating illness, and from the very highly acid urine secreted by them under very slight disturbing influence. It is important to bear this in mind, since the tendency to the recurrence of stone is far less in children than in elderly persons. With regard to mixed calculi of uric acid with other constituents, that of phosphate of lime is the most common, then oxalate of lime, whilst triple phosphate will be deposited whenever the urine becomes alkaline from ammoniacal decomposition.

2. *Urates.*—These bodies are very uncommon as forming the sole constituent of stone, especially in adults. Mixed with a considerable proportion of uric acid they more frequently occur in the calculi of young children; whilst combined with oxalate of lime they form the nucleus in fifty-six per cent. of all calculi examined. They are generally stated to consist of urate of ammonia, but analysis shows that urate of soda and urate of lime are also present. They never attain the large size of the uric acid calculus, but are of the size of an almond to that of a good sized marble, generally multiple, two or three being usually found together. Their colour is light fawn or greyish-yellow. They are less compact than a pure uric acid calculus, and their

nucleus under a lens often presents a ragged appearance. These calculi are always deposited in acid urine, except a form to be noticed subsequently, which consists of a mixture of triple phosphate and urate of ammonia, and which is associated with an ammoniacal condition of urine. Urates sometimes occur as gravel, when they are precipitated in the urinary passages as spiked granules, but their chief interest lies in their forming *infarcts* in the renal tubes of young infants. These consist of irregular masses of urate of ammonia and soda, forming yellowish-red lines, which radiate from the papillæ to the bases of the pyramids. They are said to have never been met with in the kidneys of children born dead; they usually occur from the second to the nineteenth day after birth, though in some instances they have been met with as late as three or four months. They are generally regarded as physiological rather than pathological; they are no doubt deposited from a concentrated urine, the first effort of the kidney at elimination, for just as meconium consists almost entirely of biliary matters and mucus, so we may suppose the urine at birth to consist chiefly of urates, and to be in a concentrated condition till the proper elaboration of the urine is perfected by the usual metabolic changes under the influence of respiration. These infarcts may be taken for the granules of bilirubin sometimes deposited in the renal cells of icteric patients, or granules of bilirubin may be mixed with these urates. Scattered deposits of urates are frequently found in the granular kidney, these are most frequent in the cortex, and are apparently not connected with the tubes, whilst in the so-called "gouty kidney" the deposits occur in the papillary portion of the pyramids, and are decidedly intra-tubular. Although calculi composed mainly of uric acid are frequent, and those of urates rare, yet with regard to the

nucleus, according to recent observations, the reverse obtains, a mixture of urates and oxalates being the most common.

164. **Oxaluria.**—There are few subjects in urinary pathology which have excited keener controversy than that which concerns the causes tending to produce a deposit of oxalate of lime crystals in urine. Originally discovered by Wollaston, in 1803, as the constituent of the mulberry variety of calculus, its presence as a crystalline deposit in the urine was for a long time overlooked. In 1842, Dr. Golding Bird, in the "Medical Gazette," drew attention to the fact that oxalate of lime was frequently present as a crystalline deposit in urine, and detailed a series of nervous and dyspeptic symptoms which he alleged were associated with the appearance of this salt in the urine, and which he supposed to be intimately connected with an increased production of oxalic acid in the system. Dr. Golding Bird's observations were at first accepted with some degree of hesitation, but subsequently they received the support of Beneke and Begbie. As more extended observations were made it was found that crystals of oxalate of lime were of very frequent occurrence, that they were found in urine under a variety of pathological conditions, that they were so far from being invariably associated with a train of nervous and dyspeptic symptoms that they were frequently met with in the urine of persons apparently enjoying robust health. Hereupon a reaction ensued, and the opinion gained ground that these deposits had no clinical significance whatever, and it was even questioned whether the oxalic acid found in the urine ever existed in, or was excreted as such, from the blood, and it was suggested that oxalic acid was merely a product produced by changes occurring in the urine after emission. In England these views have been advocated

by Basham, Bence Jones, and Owen Rees. The latter gentleman goes so far as to regard "oxalate of lime merely as uric acid, or urate altered after secretion," and states that he has entirely failed to detect the peculiar pathological conditions which have been said to connect themselves with the so-called oxalic acid diathesis, and is convinced that it must be regarded as an accidental and unimportant modification of that most significant variation from health which consists in the excretion of uric acid, or its compounds, in abnormally increased proportion. Facts which we will now consider, however, are now known which point to the conclusion that oxalic acid is formed in the organism and excreted with the urine, and that uric acid, though it may be a factor, is not the only source from which it is derived, either by oxidation within the system or by decomposition after it has been excreted. The following, then, are the chief pathological and clinical conditions, under which oxalic acid combined with lime makes its appearance in the urine as a deposit of calcium oxalate.

1. *Directly from food by the ingestion of substances containing oxalate of lime.*—It is a well-known fact that oxalate of lime crystals have been found in abundance in the urine of persons who have attempted to poison themselves with oxalic acid; and experiments have shown that when non-poisonous doses are taken about twelve per cent. of the acid taken by the mouth appears as a lime salt in the urine. Many fruits and vegetables, such as rhubarb, sorrel, tomatoes, onions, and turnips, contain crystals of oxalate of lime; and to many persons in weak health, indulgence in such articles is invariably followed by an attack of indigestion and the appearance of crystals of oxalate of lime in the urine. It has, however, been urged that oxalate of lime cannot thus be absorbed from the in-

testine into the system and pass out unchanged into the urine, on account of its great insolubility in water. Reoch, however, has demonstrated that the insolubility is exaggerated, and he points out that Storer, in his "Dictionary of Solubilities," gives the solubility of oxalate of lime in water as $\frac{1}{500000}$. This, no doubt, appears small; but as oxalates are never recognisable without the microscope and seldom appear larger than a blood corpuscle, so that, as Reoch argues, by taking the specific gravity of an average crystal as equal to a cube of water $\frac{1}{3000}$ of an inch in the side, since cubes are to one another as the cubes of their sides, it follows that a cubic inch of water would be equal to 27,000,000,000 of these crystals, and would therefore, according to Storer, dissolve 54,000; and ten ounces of water would dissolve 1,000,000 of these crystals; hence, as we do not often meet with a larger proportion than this in the urine, the amount of blood circulating in the body is more, considerably more, than sufficient to keep this quantity in solution. Urines containing oxalate of lime directly derived from the food are rarely altered in their general characters, and the crystals cease to be deposited at no very distant period after their ingestion. No sense of discomfort may be occasioned by their passage through the system, at most, a mere passing attack of indigestion or increasing urgency during micturition, if there be any urethral or vesical disease, caused by the passage of the crystals over the already sensitive mucous membrane.

2. *Indirectly from food, incomplete oxidation of the saccharine, amylaceous, and oleaginous principles of the food.*— Before their final conversion into carbonic acid and water, these principles yield several intermediary non-nitrogenous acids, of which the chief are glycollic, lactic, and oxalic acids. The albuminous principles, besides yielding certain nitrogenous bodies, as leucin, kreatin, uric acid,

and urea, also furnish a series of non-nitrogenous fatty acids similar to those obtained from the saccharine and amylaceous principles. Now, in the downward progress of these acids towards their lowest term, carbonic acid and water, it is quite possible that arrest of oxidation may take place at any one of them; and that whilst perfectly normal action produces carbonic acid and water, a check to the process will lead to the appearance of oxalic acid in the urine. Indeed, it is probable that there are many conditions, within physiological limits, in which power is economised in the system by eliminating the lower oxidized product, oxalic acid, by the urine, instead of in its completely oxidised state, as carbonic acid, by the lungs. Oxalic acid formed under these circumstances will only occasionally be present in the urine, and will often appear and disappear without any apparent alteration in health. When the crystals of oxalate of lime are deposited in these cases, they will be found in the urine passed within a few hours after food, their presence often inducing profuse urination.

3. *From increased tissue metabolism.*—As stated above, the albuminous principles by oxidation break up into two parallel series; nitrogenous bodies and non-nitrogenous fatty acids. When, therefore, increased metabolism of tissue occurs within the body, we have an increase of these products in the urine. This is probably the most frequent cause of the appearance of oxalate of lime deposits in the urine, and they are met with under a variety of pathological conditions, frequently during the course of most febrile diseases, in pulmonary and cardiac affections in which respiration is impeded, and in disorders of the hepatic functions and depressed conditions of the nervous system. The urines in these cases are generally of a deep orange colour, of high average specific gravity, with an

excess of urea and phosphoric acid, and are usually turbid with mucus and urates, while the deposits of oxalate are not usually persistent, often disappearing for a few days, to return again in great abundance. The oxalic acid in this case probably is, from reasons already stated, not derived from the decomposition of uric acid, either in the blood, or subsequently in the urine after emission. The most rational explanation of its appearance being, that the process of oxidation within the body, under circumstances of increased tissue metabolism, is only sufficient to reduce a certain quantity of non-nitrogenous fatty acids formed within the body to their lowest term of carbonic acid, and consequently oxalic acid, which is one of the series, appears in the urine.

4. *From the mucus of the urinary passages.*—Crystals of oxalate of lime have been found in the mucus of the gall-bladder and in the gravid uterus, and it has therefore been suggested that the crystals that appear in the urine may have their origin in the mucus of the genito-urinary passages. In some cases this is probably true, but in the majority of instances we have no evidence of any morbid condition of the urinary passages to account for their appearance. It is probable, however, that calculi composed of oxalate of lime may result from chemical changes taking place in the mucus of the urinary passages, for, as Professor Parkes (*op. cit.*) has remarked, "no one can observe the enormous amount of oxalic acid in calculi, and believe that such abundance could ever come from the blood." A very ingenious hypothesis has been advanced by Meckel to account for this formation of oxalate of lime in mucus, by assuming that the mucous membrane of the urinary passages becomes the seat of a specific catarrh. In this catarrh a tough adhesive mucus is secreted, which has a tendency to undergo acid fermentation, and in which

oxalate of lime appears when such fermentation occurs. At first this oxalate of lime mucus is of gelatinous consistence, but gradually it takes up more and more oxalate of lime from the decomposed urine, and thus, growing more and more firm, a stony concretion is at length formed. The large and numerous crystals of oxalate of lime so frequently observed in the urine of persons suffering from spermatorrhœa, are most probably derived from the mucus of the genito-urinary passages; for if a patient suffering from this malady be directed to collect the urine passed at stool in a small vessel, and also the seminal and mucous discharge which generally follows micturition during the act of defæcation, separately in a test-tube or on glass-slide, it will be found that both the urine and the discharge contain oxalates, which are, moreover, intimately mixed up in the latter, thus indicating an intrinsic origin. It is not improbable that the oxalate of lime deposits so frequently observed in the urines of ataxic patients, especially during the so-called *urinary crises*, may originate in this way, owing to an abnormal condition of the mucous membrane of the urinary passages resulting from disturbed innervation.

5. *From excess of acid in the system.*—Beneke (*op. cit.*) has pointed out that the increased production of lactic and butyric acids in the alimentary canal is frequently associated with oxaluria, since, as he thinks, the excessive formation of these acids prevents the development of the red corpuscles, so that oxidation is insufficiently performed. A catarrhal condition of the mucous membrane of the intestines he also pointed out as being frequently found accompanying this condition; he does not, however, consider it as being a proximate, but only a determining, cause of the disorder. Whilst endorsing Beneke's statement that deposits of oxalate of lime are met with in per-

sons suffering from dyspepsia, attended with excessive formation of lactic and butyric acids, I do not consider his explanation to be the correct one, since in these cases I believe a catarrhal condition of the mucous membrane of the digestive canal to be the proximate cause, which, by hindering the onward passage of the food, favours fermentative changes and the production of lactic and butyric acids. These acids, which are formed in small quantities in the large intestine in health, being absorbed into the blood, are normally reduced to carbonic acid, which under ordinary circumstances passes off with the other carbonic acid formed in the body by the lungs. If, however, the process of respiration be at all impeded, some of the carbonic acid may be eliminated by the urine, combined with the oxides of potash and soda, in the form of alkaline carbonates, causing an alkaline condition of that secretion.* Or if the acids absorbed from the intestinal canal into the circulation be formed in excess, their reduction into carbonic acid may be incompletely performed, and so the intermediate acid, oxalic, appears in the urine in combination with lime. It is this condition, and this condition alone, to which I think the term "oxaluria" may be clinically applied with a fair show of reason, since the chief and most persistent urinary phenomenon is the deposit of oxalate of lime crystals in the urine.

The symptoms attendant on oxaluria, are in typical cases sufficiently characteristic to distinguish them from those which accompany the derangements associated with deposits of uric acid, and which the late Dr. Murchison (*op. cit.*) so graphically portrayed in his account of the condition he termed "lithæmia." Thus the sufferers from oxaluria are to be found chiefly among the careworn, the

* *Lancet*, July, 1880. "A Form of Dyspepsia associated with an Alkaline Condition of the Urine." By the Author.

harassed, the overworked, and underpaid members of the community, and form a marked contrast in appearance to the generality of those troubled with uric acid tendencies; whilst high living combined with sedentary habits tends to promote a condition of "lithæmia," so that persons suffering from that form of dyspepsia, instead of feeling refreshed by food, are seized "with a feeling of oppression, often of weariness and aching pains in the limbs, and an insurmountable sleepiness after meals" (Murchison). On the other hand, patients with oxaluria feel for a time better after food and improve on a generous, if suitably selected, dietary. Again, a tendency to uric acid deposits is more frequently met with among dwellers in towns, whilst, as far as my experience goes, the victims of oxaluria are most frequently country patients, especially those residing in damp and marshy districts, or on cold ill-drained clay soils: situations, in fact, in which catarrhal affections of the intestinal canal are likely to be engendered. Although in both conditions the mental state is more or less affected, still it assumes a different aspect in each. In "lithæmia" the patient is irritable, fretful, peevish, and discontented with those around him, but he is rarely at fault with himself or hypochondriacal. In oxaluria, however, the patient is generally amiable and easy tempered with his relations and dependents, but is himself filled with the deepest gloom and forebodings, and is painfully hypochondriacal. In oxaluria the bowels are irregular, constipation at times alternating with a colicky diarrhœa of frothy, yeasty character, and not infrequently accompanied with considerable discharges of blood. The urine is usually of a pale greenish colour, and the quantity passed in the twenty-four hours normal in quantity and specific gravity. Its chief characteristic is the deposit of crystals of oxalate of lime, which are found most abun-

dantly in the morning urine passed on first rising. Owing to the presence of these crystals causing irritation of the mucous membrane of the bladder, micturition is frequent and urgent, though the quantity of urine passed is not large. Traces of sugar are not infrequently present, and sometimes sugar for a while replaces the deposit of oxalates, and *vice versâ*. This transformation has been accounted for by the hypothesis, that whilst oxalic acid denoted a condition of imperfect oxidation, sugar represented a still lower. The appearance therefore of oxalates with a diminution of the excretion of sugar has frequently been taken as a favourable symptom of diabetes, an opinion, however, which I do not think altogether warranted. The urine occasionally contains an excess of phosphate of lime, though this condition is not nearly so frequently observed in this form of oxaluria as in the case where the deposit of oxalate of lime results apparently from increased tissue metabolism, and in which, as has been already stated, an increase of urea is also generally noted. Various reasons have been assigned to account for the association of deposits of oxalates with occasional excess in the elimination of phosphate of lime in the urine. The most probable explanation is that it originates in two ways:—*a*. In those cases where there is an excess of urea the increase in the elimination of the phosphoric acid is the result of the increased metabolism of the tissues generally. *b*. Where the deposits of oxalate of lime are associated with catarrh of the intestinal canal, and the formation of lactic and butyric acids is excessive, the phosphate of lime is derived not from the tissues, but from the alimentary canal, the lactic acid having a powerful solvent action on this salt; so that if it is introduced in excess with the food, a larger proportion will be dissolved out and pass into the system than would otherwise be the case.

In addition to the mental depression already mentioned, patients suffering from this form of oxaluria are troubled with many anomalous symptoms indicative of nervous disturbance. Thus, a burning sensation is usually felt across the loins, accompanied by a feeling of tightness and dragging round the abdomen, shooting and burning pains in the lower limbs, twitching of certain groups of muscles, with often a feeling of numbness, deadness, and coldness in different parts of the body. These symptoms, when present together, may lead us to infer that the patient is suffering from an early stage of locomotor ataxy, as was the case with an out-patient under my care at the London Hospital, when he first came under observation. The fact, however, that other characteristic symptoms were absent, and did not develop, and that he improved on a treatment directed to the relief of the dyspeptic condition, soon dispelled any doubts on that point. In another case the patient had been actually treated for some time for incipient locomotor ataxy, and also for syphilitic disease of the spinal cord, his symptoms being ultimately relieved by the discharge of a small concretion of oxalate of lime (p. 512).

Oxalate of lime calculi present themselves in two forms. The most common, a large rough calculus commonly called the "mulberry calculus" (figs. 38, 39), and less frequently as numerous small rounded concretions, resembling and known as "hemp-seed" calculi. The mulberry calculus often attains a considerable size. It has a rough irregular surface, and is of a dark colour. It is extremely hard, and on section (fig. 39) presents an angular structure with dark coloured laminæ, which are very compact, and are often marked with fine parallel lines. The nucleus most commonly consists of a mixture of urates, uric acid and oxalate of lime; more frequently,

however, than with other calculi the nucleus is sometimes purely hæmic. Although calculi of pure oxalate of lime are by no means rare, still it is most frequently mixed with other constituents, the most frequent is that of oxalate of lime and uric acid in alternating layers round a

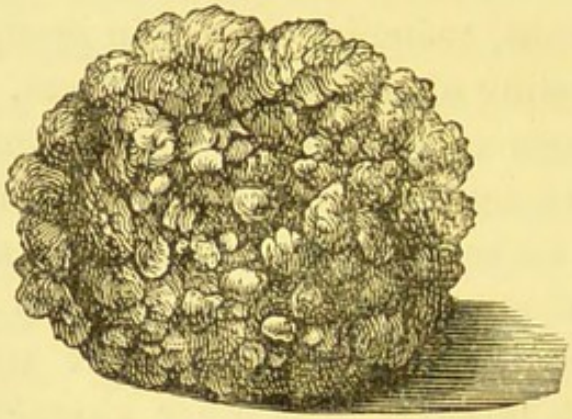


FIG. 38.—Mulberry calculus—oxalate of lime.

mixed nucleus of both substances (fig. 40), whilst next in frequency comes the calculus formed by an external crust of calcium and triple phosphate on a mass of oxalate of lime, these calculi often attain a prodigious size.

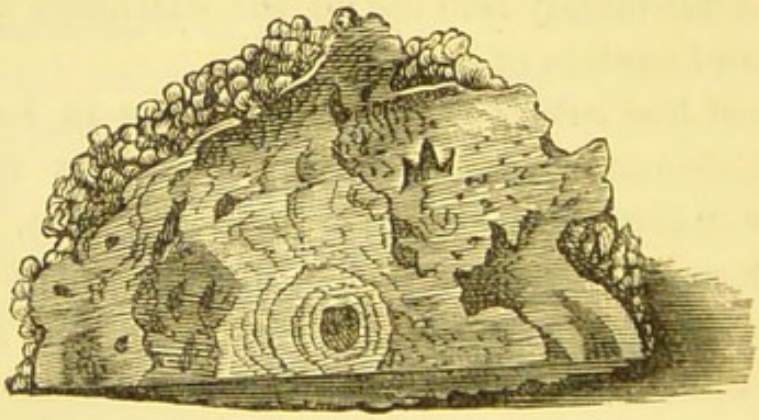


FIG. 39.—Section of mulberry calculus.

Oxalate of lime is sometimes, but very rarely, deposited on other calculi in a crystalline form (*Path. Soc. Trans.*, vol. xxv.).

The small "hemp-seed" calculi vary in size from a pin's

head to that of a hemp-seed, smooth and dark coloured. They are often discharged in considerable numbers, and like the pisiform calculi of uric acid, the tendency to form is long continued.

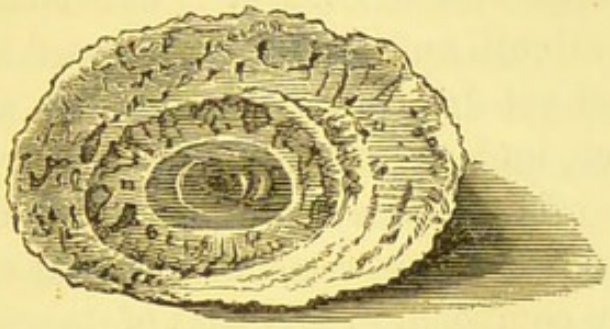


FIG. 40.—Calculus composed chiefly of uric acid ; with a mixed nucleus of uric acid and oxalate of lime.

165. **Cystinuria.**—Cystin calculi are comparatively rare in actual practice, though if we judge from the numbers preserved in pathological museums, we should think them by no means uncommon. Cystin calculi rarely attain to considerable size like uric acid, or phosphatic calculi, but are generally of medium size ; they are usually oval, but some times cylindrical ; their surface is finely granular, with small crystals often dispersed over it of a pure yellow colour ; they break with a crystalline fracture, and are soft and somewhat compressible. Their cut section presents a yellow colour, turning pale green on exposure to light, with a somewhat radiated appearance. Usually they consist entirely of cystin, but some have a nucleus of uric acid on which the cystin is deposited, cystin also occurs as a urinary deposit and as gravel. The urine in these cases has generally a yellowish-green colour, and a peculiar smell said to be like sweet briar when fresh, but rapidly acquiring a putrescent smell when kept, whilst an oily looking film speedily forms on the surface. Should the urine be acid at the time of passing, the cystin may be kept in solution, but as soon as ammoniacal

decomposition sets in it will be deposited; since, though cystin is freely soluble in ammonia, it is not so in carbonate of ammonia or any of the alkaline carbonates. Some observers have stated that urines containing cystin are poor in urea and uric acid. The conditions under which cystin calculi, and gravel, are formed in the urinary passages is not yet determined. Heredity seems to have some influence, undoubtedly it is frequently met with in the members of the same family. From its containing sulphur, and the close correspondence that exists between its elementary composition and that of taurin, it has been supposed that under certain circumstances its excretion compensates for the deficient action of the liver in the elimination of sulphur. The view I am disposed to take, is that cystin is formed directly from taurin, in a manner perhaps analogous to the formation of indigo from indol. The observations of Naunym and Dragendorff have shown that normal urine contains traces of bile acids, of which glycocholic acid is the chief, so that it is probable that some portion of the taurocholic acid is oxidized, and furnishes the partially oxidized sulphur product, which in minute quantities is always present in normal urine. Moreover, Dr. Oliver has recently shown, by means of his peptone test, that the bile acids are often enormously increased in the urine in many morbid conditions, especially those connected with functional derangements of the liver and anæmia (*Lancet*, April and May, 1885). It may be, therefore, that under certain conditions, the quantity of taurin eliminated by the kidney is increased, or its excretion checked, whilst the transformation into unoxidised sulphur is incompletely carried out, so the intermediate product cystin is the result. However that may be, the frequent association of cystinuria with some disorder of the hepatic functions has been fairly established. Prout regarding

the peculiar tallowy and waxy character of the complexion so frequently noticed in these cases, suggested the probability of its connection with fatty liver. Cystin calculi and cystin gravel have been frequently met with in patients whose kidneys have undergone extensive disorganisation. Strumous children are said to be especially liable to deposits of cystin, and it has been frequently found in the urine of chlorotic females. Benefit is experienced by the employment of oxidising remedies, sea bathing, iron, and nitro-muriatic acid. All these circumstances, as well as the statement that the amount of urea excreted is diminished in these cases, strengthens the view that the formation of cystin depends on a local, as well as a general, deficiency of oxidation.

166. **Xanthin** calculi are the rarest of all urinary concretions. In all recorded instances they have been removed from young persons. The largest calculi was that removed by Langenbeck from a boy aged eight, and was the size of a small egg. The stone in the College of Surgeons, analysed by Mr. Taylor, weighed when entire a quarter of an ounce, and was taken from a child aged four. These stones are smooth and of a cinnamon colour, and acquire a polish when rubbed. A few cases of xanthin gravel have been recorded, these all occurred in young persons. Dr. Bence Jones considers that the tendency to deposit xanthin in youth is to be explained by the fact, that it is in the earlier period of life, the greatest chemical variations of the body are to be expected, and the imperfect oxidation of xanthin into uric acid most likely to occur.

167. **Phosphaturia.**—We have already, when considering the chemistry of the alkaline and earthy phosphates (p. 90), stated that only the latter are deposited, and that this deposition occurs under three conditions. 1. When the urine is alkaline from *fixed alkali* as when the

carbonates of potash and soda are in excess in the urine. 2. When the earthy phosphates are themselves eliminated in excess. 3. When the urine is alkaline from *volatile alkali*, as when owing to the decomposition of the urea in the urinary passages carbonate of ammonia is formed, which combines with magnesium phosphate to form the triple salt ammonio-magnesium phosphate. Each of these conditions must now be considered seriatim.

1. *Deposit of earthy phosphates when the urine is alkaline from fixed alkali.*—The urine is usually alkaline when passed, and is slightly cloudy from the precipitated calcium phosphate, though it does not necessarily contain an excess of this body. The urine is usually increased in quantity. The specific gravity is above the average, and the urine effervesces when hydrochloric acid is added, the deposited phosphates at the same time clearing up. Very frequently it happens that owing to a partial deposition in the bladder of the calcium phosphate, the phosphates are discharged like a creamy fluid at the end of micturition, the passage giving rise to a considerable amount of irritation at the neck of the bladder. Patients very often consider this creamy discharge an evidence of spermatorrhœa, but it has no connection with that condition, and a few drops of hydrochloric acid will at once clear up the deposit, and make its character evident. Occasionally it happens that the urine instead of being alkaline is slightly acid; when this is the case the phosphates are not deposited *unless the urine is boiled*, when it at once becomes turbid from the precipitation of the calcium phosphate. The cause of this deposition of phosphate on boiling is explained at p. 94. Urines depositing calcium phosphate often contain an excess of uric acid, but so long as the secretion continues alkaline the uric acid will not of course be deposited, but should the urine become acid it will crystallize out. This

has made some physicians consider that the two conditions alternate, but in reality it only depends on the alteration in the reaction of the urine, for if we render the urine artificially acid when it is alkaline, an abundance of uric acid will generally crystallize out. The conditions leading to the passage of urine alkaline from excess of the fixed alkalies have been already considered (p. 62). They are generally met with in debilitated persons, and those suffering from flatulent dyspepsia.

2. *Deposit of calcium phosphate from excessive elimination.*—In these cases both the alkaline and earthy phosphates are eliminated in increased quantities, the total amount of phosphoric acid excreted in twenty-four hours being often as much as 7 or 9 grms., instead of the normal amount 2·5 to 3 grms. The urines are generally alkaline, copious, of medium specific gravity, and deposit a dense mealy precipitate of phosphate of lime, this being partially deposited in the bladder; the last portion of the urine passed is much thicker than the first and consequently comes away with great straining and irritation. Occasionally, the urine is acid, so that no deposit occurs, and till a quantitative estimation is made it is impossible to tell that phosphoric acid is draining away from the body in such quantities. When we have to deal with the persistent elimination of phosphoric acid in excessive quantities, very distressing constitutional symptoms are associated with its discharge. The symptoms vary considerably in individual cases, but they are all more or less characterised by great nervous irritability, derangements of digestion, great emaciation, severe aching pains in the back and loins, especially affecting the pelvic viscera. As the disease advances, symptoms analogous to those of diabetes, especially of the insipid form, make their appearance; indeed, the disease seems to merge into that con-

dition, insomuch that it has been proposed to give to this disorder the distinctive title of "phosphatic diabetes" (see Polyuria, p. 400).

With regard to the conditions that lead to this excessive elimination of phosphoric acid, very little is known. Indeed, there is no question in scientific medicine on which we have fewer facts to generalize from than that concerning the elimination of "phosphates in disease," and consequently there are few subjects which have yielded a richer harvest to the quack. Physiology can only tell us that the element phosphorus is absolutely essential for the growth and nutrition of the tissues, but cannot explain its *rôle*. Whilst, therefore, our information with regard to the physiological action of phosphorus within the body is still so scanty, it is obvious we are not yet in a position to indulge in speculations concerning the part played by it in the production of certain pathological phenomena with which it has been associated. It is satisfactory, however, to know that the attention of scientific workers has been called to this subject, and we may hope that shortly a sufficient number of trustworthy facts may be collected, which will enable us to gain a clearer insight into the part played by this important element with respect to the nutritive changes with which it is concerned within the body. Nor is clinical observation in this instance much in advance of our physiological and pathological knowledge. Excessive elimination of phosphoric acid has been noticed in acute inflammation of the membranes of the brain (Bence Jones), in the acute paroxysms of certain forms of mania (Sutherland and Beale), and after injuries to the head (George Harley). And the late Dr. Golding Bird attributed some of the cases of phosphaturia that came under his observation to spinal lesions, probably functional in character. But whether in

these conditions it is due to increased metamorphosis of the nervous matter, or to the irritation of a still hypothetical "coördinating chemical centre," or to the influence of a disturbed condition of the nervous system upon nutrition generally, it is at present impossible to decide. Increased elimination of phosphoric acid, again, Beneke has considered in some cases to be due to excessive formation of acid in the tissues, dissolving out the earthy phosphates; in these cases oxalates and phosphates of lime will both be found in excess in the urine. Similarly in certain cases of dyspepsia associated with excessive formation of lactic acid in the stomach and intestines, more phosphate of lime may be rendered soluble, and absorbed into the system, and thus pass out by the urine instead of by the bowel. Marcet has shown from analyses of pulmonary tissue in consumption, that a considerable reduction of phosphoric acid and potash takes place both in the insoluble tissue and nutritive material, as compared with healthy lung tissue. And Edlessen (*op. cit.*) has shown that the excretion of phosphoric acid is increased in cases of anæmia, especially pernicious anæmia. The observations of the authors I have quoted are, however, too limited to draw definite conclusions from as yet. All that we are warranted in assuming from them is, that increased excretion of phosphoric acid is met with in those states of the system which we characterise as "nervous," and that it is often met with accompanying or preceding diseases in which disorder of nutrition is usually well marked, such as phthisis, diabetes, and cancer.

3. *Deposit of ammonio-magnesium phosphate in urine alkaline from volatile alkali.*—We have already when considering the variations that occur in the reaction of the urine in disease (p. 68), described the nature of the fermentation that leads to the decomposition of the urea in

the urinary passages, and the formation of carbonate of ammonia, which combines with the magnesium phosphate in the urine to form a triple salt. The presence of crystals of ammonio-magnesium phosphate in urine at the time of its passage from the bladder is indicative of local (catarrhal) disease of some part of the urinary tract, and not of constitutional disease. The ferment which sets up the decomposition of the urea is, in most cases, introduced by means of dirty catheters, but it may be introduced by other means. Unless, however, according to the experiments of Feltz and Ritter, the ferment be present in the urinary passages, no decomposition of the urine will occur, however diseased the mucous surface may be. The urines containing crystals of the triple phosphate are generally alkaline, sometimes slightly acid (p. 96), turbid from mingled pus and mucus, containing the characteristic prismatic crystals of the triple phosphate, whilst phosphate of lime is also deposited in an amorphous form. Sometimes the pus and mucus combine to form ropy masses of muco-pus, which may be sufficiently bulky as to obstruct the flow of urine from the bladder. This form of alkaline urine is important from the part it plays in producing uriseptic conditions in what is known as the "surgical kidney." It also is especially characteristic of the vesical catarrh that follows on paraplegia, the result of lesions of the spinal cord.

Crystals of triple phosphate occasionally form in the urine sometime after it has been passed, from decomposition setting in; this, however, has no pathological significance, and I have already (p. 64) described how the iridescent film occasionally found on the surface of the urine is caused. Fermentation outside the bladder, however, takes place more readily if the urine is alkaline from fixed alkali, than if the urine were

acid when passed, consequently, the urines of those persons who suffer from dyspepsia, and pass alkaline urine, more frequently exhibit the iridescent pellicle than healthy persons.

Phosphate of lime calculi.—Bone-earth calculi composed entirely of that substance are rare. They may be met with in two forms. 1. Rounded or oval, varying in size from a small bean to a hen's egg, of white chalky appearance, with a very friable surface and breaking with an earthy fracture. 2. Irregular in shape, sometimes branched, of a greyish-white colour, of compact texture, brittle, and with a porcelain-like fracture. The former are generally met with as vesical calculi in elderly people, and especially in those who have suffered long from that form of dyspepsia attended with alkaline urine, due to the presence of fixed alkali, or in those who have taken excessive quantities of alkaline waters or remedies, though as Dr. Roberts has pointed out, that owing to its uncrystalline condition bone-earth has very little tendency to agglomerate into concretions. A fortunate circumstance, since, if it were otherwise, these calculi would probably be nearly as frequent as uric acid. The second variety of phosphate of lime calculi is usually found in cysts and cavities of the urinary organs, and seems to be entirely of local origin. I have in my collection a beautiful specimen of this form of calculus, taken from the left kidney of a sailor, who died in the Seamen's Hospital from ruptured liver, the effect of a blow from a capstan bar; up to the day of the injury he had performed all his duties efficiently though this calculus must have been forming for some years. The kidney was completely disorganised and the calculus occupied the whole of the pelvis of the kidney, and branched off to occupy the cysts in the body of that organ, when removed it resembled a mass of coral.

Phosphate of lime sometimes forms alternating layers with uric acid this is specially the case when alkaline solvent remedies are employed to dissolve the calculus, and are too long-continued. In this case the urine being rendered alkaline, a thin deposit of phosphate of lime forms on the surface of the uric acid calculus, when the alkaline remedies are discontinued, uric acid may be again deposited and so on.

Phosphate of lime associated with carbonate of lime, is deposited in irregular masses in the kidney, lungs, and other organs in cases of re-absorption of the bone salts, as in osteomalacia.

Mixed phosphatic calculus.—Although calculi composed entirely of phosphate of lime are rare, yet mixed with other calculous deposits it is of tolerable frequent occurrence.

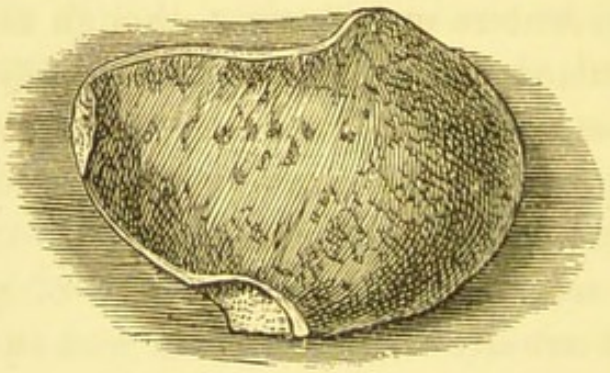


FIG. 41.—Friable crust of phosphate of lime and triple phosphate.

The commonest variety is that composed of a mixture of phosphate of lime and the triple phosphate of ammonia and magnesia. It generally attains a large size, is of a greyish-white colour, very friable and loose in texture, breaking off into thin laminæ (fig. 41), between which the triple phosphate sometimes is deposited in a crystalline form. This concretion is also known as the "fusible" calculus since under the blow-pipe it fuses into an enamel-shaped mass. This calculus is generally

formed upon some other variety, either uric acid or oxalate of lime; it may also encrust growths in the bladder. Its formation depends upon the urine being ammoniacal for a considerable length of time, a condition which ensures the precipitation of both calcium phosphate and ammonium-magnesium phosphate. It may therefore be regarded as having quite a local origin.

Ammonio-magnesium phosphate.—Calculi composed entirely of this salt are very rare, but as a crust or layer of other calculi it is very common. Its presence denotes an ammoniacal condition of the urine. Its most frequent association is with phosphate of lime, with which it is more or less intimately blended, forming the "mixed phosphatic" or "fusible" calculus of which a description has been given above. Although rare as a sole calculous concretion it is frequent as gravel, when the urine is ammoniacal, coming away as a brownish deposit, partly crystalline (prisms) and partly sub-morphous. As such, it is met with in chronic diseases of the bladder, after the introduction of dirty catheters, or in urine containing organisms, sarcinæ, bacteria, etc.

Carbonate of lime calculi are very rarely formed in the kidney, though it may sometimes be present as an in-



FIG. 42.—Calculus from prostate gland.

gredient of other calculi, their chief seat of formation being the prostate gland. In this organ two varieties are met with:—1. Of small size, poppy and mustard seeds, of yellowish-brown colour, often pyramidal and cubical in shape, and their section marked with concentric rings, and

by polarized light sometimes displaying a shaded cross band. 2. Are larger, often the size of a hazel nut, and have a porcelain-like appearance, on section the surface is found marked with radiating striæ (fig. 42), these larger concretions are usually found lodged in a cyst or abscess of the prostate. The smaller concretions may pass away with the urine, or they may collect in the gland, or as a rare event one may find its way into the bladder, and so become the nucleus of a vesical calculus of different composition.

Miscellaneous concretions.—There are other varieties of urinary concretions such as fatty, indigo, hæmic and fibrinous. The *fatty concretions* are composed of an admixture of fatty matters, rendered saponaceous by the alkaline bases of the urine. This material is known by the term *uro-stealith.* They may occur in large rounded masses or as small rounded concretions. They are, when recently removed, soft and elastic, generally of a brownish colour and encrusted with phosphates, in fact they may form the nucleus of a large phosphatic calculus. The fatty matter which forms their basis is probably derived from some old purulent collection which has dried up. Mr. McCarthy (*Med. Chir. Trans.*, vol. lv.) has given an account of some renal calculi of unusual shape found in the left kidney of a woman, who died of cancer of the uterus. These calculi were accuminated, soft and greasy when first removed and contained 36·5 per cent. of fat and cholesterin. In this case the medullary portion of the kidney was altogether absorbed, and the cortical substance the seat of suppurative nephritis. *Indigo* has been met with in rare instances both as a concretion and as a deposit. The best recorded case is that by Dr. Ord (*Path. Soc. Trans.*, vol. xxix.). When it occurs it is probably derived from the indican of the urine, which if retained and acted upon by highly acid urine, may be converted into indigo. Prout has

recorded a case in which indigo was occasionally voided in considerable quantity, the patient was in the habit of taking Seidlitz powders, and the deposit generally appeared in the urine after taking one of these powders. *Fibrinous concretions* are of extremely rare occurrence, they may be taken for hardened masses of uro-stealith, but they are insoluble in ether, and decompose peroxide of hydrogen, they never attain a large size rarely larger than a small pea, rough, uneven, and somewhat resembling beeswax. They are probably the result of some old hæmorrhage, and are the shrunken remains of the clot that has become decolorized. *Hæmic concretions* are also the result of hæmaturia, they are seldom found free, being usually encrusted with uric acid and oxalate of lime, and then form the nucleus of these calculi. When free they form small rough darkish concretions, extremely light, crushing with a cinereous fracture when dry. Examined chemically and microscopically they show they are derived from blood.

168. **Analysis of Calculi.**—The following procedure is the best adapted for clinical purposes. Note the size, colour, and general appearance. Also whether section presents an uniform surface, or is made up of concentric layers. A portion of the calculus is then reduced to a fine powder; if made up of several layers a portion of each layer must be taken, and the nucleus examined microscopically as well as chemically.

1. Analysis of the Common Varieties of Calculi:—

Powder a small portion of the calculus, divide the powder into two portions, and place one at one end, and the other at the other end of a glass slide. Label them respectively A and B.

(A.) *Soluble in liquor potassæ.*—The powder labelled A is touched with a drop of liquor potassæ, by means of a

stirring rod. It dissolves (or only partially dissolves, if there are traces of phosphates or oxalates present), a drop of HCl added to the alkaline solution causes a white precipitate; indicates uric acid or urates.

1. URIC ACID . . . — Chars under blow-pipe leaving little residue. Gives murexide reaction with nitric acid and ammonia (p. 8).

2. URATES . . . — Chars under blow-pipe, leaving considerable residue. The urates are soluble in boiling distilled water, while uric acid is not. Dissolve in boiling distilled water; filter and evaporate. The residue if urates are present will give murexide reaction.

3. CYSTIN . . . — Does not give the murexide reaction. Boiled with liquor potassæ, and lead acetate a black precipitate of lead sulphide is formed.

4. XANTHIN . . . — Does not give murexide reaction but a purple coloration, with nitric acid and liquor potassæ.

(B.) *Soluble in hydrochloric acid.*—Touch the powder labelled B with hydrochloric acid, it dissolves without effervescence* (or partially dissolves if there are traces of uric acid). The acid solution gives a white precipitate when touched with ammonia, and indicates:

1. PHOSPHATE OF LIME . — Chars but slightly under blow-pipe, leaving friable white ash, *infusible*. Ash dissolves *without effervescence* in dilute HCl. The acid solution gives a white gelatinous precipitate with ammonium oxalate solution denoting lime; also a precipitate with uranium nitrate denoting phosphoric acid.

* If there is effervescence it denotes the presence of carbonate of lime, traces of which are often found in phosphatic calculi.

2. Ammonio-magnesium phosphate, or triple phosphate . . .	Chars slightly, leaving greyish ash which *slowly fuses*. Soluble in HCl *without effervescence*, from which excess of ammonia throws down a characteristic crystalline precipitate of triple phosphate (*vide* p. 96).
3. Phosphate of lime with ammonio-magnesium phosphate. (Syn. *Mixed phosphates* or *fusible calculus*) . .	Chars slightly, the ash *fuses readily* into a porcelain-like mass; soluble in dilute HCl *without effervescence*. Acid solution gives a white precipitate with ammonia, consisting of amorphous phosphate of lime with crystals of triple phosphate.
4. Oxalate of lime . .	Chars considerably under blow-pipe, often with considerable decrepitation, leaving a white ash which dissolves *with effervescence* in HCl. A fragment of the calculus will not dissolve in oxalic acid.

2. Rarer Forms of Urinary Calculi :—

1. Uro-stealith . .	Soluble in ether. Will yield fatty acids by boiling with baryta water; and cholesterin, if present, by treating the etherial residue with boiling alcohol. N.B. These calculi often contain in addition, phosphates or uric acid.
2. Fibrinous . . .	Insoluble in ether, the powdered calculus decomposes peroxide of hydrogen.
3. Blood concretions .	Insoluble in ether, test for hæmin crystals. The ash contains abundance of iron.
4. Indigo	Insoluble in ether, soluble in boiling chloroform. Converted into indigo-white when boiled with an alkaline solution of glucose.

169. **Etiology.**—In speaking of the origin of stone, it was stated that two conditions were necessary for its

formation, (*a*) those that originated the nucleus, (*b*) those that favoured its subsequent growth. It no doubt frequently happens that uric acid, urates, or oxalate of lime in a submorphous condition, and in a state fitted to form the nucleus of a calculus, passes into the urinary passages, and is either there disintegrated or immediately passed out with the urine, because the conditions favouring its development are not present. On the other hand we have occasion frequently to observe, that the urine for long periods of time is often thick with mucus and urinary deposits, a condition most favourable for the development of stone, and yet none results, because in this instance no nucleus has been formed. It was also stated that the nucleus has its origin probably in all cases, certainly in most, in the tubules of the kidney, but that the pelvis of the kidney, and the bladder are the seat of its development and growth. In considering the etiology of calculous affections, our object will therefore be to trace the action of certain causes in bringing about an alliance of the two conditions necessary for the formation of stone.

Age.—Stone is incontestably more frequent during the early and late years of life than during middle age. Sir Henry Thompson (*op. cit.*) has shown that out of 1827 cases operated on for stone, 1158 were under twenty-five years of age, 1001 being under fifteen years, and that in the thirty years from twenty-five to fifty-five there were only 231 cases, whilst in the twenty succeeding years the number rose to 303. The causes that lead to this frequency of stone in youth may be thus summarized; it is a period when conditions of "vital impairment" of the renal epithelium, the result of overgrowth, sickness, etc., are likely to be present, and if the views I have expressed with regard to the origin of calculi be correct, then such a condition is particularly favourable to the

formation of the nuclei. In many cases the nuclei are undoubtedly derived from the remains of the urates deposited as infarcts in the urinary tubules soon after birth, a time when the renal epithelium seems not to have acquired the power of separating the more solid constituents from the concentrated urine. In youth, too, the retention and growth of the calculus is favoured by the fact, that whilst the nucleus is probably no smaller than those formed in adult life, the urinary passages are considerably smaller and narrower, so that the onward passage of anything, save the very smallest concretion, is more or less hindered. And again, since it is during youth that the greatest chemical variations in the body are met with, we may expect to find uric acid generally in excess; but what is of more importance, the urine is often unduly acid for long periods, a circumstance that ensures the precipitation of uric acid or urates. In adult life the circumstances favouring the formation of stone are less prominent. It is a period of the greatest functional development of the kidney, when conditions leading to retardation of the flow of urine through the tubules have hardly had time to come into play, and when also the calibre of the urinary passages is fully developed. In old age on the other hand, we have again circumstances favouring the formation of nuclei, in the impairment of the renal function, as is shown by the senile changes taking place in the kidney, whilst the flow of urine through the tubules is often diminished by the obstruction afforded by an enlarged prostate, or the effect of old strictures; moreover, the expulsive powers are diminished by the enfeeblement of the organic and voluntary muscles which aid in micturition.

The calculi met with in early life are chiefly composed of uric acid, mingled with urates, the nucleus almost invariably consisting of the latter substance. After removal they

rarely recur, if they do it is during the period of childhood, a fact which points strongly to the local circumstances that favour their formation at that period, and a circumstance that should be borne in mind in considering the the propriety of performing nephrectomy in any given case. If from the history, we gather that the impacted calculus was formed during the earlier period of life, its removal may be determined on as a means of permanent relief; if, however, the retained concretion has formed during the middle period of life or in old age, especially in persons subject to frequent attacks of gravel, we have to consider whether the relief afforded is worth the risk attendant on the operation since the condition is likely to recur. In middle life, although calculi of uric acid are still more frequent than other varieties, yet this is the period when oxalate of lime calculi are particularly prevalent, for even if this substance does not form the main constituent of the stone, yet it may almost invariably be demonstrated as composing a part of its nucleus. Calculi formed at this period of life have a great tendency to recur. In old age, uric acid calculi numerically retain the lead, as they do at all other periods of life, but the tendency to the formation of oxalic calculi is diminished, The most common form at this age are the "pisiform" calculi composed of uric acid, which are often passed in great numbers for a considerable length of time. Calculi composed almost entirely of phosphate of lime are more common now than at any other period of life; whilst the tendency for the urine to become ammoniacal under conditions of urinary irritation being more marked, the calculi of old people are more frequently encrusted with triple phosphate than is the case of those removed at an earlier period.

Climate exercises a marked influence on the tendency to

calculus formations. Dividing England into three strips, excluding London on account of the number of patients sent from all parts of the country for operations, out of 671 deaths from stone, 144 occurred in the Western counties, 244 in the Midland strip, and 283 in the Eastern counties. Now when we come to consider the density of the population of the Midlands as compared with the Eastern district, the relative frequency of stone in the latter district will at once be perceived, whilst supposing the Eastern countries to be as populous as the Western, which is not the case, since the Western district includes such towns as Liverpool, Manchester, Bristol, Exeter, Plymouth, etc., then the mortality from stone in the Eastern districts is twice that of the Western, and this proportion no doubt would be increased if the stone cases of London were included, the majority of which are sent up from the South Eastern and East Anglian districts.

Climate exercises its influence apparently in three ways:—1. Meteorological conditions. 2. Nature of the soil. 3. The water supply.

Meteorological conditions act probably by inducing catarrhal conditions. In the Eastern counties the wind passing over the fen lands is rendered cold and damp, whilst the East wind, which is more prevalent than in other districts in England, often brings with it cold raw fogs, which unlike the sea fogs of the West and South Western coasts, are not warmed by the genial influence of the gulf stream.

Dry cold has apparently little effect in the production of calculus. In Sweden, where in winter the cold is intense but the air dry, stone is almost unknown. In America, according to Gross, urinary calculi are rare in Canada, in Mexico and California, but more common in Ohio, Tennessee, and Alabama. In Canada the air is particularly dry, as is the case in the mountainous regions of Mexico

and California, whilst the alluvial plains of the latter States are damp and subject to frequent floods. Dr. Gross also states that stone is of rare occurrence in the coloured races of America, in ten years he never met an instance.

The soil acts, too, in the same way, but it also plays an important part in impregnating the water with calcareous salts. In the purely fen districts in the East of England, where stone is very prevalent, the chief factors no doubt are the cold raw air, and the sub-soil damp in the fenny lands; whilst on the chalky hills round Cambridge, and some parts of Norfolk and Essex, the hard water from the chalk is the chief exciting cause. But the tendency to the formation of calculus in chalky districts is not altogether due to the hardness of the drinking water, since chalk, though it rapidly dries on the surface, is, except in long periods of drought, really a damp soil. To convince one's self of this it is only necessary to inspect the basements and cellars of many houses built on this formation, and it should not be forgotten that whilst chalk absorbs water, like a sponge, it also retains it. This circumstance was originally pointed out by White of Selborne, who remarked, that on the huge chalk masses of the South Downs, the little ponds on the summit rarely dried up, even in the hottest summer, though fed by no apparent spring. This dampness of a chalk soil also probably explains why it is that it does not suit rheumatic patients. The difference of soil, too, explains the reason why calculous affections are more frequent on the chalky soil of the South Western, than on the lime-stone formation of the North Western districts; the deaths from stone in every 100,000 inhabitants, according to the Registrar-General's returns, being forty-six in the former, to thirty-four in the latter.

Nevertheless, hard water undoubtedly acts as an important exciting cause in cases where there is a predisposition to calculous formations. A patient of mine, who for some years had suffered with uric acid deposits, but who had never had an attack of gravel, spent, last autumn, a fortnight or so at Brighton, towards the end of that period he had a severe attack of gravel and passed numerous pisiform uric acid calculi; he immediately returned to town, and since then has had no symptom pointing to the formation of any kind of renal concretion, though his urine still continues to deposit uric acid crystals whenever his digestion is deranged. Another patient, permanently resident at Brighton, has suffered from the passage of small stones for years, on my recommendation he uses now only distilled water, and he tells me that so long as he employs it he is free from colic, but should he by any chance be driven to use the Brighton water for a few days, he is sure to pass a small stone shortly afterwards. In both these cases I think the attacks may fairly be attributed to the hard water, the lime forming an insoluble urate, and also probably an oxalate, since both urates and oxalates are generally found composing the nuclei of the calculi of persons who have resided in chalky districts. Whilst on this point, it is interesting to observe that horses and cattle instinctively prefer soft to hard water, and they will turn from a bucket of clear spring water to the muddy and polluted, but soft, water of the horse pond. Now, in these animals, the urine is almost entirely deficient in phosphoric acid and lime salts, a fortunate circumstance, since as their urine is alkaline, they escape the risks of the deposition of phosphate of lime. Their preference for soft water may be, therefore, explained by some instinctive taste which leads them to select the fluid best suited for their requirements. Parkes has told us that with

horses the change from soft to hard water causes indigestion, loss of condition, and roughness of coat. Whilst a practical grazier has informed me that calculous complaints are rare among cattle kept in the fields where they drink chiefly the rain-water from ponds and ditches, whilst cattle brought up in the farm-yard, as bulls and stock for market, and where the water-supply is taken from the well, are not infrequently attacked.

Sex.—Owing to the shortness and less complex nature of the female urethra, and its greater dilatability, vesical calculi are much rarer among females than males. Females, too, are less liable to renal concretions than men, though not nearly so much so, as in the case of vesical calculi; this, no doubt, is owing to their being less exposed to the other predisposing causes, about to be enumerated, than the male sex.

General causes.—An highly animalized diet and the immoderate use of certain alcoholic beverages, powerfully predispose to the formation of stone and gravel. This no doubt was, with the inefficient drainage of the land, an important factor in causing the prevalence of these complaints in the last century, when all who could afford it, washed down the substantial roast and boiled with strong ales, whilst port wine, Madeira, and rich brown sherries, were also largely consumed. Now, with the introduction of a lighter cuisine, mild bitter ales, cheap claret, and a better drained sub-soil, each decennium shows a marked diminution in the mortality from these complaints. The employment of a highly nitrogenous diet, and the immoderate use of saccharine alcoholic drinks, undoubtedly induce a tendency to stone, by causing indigestion, acidity from fermentation, and malassimilation; but their most important effect in this particular, is brought about by the increased metamorphosis and waste of tissue which they

cause. In this way the nitrogenous excretion through the kidney is greatly increased, so that impairment of the functional activity of the renal cells is at last induced, and such insoluble substances as urates and oxalates instead of being eliminated by them, may at length come to be retained Sedentary habits also favour the production of stone and gravel. The skin fails to discharge adequately its depurating function, especially as regards the elimination of free acid from the body, whilst the pulmonary exhalation of carbonic acid is not vigorously performed. The consequence of this retention of acid is, that the alkalinity of the blood is lessened, and in order to restore the balance, more than the normal quantity of acid has to be removed by the urine. This constant discharge of an highly acid urine may impair the vitality of the renal epithelium, whilst it certainly ensures the precipitation of the insoluble uric acid and urates.

170. **Symptoms.**—The symptoms of renal calculus arise from the effects caused by its presence in the pelvis of the kidney. Pain, irritation of the mucous surfaces (pyelitis), hæmaturia, and retraction of the testicle are the most prominent. In some cases there is more or less gastric disturbance and reflex vomiting.

Renal colic, or nephalgia, is the pain excited by the presence of a foreign body in the pelvis of the kidney. This pain may be slight so long as the irritant is quiescent, but if it is moved, or pressed onwards into the ureter, the pain becomes excessive. Thus it happens that a small calculus is generally attended with infinitely more pain than a large one. For a calculus large enough to fill the whole pelvis is more or less firmly fixed, and consequently beyond the dragging sensation caused by its weight, pain is little felt. Even a moderate sized calculus which does not occupy anything like the

whole of the pelvis may exist for a long time without exciting urgent pain, since in this case it may become partially encysted in a pouch of the pelvis, from which it is not easily dislodged, except after severe jolting, etc. But a small calculus rarely gets fixed, and every movement of the body acts upon it, and sets it moving, besides which the natural expulsive efforts are always tending to force it towards the ureters, so that at last the patient is quite worn out with the attacks of pain. From the dull aching pain caused by the weight of a large renal calculus to the agonizing colic attendant on the passage of a small stone from the pelvis of the kidney down the ureter, there are infinite gradations, but the character is similar throughout. The onset, or the aggravation, of the pain is sudden, generally brought about by some movement of the patient. The pain is referred to the loins, springing forwards, and sometimes radiating upwards to the chest, so that one is led to suppose the patient may be suffering from pleurisy, more generally downwards causing exquisite pain along the cord and testicle of the side affected, which is strongly retracted against the pubes, the latter organ being slightly swelled and exquisitely tender to the touch. The patient rolls over and over in his agony, keeping his thighs tightly flexed over his abdomen, and resting on the affected side. The pain at the onset may be so severe as to cause fainting, in severe attacks there is always vomiting. The pain is paroxysmal; even in a continued paroxysm, one can usually observe short lulls quickly followed by exacerbations. This severe pain lasts during the whole of the passage of the stone from the kidney to the bladder, when it suddenly ceases. If the stone does not pass, the colic usually subsides after four or five hours duration, to renew itself very shortly if no relief has been given by remedies, but fortunately in the majority of cases, the rest and the

medicinal treatment that follow such an attack, are sufficient to ensure against an immediate return, till some fresh movement disturbs the stone again. Short of these attacks of severe pain, there may be, generally in the interval, but often as the only attendant manifestation, reflected pain; this may present itself in the testicle, and may be mistaken for neuralgia of that organ, or it may manifest itself in painful irritability of the bladder, so that we may be led to fancy that the stone is forming there whilst it is still in the kidney, by no means an uncommon mistake, or by a numb sensation down the thighs; or a burning pain may be constantly present in one of the heels, the sole of the foot, or more rarely the outside edge of the foot, running along the border towards the little toe. As these reflected pains are paroxysmal, and often accompanied with reflex vomiting, they are sometimes regarded as dependent upon disease of the spinal cord. Thus, an American gentleman, who for years had suffered from paroxysmal attacks of violent pain on the outer side of the left foot and ankle, and who had consulted most of the leading neurologists in Europe, was kept in Paris six weeks, with ice bags more or less constantly applied to the spine for supposed congestion of the spinal cord, came under my observation in 1878, when he was suffering from a very severe paroxysm. Closely questioning him with regard to his past history I learnt he had passed bloody urine about five years before, or about six months before the commencement of the paroxysms. I regarded the case as one of nephro-lithiasis, and abandoning the galvanism, the electric baths, blisters to the spine, heated irons, etc., with which for five years he had been tormented, advised him to take a course of Carlsbad water, to diminish the amount of nitrogenous food, and keep his urine neutral. Since then he has improved considerably,

the paroxysms are much less severe, and do not occur unless he commits some imprudence with regard to diet, or the urine becomes unduly acid, whilst his general health is decidedly better. In another case, a gentleman who consulted me for some stomach derangement, told me that three years previously he had suffered from paroxysmal lumbar and sciatic pains often accompanied with retching. An eminent surgeon had told him his symptoms pointed to an early stage of locomotor ataxy, whilst a physician had told him they were the result of syphilitic disease of the cord, and gave him small doses of mercury for nearly a year. By some chance he happened to consult another surgeon, and shortly afterwards, under that gentleman's treatment passed a small oxalate of lime calculus, which relieved him of those symptoms. Such cases should impress upon us the importance of *examining the urine immediately after any attack of paroxysmal pain occurring in the lower extremities, even in the absence of any pain over the region of the kidneys themselves;* especially with regard to the detection of pus cells, blood corpuscles, and the nature of the crystalline deposit.

Pyelitis.—The irritation produced by the presence of a renal concretion in the pelvis of the kidney soon sets up inflammation of the mucous surface, so that pus is always found as one of the earliest results of calculous formation. The degree of pyelitis thus set up depends very much on the form and nature of the calculus. If smooth and rounded, like most of the uric acid calculi, and of sufficient size, so as to fill a pouch in the pelvis of the kidney, then little disturbance is caused, but if as is sometimes the case, these renal concretions have a spiny projection, or, as in the oxalate of lime calculus, the surface is rough and angular, then the irritation will be considerable, and the amount of pus formed and discharged abundant.

Should the calculus obstruct the opening into the ureter, the flow of pus will be arrested, and an accumulation take place in the pelvis, this may be discharged intermittently as the calculus shifts its position, or it may form a permanent accumulation (pyo-nephrosis) if the calculus is impacted.

Hæmaturia.—Blood corpuscles are not so invariably present as pus cells in cases of renal concretion, still they will be found after every exacerbation of pain, if the urine be examined immediately after the attack. Sometimes the amount of blood passed is considerable, tinging the urine a deep red, and sometimes, though rarely, in sufficient quantities to form coagula, which pass with great difficulty down the ureters to the bladder. The tendency to hæmorrhage is aggravated by exercise, especially jolting movements. It has been well said that a man with a stone in his kidney may walk but cannot drive; whilst a man with a stone in his bladder, often cannot take walking exercise, but may ride comfortably in his carriage. In the hæmaturia from the kidney, the urine generally maintains its acid reaction, and the first portion is as highly coloured as the last, whilst in vesical hæmaturia the urine is often alkaline, thick, and muco-purulent, and the last portion of the urine often appears more bloody than when the stream commenced, indeed the last drops are often pure blood, as in the case of fungoid disease of the bladder.

Gastric disturbances.—The reflex vomiting that so frequently occurs during renal colic, in no way differs from that occasioned by disturbance in other organs. The onset of the pain and the act of vomiting may be almost simultaneous, at first the food, if any is in the stomach, is ejected, then an acid glairy fluid, mucus and acid gastric juice, which finally after repeated vomiting becomes coloured with bile.

Retraction of the testicle.—In all cases of renal concretion, I have found this symptom invariably present. Occasionally it may give a clue in an obscure case, thus I was not long since called to see a gentleman, a stranger to myself, who whilst at breakfast suddenly complained of intense pain in the abdomen, vomited his food and then fainted. From what I heard, I thought probably there had been a rupture of an abdominal or iliac aneurism. On arriving, I therefore at once examined the abdomen, when I noticed the right testicle strongly retracted, which made me suspect the probable nature of the attack, and quiet the apprehension of his friends. The patient soon began to rally, was again violently sick, but had no complaint of pain anywhere, when suddenly he called for a chamber vessel, and then with great urgency passed a few drops of bloody urine, which confirmed the opinion I had drawn from the retracted testicle, and later in the day he passed *per urethram* a small uric acid calculi.

171. **Diagnosis.**—An attentive examination of the urine from day to day would preclude the possibility of overlooking the existence of a renal calculus, even if other symptoms were not pronounced. A difficulty certainly arises sometimes in those cases, as in cancer of the kidney, or scrofulous disease of the kidney, in which masses of softened cancerous or tuberculous matter are detached and passed down the ureters, giving rise to colic, accompanied with bloody urine. A careful examination of the urine, however, especially of the detritus, and the clinical circumstances of the case, generally enable us to arrive at a conclusion without much difficulty (see Cancer and Scrofulous kidney). A rapidly growing renal calculus, such as those composed of triple phosphate and phosphate of lime, or large oxalate of lime concretions, by causing a tumour in the loin, may be taken for cancer, the following points,

however, will serve us to discriminate between the two. In cancer, the amount of blood is generally more considerable than with calculus, and occurs often independently of unwonted exertion. Small red-coloured gelatinous looking lumps may sometimes be observed in the urine after attacks of hæmaturia in cancer. Examination of the urine may show cancer cells if fragments come away; if this sign is absent, then the character of the urinary deposit may help us; in cancer, it has often a mashy appearance, and is more free from pus, mucus and crystalline deposit, than that caused by calculus. In cancer, nausea occurs frequently independently of pain or hæmorrhage, in renal calculus it is not generally observed except during attacks of colic. It should, however, be borne in mind that cancer may be secondary to long-standing calculus disease of the kidney, though this contingency is not nearly so frequently observed as with gall stones. Nor should the fact be overlooked that irritation of the kidney may exist without there being any symptom referrable to that organ, whilst the pain and irritability of the bladder may lead one to suppose that viscus is affected, and *vice versâ*. Thus in the case of an old lady, I used sometimes to see, in whose left kidney was lodged an enormous calculus, all her trouble, was referred to the bladder, and nothing could convince her that she had no stone in that organ, though she was sounded, with no result, by Sir Henry Thompson and Sir Prescott Hewett. In another case, the reverse of the one just quoted, in which an abscess opened into the base of the bladder, all the symptoms pointed for many weeks to pyelitis of the right kidney, and it was not till I asked Mr. John Wood to examine the bladder for me with a sound, thinking from a change of symptoms that a stone had passed from the kidney to the bladder, that the real

nature of the lesion was determined. In these doubtful cases a careful examination of the bladder should always be resorted to.

In undertaking the treatment of stone, it is of course of importance to diagnose the leading chemical characteristic of the calculus deposit. For medical reasons, in order to select the appropriate remedy; and for surgical, as to its probable hardness and power of resistance to the lithotrite, and also its tendency to recur. In order to come to a conclusion on this point, every detail concerning the past urinary history of the case should be carefully reviewed. The prevailing character of the crystalline deposits at an early stage, the subsequent variations in the reaction of the urine, and the nature of the crystalline deposit at the present time, the amount and character of the hæmorrhage, will aid us in coming to a right conclusion. Thus if we have a history of long continued uric acid deposit, which has nearly ceased for some time, if the reaction be acid, and much mucus is diffused through the urine, that in addition to the hæmaturia, which though frequent is never excessive, caused by exercise, there is also a periodic hæmorrhage apt to occur at tolerably regular intervals independently of exertion, and the mucous deposit in the urine has a yellowish, or rusty tinge, then we may assume that the concretion is composed of uric acid. If on the other hand the patient has suffered from oxaluria, or we have the history of a dyspepsia attended with great mental depression, and the urine though acid is not so to a very high degree, whilst the hæmorrhage is abundant and very dark coloured, and the mucous deposit, when blood is absent, is of a glairy greenish colour, then an oxalate of lime concretion may be suspected. With phosphatic calculi, there is the history of long continued alkalinity of the urine, either fixed or volatile, or both; whilst the urine either contains abundance

of muco-pus, or else an abundant flocculent precipitate of mucus, whilst decided hæmorrhage is a rare event, yet the urine and mucus are generally tinged with blood.

172. **Treatment.**—A renal calculus may pass downwards from the kidney to the bladder, and then if prompt treatment be adopted, it may whilst still small, pass out *per urethram*. If this fortunate event is not accomplished, it remains in the bladder and developes into a vesical calculus. Or the stone may be retained in the kidney, in which case it may become impacted and gradually enlarge without giving rise to much trouble, or it may remain loose in the pelvis of the kidney, setting up a degree of pyelitis which either induces renal abscess and peri-nephritis, and then leads to the discharge of the stone by means of a fistulous opening in the abdominal walls, or surgical means have to be employed for its removal. Our treatment, therefore, has to be adapted to these various circumstances, and we have now to consider seriatim the means to be employed during the passage of the stone down the ureters, for its early removal from the bladder, for its relief should it be retained in the kidney, and the measures to be adopted to prevent recurrence after it has been removed either by medical or surgical means.

Treatment of renal colic.—Our efforts must be directed towards the relief of pain, and facilitating the passage of the stone down the ureter. The first step to be taken is to ensure the thorough evacuation of the bowels. Not only does a loaded condition of the bowels in itself act as a hindrance to the passage of the stone, but owing to the relation of the large intestine to the anterior surface of the kidney, considerable pain is caused by its pressure on the tender organ. The act, too, of emptying the bowel also aids the expulsive efforts directed towards forcing the concretion down the ureter; in the case of small calculi

I have known immediate relief to follow a copious evacuation of the bowel. The best means to effect this is by enemata of warm water, followed by the injection of olive oil, if there is reason to think the fæces are hardened or scybalous. Even if the bowels are not loaded, an enema is of service for the relief of the flatulent distension which is usually very great in these cases. As soon as the bowels are relieved the patient should be placed in a hot bath of 98° F., gradually raised to 100° F., for twenty to thirty minutes. On leaving the bath, a full dose of solid opium, if there is no chronic renal disease to contra-indicate its administration, should be given, and gentle but firm shampooing in a direction downwards from the loin towards the groin, frequently applied. During the paroxysm of severe pain, chloroform may, from time to time, be administered; it not only subdues the pain, but also by relieving spasm facilitates the escape of the stone. The patient should also be encouraged to drink copiously of barley-water, or better still if it is handy, of distilled or soft water. After the continuance of some hours, the colic will abate, somewhat suddenly if the stone has passed into the bladder, more gradually if it is still retained in the pelvis or the ureter. If the latter is the case, we must ensure the patient a period of rest after his severe suffering, by placing him in a comfortable position in bed, which is generally effected by letting him lie on the side affected with his thighs well flexed, and by giving him a morphia injection, sufficiently strong to secure some hours of sleep, if the dose of opium first given is not sufficient for the purpose. The subsequent treatment is determined by the course of events. Should the concretion, however, fortunately have passed into the bladder, we must proceed at once to take measures for its expulsion from that cavity before it has time to increase its bulk.

The renal concretion has passed into the bladder.—A calculus that has just passed down a ureter, is certainly not too large to pass through the adult urethra, always supposing no stricture or prostatic enlargement is present. To secure its early expulsion it is often sufficient to direct the patient to retain his urine till the bladder is full, and then gently compressing the orifice of the urethra with the thumb and finger, to make a strong expulsive effort to micturate, then suddenly to release the pressure at the orifice, and half empty his bladder, then again to compress the urethra, and again release the stream till the bladder is emptied. In this way the concretion is carried by the strong stream outwards towards the urethra, and may thus happily be discharged. It often happens, however, that the patient feels the stone carried to the entrance of the urethra and then feels it fall back again, this is generally the case with long oval-shaped concretions which have passed with their long axis downwards through the ureter, but present themselves transversely at the entrance of the urethra. In this case, the patient should be encouraged to persevere in filling and emptying his bladder, as we hope that on one such an attempt, a presentation favourable for its outward passage may occur. In cases were there is atony of the bladder, it is a good plan to introduce a full-sized catheter, half empty the bladder, then withdraw the instrument, when the stone will very frequently follow after the catheter into the urethra. The concretion in passing down the urethra, may give rise to much pain, especially if its surface is rough or irregular. It may also become fixed, but in most cases the pressure of urine from behind it, is sufficient to force it on, or if in the anterior portion of the urethra, it may be squeezed forward by the fingers; but if it does not pass it must be removed by surgical means. Should

these attempts fail to remove the stone from the bladder, it is worth while employing the use of solvents, since it is in these early cases of vesical calculi that their action is most marked. This mode of treatment will be described in the next paragraph, where we speak of the solvent treatment of renal calculi.

The calculus remains in the pelvis of the kidney.—In this case the colic is either frequently repeated, or else after a certain period of more or less pain and discomfort, the symptoms gradually subside, owing to the calculus becoming encysted. Our treatment, therefore, will be guided by these natural indications. If there should be frequent attacks of colic, we ought in the first instance to endeavour to effect the passage by trying to diminish the bulk of the calculus by means of solvents, and also to render the urinary passages more favourable to its passage by diminishing the catarrh. *Solvent remedies* were much in vogue during the century before the introduction of chloroform and the employment of lithotrity, and considerable success no doubt attended their employment, and in spite of Sir Henry Thompson's statement, that he cannot find that any patient certified to have stone, after sounding by a competent surgeon, after a course of any solvent was subsequently found free from stone; four cases are reported (*Tracts B, No. 4, 250 Library Royal Med. Chir. Soc.*) in which stones were detected by Mr. Nourse of St. Bartholomew's, Mr. Sharp of Guy's Hospital, and Mr. Cheselden of St. George's Hospital, by sounding, and the patients after a course of solvents, during which a large quantity of grit was passed, were found by the same surgeons, on again sounding, to be free from stone. To these may be added the well authenticated cases of Dr. Jurin and Dr. Whytt, whilst besides these I have collected from various sources some 130 cases in

which the use of solvent remedies was followed by either complete relief, or diminution of suffering. The solvent remedies employed in those days were either solutions of soap, lime-water, or else strong infusions of wood ashes. In this form though they rendered the urine powerfully alkaline, they had the disadvantage of disordering the stomach, and were by no means so perfect or so easily applied as the remedies now at our command. In considering the efficacy of the solvent treatment we must bear in mind one important fact, and that is, it is better suited for the solution of vesical than renal calculi. The reason of this is, that the urinary bladder is capable of holding three or four ounces of alkaline fluid, which can be retained for some hours, and which thus completely surrounds the stone, whilst in the kidney the urine in contact with the stone at any given time, is only small in quantity, and as it passes away directly to the bladder, it is therefore much more difficult to keep the urine constantly alkaline, a greater quantity of alkali having to be administered. The solvent treatment is therefore best adapted for the solution of small calculi just passed into the bladder. The treatment is carried out as follows: the patient having emptied his bladder, twenty to thirty drops of liquor potassæ, or forty to sixty grains of citrate of potash as recommended by Dr. Roberts, should be administered in some bitter infusion, every four hours, in the meantime the patient is to drink as little water as possible, so that the urine should be concentrated and the degree of alkalescence kept as high as possible, whilst he should be directed to retain his urine as long as he can, so that the stone may be kept immersed in the alkaline fluid. This solvent treatment is only available for uric acid stones, alkaline solutions having no effect on phosphatic or oxalate of lime calculi; whilst with those which

are soluble in acid solutions, it is found practicably impossible to administer acid in sufficient quantities to have the slightest effect, though in the case of phosphatic calculi in the bladder, washing out that organ frequently with a dilute solution of HCl, may check their growth. In renal calculi, for the reasons already stated, the alkaline solvent treatment has little effect unless the calculus is very small and quite recent, in fact, still in almost a nuclear condition. Then the continuous administration of liquor potassæ or citrate of potash for some days or weeks, or the use of the alkaline waters of Vichy or Contrexéville, will perhaps bring away the concretion in a partially disintegrated condition. Should, however, the calculus have attained a fair size, the administration of alkaline solvents will not only do no good but may do positive harm, the amount of alkali taken, especially if in the form of bicarbonate, having a tendency, as has been shown by experiments by Parkes, Beneke, Bence Jones, and myself (*Lancet*, Nov. 9th, 1878), to render the urine more highly acid after the immediate effect of the alkali has passed off; whilst with large and long-continued doses of alkali unless carefully watched, there is a danger of inducing an ammoniacal state of the urine, which greatly aggravates the existing evils. In these cases I fall back upon the method suggested by Dr. Murray of Newcastle, some few years back, which consists of administering large quantities of soft or distilled water. This method, which is suited for all kinds of calculi, has in the case of renal concretions been successful in my hands, especially when alternated with alkalies, in the case of uric acid calculi. In one case which I reported to the Pathological Society (*Trans.*, vol. xxxiii., p. 206), the calculus was passed as a mere shell after two years persistence in the use of soft water, with occasional doses of alkali. In other

cases with smaller calculi the treatment has been less prolonged, and they have come away much eroded on the surface, showing that a diminution of their bulk had been effected. In carrying out this treatment, about four pints of distilled water are administered daily, the patient having no other supply, the tea is made from distilled water supplied in gallon jars by the chemist, and for drinking water, the distilled aërated water supplied by the "Salutaris" company may be relied on. The continued use of distilled water exercises a powerful diuretic action, and the specific gravity of the urine becomes very low, whilst the inorganic constituents, especially the lime salts, are reduced to a minimum. The solvent action of distilled water is due to several influences. In the first place by causing a low specific gravity of the urine it induces disintegration; since Rainey has shown experimentally that bodies placed in solutions of different density to those in which they were formed undergo molecular disintegration. Again, chemical analysis has shown that those calculi that undergo spontaneous disintegration are always poor in inorganic constituents, the use of soft water diminishes the supply of these as already stated, even if it does not actually act as a solvent on those forming the outer crust of the calculus, and so increases the tendency to disintegrate. Lastly, soft water probably diminishes the catarrh of the urinary passages, and by diminishing the swelling of the mucous membranes allows a small stone to pass, which was before obstructed. And this brings us to the second consideration named at the commencement of this paragraph, viz., the treatment necessary "to render the urinary passages more favourable to the passage of the stone." A renal concretion cannot exist for long without setting up a considerable amount of pyelitis, and it is easy to see how the swelling of the mucous membranes of the

pelvis of the kidney, especially the folds near the orifice to the ureter will obstruct a calculus in its passage. Although soft water relieves this condition, still we have a more sure and rapid agent in turpentine. This medicine which has gone out of fashion of late years, had formerly a great reputation in calculous affections. The late Dr. Henery, of Manchester, thought the subject important enough to bring before the Royal Medical and Chirurgical Society, and related a case in which a single dose brought away an enormous accumulation of uric acid concretions. Pepys, the Diarist, a martyr to stone and gravel, records his favourable experience of it. For my part I have found it of considerable value. After a few doses, even if the calculus does not pass, the patient becomes easier, and the urine less purulent, whilst in many, the administration is followed by the discharge of the concretion. It is valuable, too, as a prophylactic agent, since whilst it renders the urinary passages more free, by diminishing the excessive amount of mucus, and the swelling of the mucus surface, it removes the conditions favourable for the retention and growth of any subsequent nucleus that may be discharged into the pelvis of the kidney. The best mode of administration is in the form of capsules, one or two every night or morning.

Encystment.—It often happens that after death we find the kidneys the seat of calculous disease, which was unsuspected during life, or had given rise to little or no disturbance. Thus, in the case of a lady I attended a few years since, and who died at the age of eighty-four, her left kidney had attained an enormous size, but gave her little pain; this calculous mass had been growing since 1840, when she first consulted Dr. Prout for irritability of the bladder, which he pronounced was due to the presence of this stone in the kidney. In a

post-mortem made on a sailor in the Seamen's Hospital, a huge branch-shaped calculus in his left kidney was found, this had given rise to no symptoms during life, as he had for years performed his duties as an able seaman, the cause of his death being rupture of the liver by a blow from a capstan bar. These cases, and many similar ones, may lead us to hope that if a calculus is allowed to remain quiescent and increase in size, it may form a pouch for itself in the pelvis of the kidney, and give rise to little or no trouble unless disturbed by some unwonted exertion. If therefore it happens that the employment of the solvent mode of treatment gives no relief, and if after a fair trial there is no amelioration of the symptoms, and that the stone does not pass, this mode of treatment ought to have a fair trial before operative procedure with its attendant risks be decided on. The most successful case, that has come under my notice, is that reported to me by my friend Mr. Hicks of Ramsgate. A lady who suffered from repeated attacks of colic, and considerable pyelitis, dependent on an oxalate of lime calculus in the kidney, and who was completely worn out with suffering, was induced by Mr. Hicks to remain in a recumbent position for six months. At the end of that time all symptoms of pyelitis subsided, and the patient was able to walk about and be driven without any feeling of discomfort whatever. In the case of a sailor, admitted at the Seamen's Hospital, with hæmaturia due to renal calculus, and who was unable to walk across the ward without inducing an attack of colic, I tried this treatment. After some failures caused by his restlessness, I managed to keep him in bed for nearly two months, more or less on his back. At the end of that time he was able to walk about the grounds of the Hospital, and was free from pain, and ultimately was discharged with a view of joining his ship; from that time I have

heard nothing of him, so I cannot say if the relief was permanent. In order to ensure complete success by this mode of treatment, the rest must be complete, and the position nearly always the same, viz., dorsal but rather inclining to the affected side. The discipline is severe, but if rigidly carried out is likely to be rewarded in suitable cases with success. It should I think always be resorted to in cases manifestly unsuited to operative relief. Lastly, if we fail in our efforts to cause the stone to pass into the bladder, or to render it quiescent in the pelvis of the kidney, then if the patient continues to suffer from repeated attacks of colic, with considerable pyelitis, the case becomes one for the surgeon, and operative procedure must be resorted to without further delay.

Prophylactic Treatment.—A patient having got rid of a stone, it must be our endeavour to prevent the formation of another. For this purpose the patient must be placed under the best hygienic conditions. If he lives on a cold damp soil, it should be drained, if exposed to cold easterly winds, he should if possible winter in the South, and on a dry sub-soil, if that is not possible he should clothe himself in flannel, especially a flannel binder round his loins, the waistcoats and drawers may also be advantageously lined with chamois leather. He should continue the use of soft water. If the tendency be toward *uric acid* deposits, the condition of the urine must be attended to, and should never be allowed to become highly acid or concentrated. Occasional doses of biborate of soda and citrate of potash will best effect this; whilst on the slightest suspicion of lumbar pain, he should take a few doses of turpentine with a view of clearing the urinary passages of mucus, and diminishing any catarrh.

The food must be light and easy of digestion, and should be as varied as possible. Fish should be the

chief article of animal diet; white meat such as poultry and lamb, veal and pork excepted, should be preferred to red meats. When these are partaken of, it is as well to remember that the neck cutlets of mutton and the fillet of beef are more juicy and tender than the loin chop or rump steak. All roast meats should be cooked with the gravy retained in them. Bread should be eaten stale, better as toast. Potatoes, except in the form of "chips," and those only in small quantity, are to be avoided, so also all flatulent vegetables—cabbage, spinach, onions, turnips and peas; in their place, simple salads should be freely partaken of. Tomatoes cooked in various ways, the soft white flower of the spring broccoli, French beans, stewed celery, sea-kale, laver, may all be used. Watercress should be served at every meal. Sweet fruits and cooked fruits, with added sugar, must be forbidden. But the subacid fruits may be employed in moderation, but even these may occasion heartburn and acidity, and give rise to cramp. Pastry, on account of its richness and the sugar it contains, should be abstained from, but plain rice, bread and butter, and custard puddings, with but little sugar, may be eaten each day at dinner with advantage. Savoury omelettes, caviare, olives, &c., need not be forbidden if partaken of in moderation. With regard to the use of alcohol, the special requirements of each patient must be taken into consideration. It should be taken in as dilute a form as possible, and the beverage selected must also be comparatively free from sugar. It is impossible to decide what wine will suit the patient best. It often happens, as Dr. Prout remarked many years ago, that those individuals who have long been accustomed to the use of the stronger wines, as port and sherry, or who have been drinkers of ale, often suffer from pains in the back and gravel when they are first placed upon light wines, such as claret, hock, and

champagnes, and this is especially noticeable in cold weather. It is, therefore, as well to make no sudden change, especially with elderly people, beyond reducing the quantity and substituting a dry and lighter port or sherry, if the taste had previously been towards a fuller and more bodied wine. When, however, the light wines can be taken without occasioning gravel or pains in the back, the superior growths of the light clarets, such as St. Jullien and St. Estephe, are preferable to clarets of the higher class, such as La Rose or Lafitte. Zeltinger, a still Moselle, is also a wine that persons suffering from uric acid tendencies, as a rule, are able to take without discomfort. All wines should be drank directly from the cask or after they have been bottled some time. Newly bottled wines are most pernicious. Alcoholic beverages should only be indulged in once during the day, and should then be taken with the principal meal. As the digestive powers are usually enfeebled in persons who have suffered long from gout, a little *dilute* alcohol, which, as Claude Bernard has shown is, next to the saliva, the most efficient agent in stimulating the gastric secretion, should be taken at the commencement of dinner. The best form is a tablespoonful of brandy in half a tumbler of water, or a spoonful of sherry in the soup. No other alcohol should be taken during dinner, but afterwards a couple of claret glasses of some light wine or two small glasses of dry port or dry sherry. If the patient is very weak and the nights are sleepless, a little brandy or whiskey may be permitted before going to bed; this is best taken in some natural alkaline effervescing water.

With regard to the treatment of *oxaluria*, we have to consider whether the deposit manifestly arises from the ingestion of articles of food containing crystals of oxalate of lime, in which case it will be sufficient to point out

what these are and to discontinue their use. If the deposits, however, arise indirectly from the food, owing to incomplete oxidation of the saccharine, oleaginous, and albuminous principles, it will be necessary carefully to regulate the diet with regard to quantity and quality, and to promote the oxidising processes within the body by means of iron, change of air, sea-bathing, &c. In those cases where oxalate of lime deposits seem to arise from increased tissue metabolism, as evidenced by an increase in the amount of the urinary constituents more especially the urea and phosphoric acid excreted daily, inquiry must be made into the nature of the conditions producing such disturbance, and the treatment directed accordingly. In the case of calculous deposits of oxalate of lime it will be profitable to remember that the oxalic acid has possibly its origin in the mucus of the urinary passages, and not necessarily in the blood, a reflection which ought to direct our attention rather to the treatment of any local morbid condition that may exist in them, than to the employment of remedies designed to act on the system generally. Lastly, with regard to these cases of dyspepsia associated with more or less persistent deposits of oxalate of lime, and to which alone, as I have stated, the term "oxaluria" seems applicable; our effort at treatment must be directed almost entirely to the relief of the catarrhal conditions on which the dyspeptic symptoms depend. This is best effected by the systematic employment of small doses of Carlsbad salts largely diluted; a teaspoonful of the salt dissolved in ten to fifteen ounces of hot water, as hot as the patient can bear it, should be taken every other morning an hour before breakfast. This diluted warm saline solution seems to have the power of dissolving and removing a considerable quantity of the abnormal mucus, which in undergoing fermentative changes gives rise to lactic and

butyric acids, the motions which result from its use containing not only fæcal matter, but much offensive glutinous-looking slime. Thirty-grain doses of bismuth should be administered once or twice a day before meals, and Dr. Prout's mixture of nitro-muriatic acid and nux vomica may be prescribed with advantage, especially in long-standing cases when there is much mental depression, about two or three hours after food. The patient should remove to a dry soil, but if that is not possible, the greatest attention should be paid to the subsoil drainage of his house. The use of a cold-water compress over the abdomen at night will be found advantageous, not only in relieving the abdominal catarrh, but in protecting the patient against a return of the malady. The diet should be nutritious and digestible, with a liberal allowance of meat, fish, poultry, and game. The bread should be eaten stale, or better still, toasted. Sugar and all farinaceous food should be avoided as much as possible without actually restricting them, and flatulent vegetable food altogether discarded. Tea may be used in moderation, but coffee and alcohol are positively injurious.

With regard to the treatment of persistent deposition of *earthy phosphates* the main indications are rest and an endeavour to promote nutrition generally. To attain this end opium or codeia should be given in full doses, when the patient first comes under observation. As soon, however, as the nervous system is quieted, and the rheumatic and neuralgic pains are less severe, it should be discontinued, lest it interfere with digestion. General tonics, such as iron, phosphorus, quinine, nux vomica, hydrochloric acid, and cod-liver oil should be persevered with. When there is a history of syphilis, iodide of potassium should be combined with these remedies. Warm baths, followed by tepid douches, give great relief to the neuralgic

pains, and also soothe the nervous system. The soluble phosphates may be administered; but their utility in these cases is questionable. There appears to be no lack of these constituents in the system; the difficulty seems rather to lie in the want of power of the tissues to retain them. The food should be light and nutritious, and milk one of the chief constituents. Alcohol should be avoided; it invariably, even in small quantities, increases the diuresis. The same may be said of coffee. Change to dry, bracing air should be obtained if possible. The clothing should be warm, and the patient carefully guarded against cold, since in these cases a reduction of bodily temperature is always noted.

When the urine is alkaline from the presence of carbonate of ammonia, we may endeavour to prevent the formation of *ammonio-magnesium phosphate* concretions by the administration internally of boracic acid, or benzoic acid; after a fair trial of both, I think the former the most satisfactory, the prescription given at p. 290 is perhaps the best way of administering it. It may be taken for long periods of time together, without in any way affecting the general health. Turpentine too is very useful in this condition, since it diminishes the catarrh of the urinary passages which is always more or less present. The bladder, if affected, should be washed out systematically, either with a dilute solution of hydrochloric acid and quinine, or of boracic acid (p. 291). Although in spite of all our efforts we may find it impossible to restore the urine to its normal reaction, yet by persistently using the above means we can generally prevent the formation of a triple phosphate concretion, and also relieve the patient from the many discomforts attendant on an ammoniacal state of urine.

LEEDS & WEST-RIDING
MEDICO-CHIRURGICAL SOCIETY

CHAPTER XI.

Functional Albuminuria, Peptonuria, Hæmoglobinuria.

Functional Albuminuria.

173. **Classification.**—Writing as far back as 1842, Simon remarked that "albuminous urine is so frequently observed in numerous deranged states of the organism, independent of Bright's disease, that the idea that granular degeneration of the kidneys necessarily exists, when albuminuria occurs, must be abandoned." Again, in 1852, Mialhe asserted that digested albumin (peptone) occasionally appears in the urine independently of any apparent renal lesion. Whilst Gigon, in 1858, went so far as to state that albumin existed in normal urine. So little impression, however, did these observations make, at all events in England, that though Parkes, Roberts, and other writers on urinary pathology, alluded to the fact that albuminuria might occur independently of Bright's disease, and in connection with general disorder of the system, still the fact never, till quite recently, seemed to impress itself on the attention of the profession generally. Since, however, the practice of systematically examining, for albumin and sugar, the urines of all patients that come under our observation, and of those who are referred to us for "life assurance," has become general, the subject has received considerable attention, and very valuable additions have been made to our knowledge with respect to it.

And first with regard to the so-called *physiological albuminuria*. As already stated, as far back as 1858,

Gigon asserted that albumin existed in normal urine. Becquerel, however, who carefully went into the question at the time, conclusively showed that the precipitate obtained by Gigon was not albumin, but a mixture of mucin and other organic substances. With the introduction of more delicate reagents for the detection of albumin, Gigon's idea has revived, and many hold that a minute trace of albumin is present normally in all urines, or at all events in the urine passed after food or after exercise, and that an exaggeration of the physiological condition, such as an indigestible meal, or strong exercise, may lead to a very perceptible increase in the amount passed into the urine. Thus Leube, who examined the urine of soldiers after a long march, found albumin in sixteen per cent. of the urines examined; whilst Capitan who examined the urine of ninety-seven children at the Hôpital des Enfants Assistés, found albumin in thirty-eight instances, in quantities varying from ·007 to ·02 grm. in the litre. Chateaubourg also found albumin in seventy-six urines out of ninety-four, passed by soldiers five hours after a meal. On the other hand Oertels who experimented on a considerable number of individuals, some of whom were invalids, and some women and children, by making them ascend heights of various degrees of steepness, only found albumin in three per cent. of the cases submitted to the experiment. This latter observation closely accords with my experience, for out of more than sixty examinations made for "life assurance" in persons otherwise apparently healthy, I have met with temporary albuminuria but twice. The discrepancy existing between the results obtained by Leube (sixteen per cent.), Capitan (thirty-nine per cent.), Chateaubourg (eighty-one per cent.), and those of Oertels (three per cent.) requires explanation, which I believe is to be found in the

circumstance that the first named observers did not employ tests that sufficiently distinguished between serum, albumin, and other proteid bodies, such as mucin, peptones, etc., that might happen to be present, and also by not always having rigidly excluded the possibility of extra-renal albuminuria.

Thus Capitan and Chateaubourg relied on potassio-mercuric iodide, which as we know has a wide range of action, precipitating as it does mucin, peptones, hemi-albumose urates, and alkaloids, and mistakes are liable to arise unless *heat* is employed as well, to confirm the presence of serum albumin; and we are informed that in the case of ninety-four soldiers, whilst potassio-mercuric iodide gave a precipitate with seventy-six urines, heat only once proved the presence of albumin. Again, with regard to Leube's observations, though the nature of the test employed is not stated, still it is not unreasonable to suppose that among soldiers, a considerable proportion had suffered from urethral trouble at no very distant date, and though sufficiently recovered as to permit them to perform their ordinary regimental duties, a long march might still excite a muco-purulent discharge. Again, the effect of the pressure on the chest, from the weight of the knapsack and other accoutrements, would probably in some cases occasion a degree of venous obstruction sufficient to account for the albuminuria. I have repeatedly examined urines passed by apparently healthy persons, supposed to contain albumin, but with the exception of the two instances above mentioned, I have failed to satisfy myself of its being physiological albumin. Either it has proved to be some other proteid body, such as mucin, peptone, hemi-albumose, etc., or else on microscopic examination of the urine I have found the mucous membrane of the genito-urinary tract inflamed as from an old gleet, slight

cystitis from cold, or pyelitis from gravel. But though I do not believe in the existence of a physiological albuminuria, I am ready to admit that in some persons, apparently strong and well, albumin, just as sugar does in others, passes into the urine on very trifling exaggerations of ordinary physiological conditions.

But if we examine the urine of those acknowledged to be suffering from definite disease, we find a much more frequent occurrence of albuminuria. This varies with the class of cases that come under observation; thus, among out-patients with a great proportion of slight maladies, albuminuria will be noticed in about twenty-seven per cent. of the urines examined, whilst with in-patients, among whom are to be found cases of heart disease in the last stage, pneumonia, pleurisies, and other acute febrile affections, the percentage is far higher and may be placed at forty-seven; thus giving, if both classes of cases be taken together, an average percentage of thirty-six. The statistics of different observers, however, vary as regards this point; thus Parkes puts the percentage for men in hospital cases at 37·05, Dickinson at 39, both of which agree closely with mine; whilst Saundby states that out of 145 out-patients he found the urine albuminous in 104. Further, if we analyse these thirty-six cases we shall find about twenty-one per cent., according to my figures, are due to organic changes in the structure of the kidney, such as diffuse inflammation, cyanotic induration, waxy degeneration, etc., and about eleven per cent. due to disease of the lower urinary passages or to pyrexia, etc., whilst the remaining four per cent. may be fairly termed functional albuminuria, due either to derangements of digestion, disturbances of innervation, or an altered condition of the blood.

1. *Derangements of digestion.*—In the majority of cases

the albuminuria occurs only after the ingestion of food, and appears to be caused by the presence of some more diffusible form of albumin than serum albumin, such as ov-albumin in the case of the albuminuria after eating largely of eggs, or casein, as in the instances recorded by Christison, after eating cheese. But, in many cases, the presence of albumin in the urine after food seems to depend on the non-assimilation of proteid substances in the stomach and intestinal canal, just as sugar appears in the urine owing to the non-assimilation of starchy and saccharine matters in the liver. That this may be a probable cause of digestive albuminuria has been shown experimentally by Parkes, Bernard, Stokvis, and Gubler. In other cases, the albuminuria is ushered in with a feeling of nausea, and is attended with marked disturbance of the hepatic function, shown by the decided icteric tint of the skin, and vague dyspeptic attacks; in these cases the urea eliminated is usually increased in quantity. This latter form of albuminuria, which has been designated "hepatic albuminuria," resembles somewhat in its character that of paroxysmal hæmoglobinuria, only the colouring matter of the blood is absent from the urine. Many of these cases of albuminuria, apparently dependent on functional derangements of the liver, are glycosuric as well. Finally, what may be termed "digestive albuminuria," is occasionally observed, when a small quantity of serum albumin diffuses through with peptones (p. 110).

2. *Disturbed innervation.*—Experiments on animals have shown that albuminuria, accompanied by a profuse flow of urine, follows section of the renal nerves; whilst puncture of the floor of the fourth ventricle, a little higher up than is required to cause glycosuria, and irritation of the sympathetic in the neck, are also attended by the presence of albumin in the urine. Albuminuria has also been

produced, though in a lesser degree, by irritation of the sciatic nerve, or of the plexus of nerves over the intestines. Capitan has also shown, that irritation of special nerve centres—the auditory by detonations, the retina by strong light, sometimes causes transient albuminuria. Neurotic albuminuria may be observed clinically in some persons after a cold bath or exposure to cold. It has been suggested that the albuminuria thus produced is only a minor manifestation of paroxysmal hæmoglobinuria, only in this case the colouring matter of the corpuscles is not dissolved out. It may also be produced by purely mental causes, such as the prolonged study, with anxiety, attendant upon competitive examinations. These cases of albuminuria are more frequently observed, I am convinced, among students residing in London, or large towns, than among the members of the two Universities, where the conditions of life are more healthy, and where better opportunities exist for getting fresh air and exercise. One reason, perhaps, that the condition seems more prevalent among students of the medical profession than among others, is, that they are accustomed when out of health to test their own urine, and so discover a symptom that might otherwise have passed unnoticed. In one case I have seen albuminuria apparently induced by sheer anxiety. A healthy young man presented himself for "life assurance" and would have passed as a first-class life, but his urine was found loaded with albumin. His medical attendant who learnt the cause of his rejection, was unable to find in any subsequent sample passed the smallest trace of albumin, and he therefore assumed I was mistaken; it was therefore arranged he should undergo another examination, but the very morning he was to come to town for that purpose the urine was again found to be albuminous. Neurotic albuminuria, as has

been pointed out by Dr. Dukes (*Brit. Med. Jour.*, vol. ii., 1878), is not uncommon among adolescents, in many cases it may be referred to over-work and ill-health, but in some it is undoubtedly connected with the practice of masturbation. Dr. Matthews Duncan (*Med. Chir. Trans.*, 1885) has also pointed out the intimate connection that exists between the internal genital organs and the kidneys, and the frequency with which parametritis is accompanied with albuminuria. Transient albuminuria has also been met with after injuries to the head, during epileptic convulsions, in tetanus, and in exophthalmic goître.

3. *Altered conditions of the blood.*—It is often difficult to determine whether the albuminuria is caused by changes in the blood itself, or is induced by the irritation in the kidneys, set up by the elimination of poisonous substances through them. Thus for instance, in the case of the absorption of purulent collections from the body, the blood poisoning from malaria, jaundice, scurvy, purpura, syphilis, etc., or the poisoning by phosphorus, mercury, lead, etc., a certain degree of nephritis undoubtedly exists. On the other hand it is probable that variations in the specific gravity of the blood may induce transient albuminuria. Thus for instance, I have found occasional traces of albumin not at all infrequent in the urines of corpulent elderly persons, who habitually secrete a rather dense urine, containing an excess of urea. These cases are often spoken of as "gouty albuminuria," and it may be so, although in many cases I have had no reason to suppose the patient to be gouty; I have, however, satisfied myself that in some of those cases that have come under my observation, the albuminuria was not caused by any organic changes in the kidneys, nor that the albumin was derived from pus caused by irritation of the excretory tract, from deposited

uric acid, urates or oxalates. I am therefore inclined to think that in these instances, the albuminuria was caused by a functional exhaustion of the renal epithelium brought about by a long-continued over-elimination of urinary solids.

Again in the puerperal state there is often an albuminuria, which must be distinguished from the albuminuria of puerperal nephritis (p. 246) as being unattended with dropsy or eclampsia. This form of albuminuria is often accompanied with slight jaundice, and is usually somewhat intermittent, indeed occasionally paroxysmal in its character, being abundant at one time, whilst hardly a trace can be found at another. Thus in one case the morning, noon and afternoon samples contained but the merest trace, whilst the evening urine was always loaded, even when the patient was kept in bed. This form of albuminuria depends, I think, on some altered condition of the blood in the puerperal state. Albuminuria will occasionally be observed in some females about the menstrual period, often associated with a slight transient jaundice (*icterus menstrualis*).

With regard to the causation of functional albuminuria, under any of the above named conditions, we must, in accordance with the conclusions arrived at (p. 167), where we considered the causation of albuminuria generally, infer that the primary cause lies in a deranged function of the glomerular or tubular epithelium, though no doubt the secondary causes are numerous. Thus in the albuminuria referred to derangements of digestion, a more diffusible albumin may be brought to the epithelium, or as Dr. Lauder Brunton (*Lettsomian Lectures*, 1885) has suggested the albumin may be presented in a state of finer molecular sub-division. In neurotic albuminuria the functions of the renal epithelium are disturbed, by varia-

tions of pressure in the circulation, brought about by the vaso-motor nerves. In certain cases this may be so great as to lead to considerable hyperæmia. In some cases the functions of the epithelium may be arrested by the direct action of some toxic agent on them, as in Dr. Robertson's experiment (p. 161) with atropine, whilst in others the epithelium, as already stated, may become exhausted by habitual over stimulation.

As a rule there is little difficulty in determining between functional and organic albuminuria. In the former though the albumin may be abundant it is rarely persistent, and many samples may be passed throughout the day perfectly free from albumin. Again, even if the albumin should persist, functional can be distinguished from organic albuminuria, by the fact that the other evidences of organic disease are absent, thus there is no dropsy; no epithelial casts for when these occur in transient albuminuria, we must suspect that a slight degree of nephritis also exists; no great diminution in the excretion of urea as in tubal nephritis; no uræmic convulsions or cardio-vascular changes as in chronic interstitial nephritis; whilst febrile reaction serves to distinguish the transient albuminuria which often accompanies pyrexial conditions from functional albuminuria. The presence of pus in the urine will enable us to distinguish between disease of the urinary passages, and albuminuria the result of functional disturbance.

174. **Treatment.**—In the majority of cases, rest, change of air, and the administration of tonic medicines are sufficient to cause a disappearance of the albumin in the urine. In the albuminuria dependent upon digestive derangements, special attention must be paid to these organs. In most of the cases some evident derangement of the liver is manifest as marked by sallowness, and an in-

crease in the amount of urea excreted, and deposits of oxalate of lime. The albuminuria is always aggravated when the bowels are constipated, or by meals consisting chiefly of animal food. The diet therefore should be light, though nutritious, and farinaceous articles with abundance of fruit and vegetables should replace meat. I have found the continued administration of nitro-muriatic acid with nux vomica very serviceable in these cases, together with the frequent use of purgative mineral waters. The patients, too, are much benefited by the daily use of tepid saline douches (85° F.). Two cases I had under my care last year, lost all traces of albuminuria after employing the above treatment for a short while. One, a gentleman from America, aged sixty-five, sent me by my colleague Mr. Couper, had noticed albumin in his urine for some months previously, and feared he was suffering from chronic renal disease. All the specimens I examined contained albumin, but those passed after meals had it in abundance. The specific gravity averaged 1025, and there was an abundant deposit of oxalates. This patient took nitro-muriatic acid and nux vomica, and went to Hombourg where he drank the waters, which acted freely, and adopted a strict regimen. In about five weeks all trace of albumin had disappeared, and had not returned when I saw him some time afterwards. The other case was that of a medical man in the West of England, he had found albumin in his urine, which was always most abundant after suffering from dyspeptic attacks, he was sallow, and the urine had a high specific gravity, 1028, contained an excess of urea, and deposited oxalates in great quantities. He was also placed on nitro-muriatic acid and nux vomica, and was ordered to take every other morning an efficient dose of some mineral purgative water. Some months after he wrote to say he had experienced the greatest benefit from

the free purgation, and that so long as he attended to the condition of his bowels, his urine never contained traces of albumin.

Peptonuria.

175. The clinical significance of the occurrence of peptones in the urine, together with the tests by which their presence is detected, has already been discussed (see pp. 108-111).

Paroxysmal Hæmoglobinuria.

176. **Symptoms.**—The prominent symptom is the paroxysmal discharge of bloody urine. The intermediate samples being usually normal, or at all events free from blood. The next point of importance is the fact that on microscopic examination, no red corpuscles, or only a few, are to be detected in the bloody urine, a circumstance which distinguishes this disorder from hæmaturia. The paroxysm is usually ushered in with a distinct chill, or even rigor, the hands, face, or any part of the body that may be exposed, often become livid and in some cases urticaria appears on exposed parts of the skin. Other symptoms are occasionally present such as headache, drowsiness, and great thirst. Colicky pains in the abdomen, sometimes accompanied with nausea and vomiting, are by no means infrequent, whilst the kidneys are somewhat tender when pressure is made over them. The patient has usually an icteric tint at the time of the attack, which, however, generally becomes more marked as the paroxysm passes off. The temperature is often elevated at the commencement of the paroxysm, and may be followed by sweating. A rise of temperature is not, however, an invariable ac-

companiment. The URINE passed during the paroxysm in well marked cases is of port wine colour, though in slight ones it may have only a reddish tinge. When examined by the spectroscope the characteristic bands of oxyhæmoglobin can be detected, and in addition a third absorption band, that of methæmoglobin can often be detected. On standing, the urine deposits an abundant dirty brown sediment. This deposit consists chiefly of urinary epithelium, the nuclei of which are often stained with blood pigment, amorphous urates, pigment matter. In some cases, brownish looking casts may be observed, which are probably hyaline casts containing hæmoglobin or hæmatin crystals, bilirubin crystals, and the pigmented débris of disintegrated blood corpuscles may be observed; rarely granular casts may be present. Crystals of uric acid and of oxalate of lime may be observed in some urines, but their presence is by no means universal. Hæmatin crystals have been observed in some few instances, probably they are formed in the urine, subsequent to emission, owing to decomposition changes in that fluid. The blood corpuscles are entirely absent in the majority of cases, though occasionally a few may be observed, but never in quantity sufficient to account for the coloration. They may be observed in one attack and absent in the next. Afanassieu (*Archiv f. Klin. Med.*, Bd. vi., 1883) has pointed out an important fact that whilst the colouring matter generally appears in the form of granules, found with the casts and sediment, sometimes no granules are deposited, but the colouring matter remains entirely in solution. The paroxysmal urine is always albuminous, and contains serum albumin as well as paraglobulin. It has been stated that the coagulated albumin instead of sinking to the bottom of the test tube floats on the surface of the urine. This peculiarity has been absent in all the cases

that have come under my observation, and others have failed to observe it as a constant phenomenon. In the majority of cases the urea is increased, and consequently the specific gravity remains high, although the amount of urine passed is generally above the average. The reaction of the urine is generally acid, rarely alkaline, when freshly passed. Such are the characters of the urine passed immediately after the chill, the succeeding samples being either quite natural, or only containing small quantities of blood which become less and less each time the urine is passed. In cases, however, in which the paroxysms are frequent, the urine has not time to clear itself between whiles, so that the passage of bloody urine seems to be continuous. A little discrimination, however, will show us that one sample is darker than others. The albumin generally entirely disappears between the paroxysms, especially if they are not frequent, though I have seen a case in which a trace of albumin was found in the urine some months after the paroxysms had ceased; it, however, finally disappeared. I have found the interparoxysmal urine to have somewhat a lower specific gravity than that passed by the same patient during the attack, whilst the urea is never in excess but may be less than normal. Often, too, the urine remains somewhat dark, not from blood, but from a tendency to deposit orange-brown amorphous urates. In one instance (*Lancet*, Nov. 17, 1883) I have observed the interparoxysmal urine to be distinctly chylous, I believe this to be the only case in which this has been noticed. In the majority of instances the general health is little affected, beyond the initial disturbance ushering in the paroxysms, the patient may feel quite well. In some cases, however, the patient feels weak and languid and becomes decidedly anæmic. This was the case with a patient I saw last November with Dr.

Humphry of Chislehurst, who for more than a fortnight had a daily febrile exacerbation lasting some hours, ranging from 100° to 102·5°F, followed by sweating. In this instance the urine was never quite free from blood colouring matter, and it was necessary to keep him in bed; in spite of the severity of the onset, he made a good recovery, and was well by January. In another case, however, an out-patient at the London Hospital, the patient was enabled to pursue his labour in the brickfield throughout the attack.

177. **Etiology.**—Of recorded cases, that I have been able to collect, the proportion of *males* to *females* is as ten to one. This disproportion, however, is less marked among children than adults, since under the age of fifteen the number of male cases to females is about four to one. The *ages* of the patients ranged from two years to fifty-four years of age; I have not been able to find a case in which the disease commenced after the fifty-fourth year. There does not appear to be any greater liability to the disease during one period more than another, in which the disease has been noticed. The cases reported by physicians attached to large general hospitals, where there is a department for diseases of children, or who are attached to a children's hospital, naturally show a preponderance between the age of two and ten years; whilst in the cases reported by physicians attached to hospitals in which there is no special department, or where the hospital is near one specially devoted to children's complaints, the adult cases are more considerable. If there is any preponderance at all, it is, as Dr. Stephen Mackenzie has stated, on the side of young adult males. Dr. Saundby (*Med. Times*, May, 1880) has recorded an instance in which the disease was hereditary. Among the chief predisposing causes *malaria* stands foremost on the list. Long before

the clinical characters of the disease were fully recognized, Prout described an intermittent form of hæmaturia dependent upon ague. In about sixty per cent. of the collected cases there was either a history of previous malarial attacks, or else the patient had been placed in circumstances in which he might have been exposed to the malarial influence, for it does not follow that there should be any declared outbreak of intermittent fever. One of my patients had never suffered from ague, but eighteen years previously he had worked in the marshes between Arundel and Portsmouth where ague is known, and in another patient the disease declared itself immediately after a sojourn in the South of France, and a recurrence took place after visiting the same district a second time. *Syphilis* is said to play an important part in the etiology of the disease, certainly in a considerable number of the recorded cases a history of syphilis has been established.

The disease occurs not infrequently in individuals liable to rheumatism. In the interesting cases recorded by Graves, in which articular rheumatism was followed by jaundice and urticaria, it is not improbable that hæmoglobinuria might have been present, the dark colour of the icteric urine masking the blood colouring matter. This of course is only conjecture, still the clinical connexion, jaundice and urticaria, suggests it, and the possibility should be kept in mind. Among the exciting causes, exposure to *cold* must be reckoned the chief, for this reason the disease is more frequently observed in winter than in summer. It is extraordinary how slight a chill will often provoke it, such as sprinkling a few drops of cold water on the exposed skin. The disease has been known to follow directly on prolonged and severe muscular effort and strain, as after long marches, lifting weights, or a long day in the hunting field. I am not aware of

any case originating from psychical causes, but these undoubtedly will induce a paroxysm when the disease is established. Among the etiological connections of this disorder, must be mentioned Raynaud's disease, which consists in a symmetrical lividity of the extremities, often proceeding to gangrene. In a well marked instance of this disease that came under my observation at the London Hospital, the hands when exposed first became somewhat red and swollen, and then shortly became icy cold and livid, the deep purplish patches on one hand corresponding very closely in extent to those on the other. In this disease occasional discharges of urine containing hæmoglobin, and but few red blood corpuscles have been noticed. The transitory albuminuria occasionally observed after cold bathing is probably an allied, if not actually a minor, manifestation of paroxysmal hæmoglobinuria; in some of these cases hæmaturia occasionally occurs as well. On the other hand, the dissolution and destruction of blood corpuscles which occur in certain diseases, such as scurvy and purpura, in septic conditions, and also after the introduction of certain poisonous substances, such as Dr. Dreschfeld's case of chlorate of potash poisoning, can hardly be considered to be even remotely allied to true hæmoglobinuria. Since in these cases the elimination of the colouring matter is continuous, and the extraordinary paroxysmal character of the disorder is entirely absent.

178. **Pathology.**—One fact is established, viz., that in this disease the blood corpuscles have undergone dissolution. The unsettled questions are the place of their dissolution, and the pathological causes at work to produce it.

Experiments have been made on the living body with the view of destroying the red blood corpuscles and giving rise to hæmoglobinuria. The substances employed were glycerine, pyrogallic acid, and toluylendiamin, and all

induced more or less marked hæmoglobinuria. Glycerine withdraws the hæmoglobin and causes its solution in the plasma, but does not give rise to jaundice. Toluylen-diamin, on the other hand, breaks up the corpuscles so that the blood becomes filled with coloured granules, which accumulate in the liver, spleen, and in the kidneys; but unlike what occurs with glycerine, *no hæmoglobin is held in solution*, and jaundice occurs. Pyrogallic acid has an action intermediate between the two, extracting hæmoglobin and causing slight jaundice. The results of these experiments closely correspond with our clinical experience, viz., that there are cases in which we have evidence of corpuscular destruction, and others in which we have none; again, cases in which jaundice is present, others in which it is absent. This would make it appear probable that two forms of the disease exist:—(1) in which an extraction of hæmoglobin takes place in the blood and the colouring matter is eliminated with the urine; (2) in which destruction of blood corpuscles takes place in the liver, spleen, and kidneys.

An examination of the blood in this disease shows in some cases that hæmoglobin is dissolved into the serum, which acquires a tint varying from a straw to a ruby-red; in others, no change has been observed, except an increase of white corpuscles. In the cases in which the serum was found tinted, alterations of the red blood corpuscles were generally noticed. Thus they are paler than natural, there is an alteration in their colour, and the tendency to rouleaux formation disappears. Some of the corpuscles are quite devoid of contour (phantom corpuscles), whilst others are so altered in shape as to become three-cornered, oval, and spindle-shaped. In addition to these changes, blood flakes may also sometimes be observed. Boas (*Deutsch. Archiv f. Klin. Med.*, 1883), who artificially

induced attacks in patients suffering from the disease, concludes that in many cases the dissolution of the red blood corpuscles takes place only in the part exposed to cold.

The post-mortem appearances of those who have suffered from the disease, or in animals in which it has been induced, generally reveal a certain degree of nephritis. The inflammation is most evident around the glomeruli. In the artificially induced disease in animals, fatty degeneration of the renal epithelium occurs, sometimes the nephritis is of such an extreme kind that there are hæmorrhages into the tubules. The liver, in the experimental cases, also showed considerable fatty changes, and in those cases where jaundice was a prominent feature the hepatic cells were laden with bile pigment, and the products of blood disintegration, there being further, an infiltration of round cells around the hepatic and sub-lobular veins. Dr. Afanassieu, from whose account much of the preceding is taken, describes the renal lesions as hæmoglobinuric glomerulo-nephritis, which may pass eventually into an interstitial nephritis, whilst the condition of the liver he considers to be caused by interstitial inflammation, induced by hæmoheptogenous jaundice. The hæmoglobin or methæmoglobin, whether in granules, or in solution, is excreted at the glomeruli, in this respect differing from the elimination of the formed products of corpuscular destruction, brought about by poisonous substances as in Dr. Dreschfeld's case (*op. cit.*), which are eliminated by the tubular epithelium.

From the foregoing facts we venture to infer that the disease exists in two forms:—(1) in which the hæmoglobin is simply dissolved out of the blood corpuscles, and that in this form of the disease, in each attack, the dissolution takes place chiefly in the parts exposed to cold; in this form, jaundice is not well marked, nor do pig-

mented casts appear in the urine; (2) a more severe form, in which the dissolution is general, and probably attended with some destruction of red corpuscles in the liver, spleen, and even in the kidneys; in these cases the icteric tint is well marked, and casts containing crystals of hæmoglobin, bile crystals, and pigmented granules of disintegrated blood corpuscles will be distinctly visible. In most, if not in all cases, the elimination of the hæmoglobin occasions a certain degree of irritation, if not actual glomerulo-nephritis, which accounts for the presence of serum albumin in the paroxysmal urine, and of which traces may occasionally be found some time after. Should the attacks be frequent, or the disease prolonged, interstitial changes may ultimately result.

With regard to the conditions that induce the attack we are still in the dark, though there are many circumstances such as the peculiar chills, and the accompanying urticaria, that suggest a neurosal origin, probably an exaggerated sensibility of the reflex nervous system. It may be as some have suggested, that peripheral stimulation causes irritability of the vaso-motor centre, and in turn this causes local asphyxia in the part stimulated, under which condition the red corpuscles part with the hæmoglobin. Thus, Murri (*Revista Clinica di Bologna*, 1880) holds the essence of the disease to be due to an increased irritability of the vaso-motor reflex centre, and the formation, owing to disorder of the blood forming organs, of corpuscles unable to withstand the influence of cold or of carbonic acid.

179. **Treatment.**—After the occurrence of a few paroxysms the disease may disappear entirely, more usually the disease recurs irregularly for a considerable number of years. Although no patient can be said to have actually died of the disease, yet undoubtedly it is a serious compli-

cation should any intercurrent affection supervene, especially if of an acute character. Pneumonia seems to be the most frequent termination of those cases which have run a protracted course, and is usually preceded and accompanied by chronic nephritis.

As cold is the chief exciting agent in the production of the disease, so avoidance of chills of all kinds is the best prophylactic measure we can employ to prevent the recurrence of the paroxysmal attacks. The patient should be clothed in flannel, wear woolen gloves and stockings, and tightly fitting drawers. He should be careful to avoid exposing himself to cold whilst dressing and undressing. It is astonishing how hypersensitive some of these patients are to the slightest change of temperature; in one of my patients the act of getting out of bed, although the room was well warmed with a fire, and the weather was not cold, brought on a paroxysm. Dr. Barlow has suggested that this over sensitiveness may be overcome by gradually habituating the patient to cold, and mentions the case of a child who was much benefitted by being washed in cold instead of hot water. I would not, however, recommend this practice in all cases, especially in those in which the urine remains albuminous between the paroxysms, for fear of increasing the renal hyperæmia. It may be successfully tried, however, when the disease remits, and the patient for a time regains his usual health, so that the cutaneous nerves may be rendered less sensitive to cold, should the tendency recur. The best plan is to commence with a douche so regulated that at first hot water is poured over the patient, which gradually becomes colder, till a temperature of about 40° F. is reached. I have found warm (95° F.) sea bathing, or sea salt, distinctly beneficial in two cases under my care, the salt seemed to stimulate the skin and gradually render it less sensitive.

As regards general treatment the universal consensus of opinion is in favour of quinine; even in those cases in which there is no evidence of malaria it is of decided value. For in cases in which it fails to control the paroxysms or cut short the disease, it will generally improve the patient's condition. Next to quinine in my opinion, comes arsenic. Under its administration the blood corpuscles, if previously affected, acquire a better colour, and appear less translucent. Although it has not the same power that quinine often has in controlling the paroxysms, yet I think it makes the cure more complete. The patient, whose case I recorded in the *Lancet*, Nov. 1883, had previously suffered during the spring months of four successive years from hæmoglobinuria; when I saw him in March 1883, I put him on arsenic, three drops three times a day, and a daily four-grain dose of quinine. This had no apparent effect till about the middle of April, when the weather became warmer, when he made what may be considered a sudden recovery. I kept on the arsenic for some time longer. He missed his usual attack in the ensuing spring of 1884, he also stated that none of the preceding attacks had yielded so quickly, and that he had never before got rid of his complaint till the middle of summer. My practice is therefore to give one good dose of quinine, four to five grains once daily, and a mixture containing three or four drops of liquor arsenicalis, and ten grains of ammonium chloride of iron, thrice daily after meals. If there is any history of syphilis, I add to this mixture ten grains of iodide of potassium. The diet should be light and easy of digestion. In a case that has now been frequently under my observation, the patient finds that when he attends particularly to this point his urine remains clear for long periods together, whilst an attack of indigestion from imprudence will at once tinge

his urine with blood. The diet, which should be chiefly farinaceous, should be similar to that given at p. 263. Should the disease be accompanied by marked manifestations of pyrexia, the patient must be kept in bed, otherwise he may go about as usual, keeping quiet, however, for some hours during and after the occurrence of a paroxysm.

APPENDIX I.

Quantitative Analysis.

1. **Urea.** (*Liebig's method*).—When a solution of mercuric nitrate is added to a solution of urea an insoluble compound of urea and mercury is formed. If we continue to add the mercuric solution, as long as the precipitate is formed, a point is reached, when, on addition of sodium carbonate, a yellow colour is produced by the appearance of hydrated oxide of mercury. This indicates that all the urea has been precipitated by the mercuric solution.

Solutions required.—1. Mercuric nitrate solution, one cubic centimetre of which is equivalent to 0·01 grm. of urea.

2. Baryta solution, consisting of two vols. of baric hydrate, and one vol. baric nitrate, to precipitate phosphates and sulphates.

3. Sodic carbonate solution, placed on a white filter paper to indicate completion of the process.

Process.—Take 30 c.c. of urine, and add to it 30 c.c. of the baryta solution. Mix thoroughly and filter. Now carefully measure off by means of a pipette, 20 c.c. of the filtrate; this of course contains 10 c.c. of urine. Place this in a glass beaker, and then from a Mohr's burette, add at first 5 c.c. of the mercuric nitrate solution, stirring the mixture, and placing a drop on the sodic carbonate test-paper. If no reaction occurs, then add a cubic centimetre at a time from the burette, till a yellow stain appears. The number of cubic centimetres employed gives the amount of urea in 10 c.c. of urine. Then if we know the amount of the twenty-four hours' urine, the diurnal excretion of urea can readily be made; thus, the patient has passed 2110 c.c. of urine, and 12 c.c. of standard mercuric solution were used, then $\frac{2110 \times (\cdot 01 \times 12)}{10 \text{ c.c.}} = 25 \cdot 32$ grms. of urea.

Correction.—But as the urine contains sodium chloride, and as this is likewise precipitated by mercuric nitrate, we must make a correction for this. This is done, either by determining the amount of sodium chloride separately as by process 5, and making the correction directly

from this; or by adding a concentrated solution of silver nitrate to the urine, from which the phosphates and sulphates have been precipitated, till no further precipitation of silver chloride takes place; then filter and proceed to add the mercuric solution. In ordinary cases, however, (excepting pneumonia and rheumatic fever) it is sufficient to deduct 1·5 to 2 c.c. from the total c.c. of mercuric nitrate employed for the precipitation of the insoluble compound of urea and mercury.

2. **Hippuric Acid.**—The process consists of separating the uric acid from the hippuric acid, and crystallising out the latter from its solution, and collecting and weighing the deposited crystals.

Process.—Evaporate 1000 c.c. of urine to dryness. Triturate with baric sulphate, add 60 c.c. of hydrochloric acid, and then exhaust with alcohol. Neutralize the acid alcoholic extract with soda-ley. Evaporate to a syrupy consistence, adding a small quantity of oxalic acid. Then dry in a water bath. Exhaust dry mass with ether containing twenty per cent. of alcohol. Evaporate the ethereal alcoholic solution, and treat the crystalline residue with warm milk of lime. Filter. Evaporate filtrate to small volume, add hydrochloric acid. The hippuric acid now crystallises out, the crystals are collected on a weighed filter, washed, dried, and weighed; the weight gives the amount of hippuric acid in amount of urine examined.

3. **Phosphoric Acid.**—An acid solution of uranic nitrate added to a solution of phosphoric acid is decomposed, and a precipitate of uranic phosphate is thrown down. Uranic nitrate gives a reddish stain when dropped on ferrocyanide of potassium test-paper, but uranic phosphate does not give a coloration. As long, therefore, as the uranic phosphate is precipitated on the addition of uranic nitrate no brown stain will be given to a ferrocyanide of potassium test-paper, but as soon as a precipitate ceases to be formed the coloration is given, because then free uranic nitrate appears in the mixture. It is on this fact that the process for estimating phosphoric acid by means of uranic nitrate is based.

Solutions required.—1. Uranic nitrate solution, one cubic centimetre of which is equivalent to ·005 grm. of phosphoric acid.

2. Sodic acetate solution to ensure precipitation of uranic phosphate.

3. Potassic ferrocyanide solution to moisten indicating test-paper.

Process.—Take 50 c.c. of urine, add to them 5 c.c. of acetate solution, and warm the mixture. Then from a burette add a cubic centimetre at a time of uranic nitrate solution, each time stirring with glass rod, and placing a drop on the test-paper moistened with ferrocyanide solution. Continue till with the last addition a brownish stain developes on the paper. The number of c.c. from the burette used to effect this, represent the amount of phosphoric acid in 50 c.c. of urine. Then if we know the amount of urine passed in twenty-four hours, we can readily calculate the diurnal elimination; thus, the patient has passed 1450 c.c. of urine, and the amount of uranic solution employed is 16 c.c. then $\frac{1450\times(16\times\cdot005)}{50} = 2\cdot32$ grms. of phosphoric acid.

Separate determination of phosphoric acid combined with alkaline and earthy bases respectively. The foregoing process gives us the total phosphoric acid in urine, but does not tell us in what proportion it is combined with the different bases. To ascertain this, we take 50 c.c. of urine, and render it strongly alkaline with ammonia. Set aside the mixture for twelve hours. Collect the precipitated phosphate upon a filter, and wash with liquor ammoniæ. Then dissolve the precipitate with a little dilute acetic acid. Place the acid solution in a small beaker, add 5 c.c. of sodic acetate solution, add distilled water up to 50 c.c., and then proceed to add the uranic nitrate as before. Now in the 1450 c.c., instead of using 16 c.c. of the standard, we shall find that less has been used, say 6 c.c.; then, $\frac{1450\times(6\times\cdot005)}{50} = 0\cdot87$ grm. of phosphoric acid combined with lime and magnesia. And as we found the *total* phosphoric acid by the previous estimation was 2·32 grms., and as we have now found the phosphoric acid in combination with the *earthy* bases to be 0·87 grm.; then the difference between these two represents the amount of phosphoric acid in combination with the *alkaline* bases, viz. 1·45 grm.

4. **Sulphuric Acid** is estimated by adding a solution of baric chloride to an acid solution of urine, till a precipitate is no longer formed.

Solution required.—Baric chloride solution, one cubic centimetre of which is equivalent to 0·01 grm. of sulphuric acid.

Process.—Add to 25 c.c. of urine five drops of HCl, and warm the solution. Now add from a burette the standard solution, one c.c. at a time,

till a precipitate is no longer formed. The number of c.c. used to effect this, represents the amount of sulphuric acid in 25 c.c. of urine. Now if the patient passes 1450 c.c. of urine, and 5 c.c. of baric chloride has been used; then $\frac{1450 \times (\cdot 01 \times 5)}{25} = 2 \cdot 9$ grms. of sulphuric acid eliminated in twenty-four hours.

5. **Hydrochloric Acid.**—When nitrate of silver is dropped into a neutral solution of sodium chloride and neutral potassium chromate, the chlorine is thrown down in the form of chloride of silver. When the whole of the chlorine is thrown down, then it is converted into chromate of silver which gives the mixture a permanent red colour. When this occurs the process is complete.

Solutions required.—1. Nitrate of silver solution, 1 c.c. = ·01 grm. of sodium chloride, or ·006 grm. of hydrochloric acid.

2. Yellow potassium chromate solution, saturated.

Process.—Collect the urine for twenty-four hours, carefully measure, remove albumin if present. Filter a portion of this urine and measure off, by means of a pipette, 10 c.c. into a small beaker, and add a few drops of sodium carbonate solution, to render it neutral, and dilute with distilled water up to 100 c.c. A few drops of potassium chromate solution are now added and a few c.c. of the standard solution of silver nitrate run into the mixture from a Mohr's burette; agitate. Continue to add a c.c. or so of the standard solution till a red colour appears when the mixture is agitated (red silver chromate). Now since 1 c.c. of the silver nitrate solution is equal to ·006 grm. of hydrochloric acid, therefore if 6 c.c. of silver nitrate be used, the 10 c.c. of urine will contain ·036 grm. of hydrochloric acid, and if 1500 c.c. of urine be passed in the twenty-four hours, then $\frac{\cdot 036 \times 1500}{10} = 5 \cdot 4$ grms. of hydrochloric acid.

As the colouring matter of the urine, if in excess, interferes with the reaction, in these cases it is necessary to evaporate the urine and incinerate the ash, dissolve this in water, and then proceed as above.

6. **Albumin.**—The albumin is coagulated by means of heat, collected, dried and weighed.

Process.—Take 100 cubic centimetres of urine, place it in a glass beaker, and add two or three drops of strong acetic acid, to render it slightly acid, and add distilled water to bring the measure up to 200 c.c. Place the

beaker in a water-bath, 100° C., for about half an hour, frequently stirring to prevent clotting, then set aside to subside. When the coagula have fallen to the bottom of the vessel decant the supernatant fluid into another vessel, and place the coagulated material on a filter previously dried and weighed, carefully removing any portion that may adhere to the glass with a feather to the filter. Set aside to drain, add from time to time any portion of coagula that may be deposited from the supernatant fluid that was decanted. When every visible fragment of coagula has been transferred to the filter, place it in the hot-air bath and cautiously dry. When it has been in the air-bath some hours withdraw, cool, and weigh, and repeat this process till it ceases to lose weight. When it does, deduct the original weight of the filter from the amount, and the difference will give the weight of albumin in 100 cubic centimetres of urine. Thus, the weight of the filter, previously ascertained, is 0·175 grm., and the weight of the filter with the albumin after drying is 0·598 grm.; then ·598—·175 = ·423 grm., the weight of albumin in 100 c.c. of urine; and if the patient pass 1100 c.c. of urine in twenty-four hours, then the amount of albumin discharged from the system in the day will be $\frac{1100 \times \cdot 423}{100} = 4 \cdot 653$ grms.

7. **Sugar.**—Solutions of glucose possess the property of reducing cupric salts to cuprous oxide, in the presence of alkalies, p. 119. It is upon this property that the quantitative estimation of sugar is based.

Solutions required.—1. Cupric sulphate solution, (34·63 grms. of cupric sulphate and distilled water up to one litre), one cubic centimetre of which is equivalent to ·005 of glucose.

2. Alkaline tartrate solution, (potassic hydrate 80 grms., sodio potassic tartrate 173 grms., and distilled water up to one litre).

Process.—Measure off 10 c.c. of the collected urine of twenty-four hours, remove albumin if present, and dilute it with distilled water up to 200 c.c. Charge a burette with this diluted urine.

Into a porcelain basin, or a glass flask suspended to the burette, containing 50 c.c. of distilled water, measure off 10 c.c. of standard copper solution, and 10 c.c. of alkaline tartrate solution, and gradually bring the mixture to the boiling point.

When the alkaline copper solution has reached the boiling point, a few drops of the dilute urine are run into it from the burette; at first the addition only makes the copper solution turbid with a greenish-red precipitate, which subsequently on the further addition of urine, acquires a deeper red, and settles readily at the bottom of the porcelain vessel.

After each addition of urine, the precipitate should be allowed to settle and the vessel slightly tilted so as to observe the colour of the supernatant fluid; when this becomes perfectly colourless, the process is complete and the estimation can be made as follows:—

Suppose that 30 cubic centimetres of dilute urine have been employed, and as the urine was in the first instance diluted to $\frac{1}{20}$ of its volume, these 30 c.c. are equivalent to 1·5 c.c. of the diabetic urine. And as 1 c.c. of the cupric solution = ·005 grm. of sugar, and 10 c.c. of the solution was used, it is clear that 1·5 c.c. of diabetic urine contains ·05 grm. of sugar. Then if the patient passed 4110 c.c. of urine in the twenty-four hours, $\frac{4110 \times \cdot 05}{1 \cdot 5} = 137$ grms. of sugar, or the same result is more readily obtained by dividing the twenty-four hours urine by the number of centimeters of dilute urine used from the burette thus $\frac{4110}{30} = 137$ grms.

APPENDIX II.

Diet for Diabetic Cases.

The Dietetic Treatment in diabetes consists: 1. In cutting off every article of diet which contains starch or sugar in any form; 2. In replacing such articles with some kind of substitute, and also in rendering the food that can be taken as palatable, nutritious, and varied as possible.

To fulfil the first indication, the medical attendant should draw up and give the patient a list of those articles of diet he is to avoid, and those articles of which he may partake, thus :—

To avoid.—Milk (except very small quantities for cooking purposes). The liver of all animals (as the liver of oysters and all mollusca is large, and abounds in glycogen, these animals must be forbidden) so also the interior of crabs, lobsters, etc. Bread, biscuits, rusks, toast, farinaceous vegetables, such as potatoes, Jerusalem artichokes, rice, oatmeal, corn-flour, sago, tapioca, arrowroot, etc. Saccharine vegetables, turnips, carrots, parsnips, green peas, French beans, beet-root, asparagus, tomatoes. Blanched vegetables of every sort as celery, sea-kale, endive, radishes, also the stalks and white parts of such vegetables as cabbage, lettuce, broccoli, etc. Fruits of all kinds. Jams, syrups, sugars. Certain condiments, such as Chutnee and sweet pickles. Cocoa, chocolate. Liquors, sweet wines.

May take.—Meat, fish, poultry, game, butter, bacon, ham, eggs. Bread and biscuits, made with prepared gluten bran, or almond flour. Green vegetables, summer cabbage, turnip tops, spinach, broccoli tops, watercresses, mustard and cress, laver, sauer kraut, the green parts of lettuce, sorrel, mushrooms. Nuts of various kinds (except chesnuts). Cheese.

The second indication is best fulfilled by varying the dietary as much as possible, so as to prevent monotony, and by the greatest attention being paid to the preparation and selection of the food, so that it may be both palatable

and nutritious, the following hints from a diabetic patient may prove serviceable.

An egg beaten up in tea or coffee is not a bad substitute for milk. The most palatable form of prepared bread is the gluten roll (Bonthron). This cut in slices well buttered, goes very well with potted meats, anchovy paste, caviare, grated Hambro' beef. A savoury omelette (four eggs to one table-spoonful of milk) is often an agreeable change when the patient tires of "phantom crusts." A list of breakfast dishes should be drawn up, these should be as varied as possible, thus fish one day, kidneys another, eggs and bacon, grilled chicken, and so on. Sausages, since they usually contain a considerable quantity of bread should not be allowed. For lunch, a chop, steak or cutlets, with watercress or salad; if, however, the patient has eaten solid meat for breakfast, fish had better be served for lunch. At dinner, either a good clear meat soup, made without vegetables, but flavoured with herbs; or fish. The following receipt for melted butter made without flour, may be found useful. "Rub up the yolk of a hard boiled egg with olive oil till a rich paste is formed, add two ounces of butter, and heat, gently stirring; add anchovy sauce, capers, fennel, chopped parsley or sorrel, lemon juice, etc., as may be required." A green salad should always be served with the meat, it should be mixed with plain oil and vinegar, and warn the cook against adding sugar. As the number of green vegetables are limited they should be quite fresh, carefully cooked, and well served, otherwise the patient becomes disgusted with them, which is always a misfortune, since owing to the amount of animal food eaten, plenty of green stuff is required to keep the body healthy. It is astonishing in what a different number of ways a simple cabbage may be cooked, so as to make almost a daily variety. If the patient can be educated up to sauer kraut, he will find it very beneficient to his health. Watercresses should be served at every meal. Meat twice cooked should never be served. Since sweets may not be partaken of, savouries should follow the meat. Savoury omelettes, caviare, anchovies, cheese fondûs; sometimes the omelettes may be flavoured with grated cocoanut, glycerole of orange peel, essence of vanille, almonds, etc., or a mixture of sherry, glycerine and lemon juice.

The diabetic patient should be cautioned against too great indulgence of his appetite, he should just satisfy his hunger and no more. A French physician observed that during the siege of Paris many diabetic patients improved, when they could not obtain the usual amount of animal food they were accustomed to consume. "I have found the urine less saccharine, and myself in better health on a moderate diet, than when I have fully indulged my appetite. After a little restraint the craving for extra meat soon ceases."

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