Kidney diseases / by W.P. Herringham ; with chapters on renal diseases in pregnancy by Herbert Williamson.

KIDNEY DISEASES

W. P. HERRINGHAM

OXFORD MEDICAL PUBLICATIONS

Dr. Geoffrey Evans,
7, Mansfield Street,
Portland Place,
W.1.
Tel. Langham 1717.

OXFORD MEDICAL PUBLICATIONS

KIDNEY DISEASES

OXFORD : HORACE HART
PRINTER TO THE UNIVERSITY

OXFORD MEDICAL PUBLICATIONS

KIDNEY DISEASES

BY

W. P. HERRINGHAM, M.D., F.R.C.P.

PHYSICIAN TO ST. BARTHOLOMEW'S HOSPITAL, ETC., ETC.

WITH CHAPTERS ON RENAL DISEASES IN PREGNANCY

BY

HERBERT WILLIAMSON, M.D., F.R.C.P.

ASSISTANT-PHYSICIAN-ACCOUCHEUR TO ST. BARTHOLOMEW'S HOSPITAL, ETC., ETC.

LONDON

HENRY FROWDE
OXFORD UNIVERSITY PRESS

HODDER & STOUGHTON
WARWICK SQUARE, E.C.

1912

COLLEGIS MEIS

QVIBVSCVM

PRO MEDICINAE SCIENTIA

PRO SCHOLAE STI BARTHOLOMAEI HONORE

MAXIMA CVM AMICITIA

TAMDIV LABORAVI

HVNC LIBRVM DEDICO

PREFACE

I SUPPOSE that the uppermost feeling in the mind of a man who puts his work into shape is that he has produced after all a tissue made chiefly of holes, and that everywhere he has left observations incomplete, and hypotheses unverified. That I think must always be. Man is the most difficult object in the world to investigate, and conclusions must often be left doubtful. Yet experimental pathology is not more reliable, though here the uncertainty lies less in the observation than in its application. Medicine must work by both methods, and clinical experience will always be needed.

This book is the outcome of many years of work, and is drawn chiefly from my own hospital and my own wards. Of course, however, I am greatly in debt to the writings of others, especially in those rarer diseases which do not occur frequently in the practice of any one man. These obligations I hope I have acknowledged in the text.

But the largest debt of all I owe to my colleague Williamson. I have always been interested in the

connexion between renal disease and pregnancy, and years ago formed the intention that if ever I wrote a book this matter should be treated at length. I have been fortunate in inducing him to undertake this task, and every one, I think, will allow that his chapters contribute a very large share to the interest of our production.

W. P. HERRINGHAM.

TABLE OF CONTENTS

CHAPTER VII

ABNORMAL CONSTITUENTS OF URINE (*Continued*) PAGES

CHAPTER VIII

METHODS OF EXAMINATION OF THE RENAL FUNCTION

CHAPTER IX

HÆMATURIA, FAMILY HÆMATURIA, AND ESSENTIAL HÆMATURIA

CHAPTER X

HÆMOGLOBINURIA AND PAROXYSMAL HÆMOGLOBINURIA

CHAPTER XI

DROPSY. ESSENTIAL DROPSY, AND URÆMIA

CHAPTER XII

NEPHRITIS

CHAPTER XIII

ACUTE NEPHRITIS

CHAPTER XIV

SUBACUTE AND CHRONIC DIFFUSE NEPHRITIS

CHAPTER XV

SUBACUTE AND CHRONIC DIFFUSE NEPHRITIS (*Continued*)

CHAPTER XVI

THE TREATMENT OF DIFFUSE NEPHRITIS

CHAPTER XVII

CHRONIC INTERSTITIAL NEPHRITIS

CHAPTER XVIII

CARDIO-VASCULAR CHANGES

CHAPTER XIX

POLYCYSTIC DISEASE OF THE KIDNEY

CHAPTER XX

RENAL DISEASE IN PREGNANCY DEPENDENT UPON TOXÆMIA

CHAPTER XXI

PREGNANCY AND CHRONIC NEPHRITIS

CHAPTER XXII

HÆMATURIA IN PREGNANCY

CHAPTER XXIII

PYELITIS AND PYELONEPHRITIS—I. IN PREGNANCY

CHAPTER XXIV

CHAPTER XXV

CHAPTER XXVI

CHAPTER XXVII

CHAPTER XXVIII

CHAPTER XXIX

LIST OF ILLUSTRATIONS

KIDNEY DISEASES

CHAPTER I

ANATOMY, NORMAL AND ABNORMAL, AND MOVABLE KIDNEY

1. Anatomy.

The kidneys lie obliquely in the abdomen opposite the last dorsal and the upper two lumbar vertebræ and are about 4 inches long and 2 inches wide. The upper ends are about 3 inches, and the lower 5 inches apart. The line drawn across their upper margins is about 5 inches above the umbilicus. The lower end of the right kidney is ½ inch, and that of the left 1 inch above it. In the supine position they hang like saddle bags across the spine, having the psoas on their inner side, and the quadratus lumborum behind them, though separated from them by the deep fascia. What is usually called the anterior surface looks outwards as well as forwards. On the right side it is covered for more than its upper half by the hollow on the liver called the impressio renalis. Below this the duodenum covers its inner, and the ascending colon its outer margin.

On the left side the spleen lies outside the upper part of the kidney, the stomach in front of it. The tail of the pancreas runs over its lower part and separates it from the upper end of the transverse colon as this piece of gut runs upward and backward to the costo-colic ligament which attaches it to the end of the eleventh rib. As the gut turns down from this point it lies along the outer margin of the kidney.

On each side the supra-renal capsule is fitted against the rounded inner margin of the upper end of the kidney.

The organs are imbedded in loose fibrous tissue and fat. In youth and health this shells off easily. But in cases of

chronic nephritis with much fibrosis it is closely connected with the proper capsule of the kidney, and becomes itself very hard and fibrous. It is in this tissue that a peri-renal abscess forms.[a]

If these measurements are plotted out on the surface of the body it will be found that in an ordinary person the long diameter of the kidney lies just behind the oblique line of the margin of the thorax, where it is formed by the seventh and eighth costal cartilages.

In the majority of healthy persons neither kidney is palpable.

The renal vessels come off nearly at right angles from the aorta and vena cava. They are large vessels. The vein lies in front of the artery. The left vein, which of course is the longer, receives the left spermatic vein.

The lymphatics go from the hilum into the lumbar glands.

The sympathetic nerves controlling the blood-supply come from the lower seven dorsal, and the first lumbar roots. The last two dorsal and the first lumbar are the chief source.

Like other viscera, the kidney does not in health give rise to definite sensations. It is painful enough when diseased, and these sensations are carried by the myelinated fibres which are found in the sympathetic nerves. But the exact course of these sensory nerves is not known.

2. Abnormalities.

It is not very uncommon to find one kidney either entirely absent or represented by a mere fragment of connective tissue. We have had six such cases in about 4,800 autopsies at St. Bartholomew's Hospital. (1) A man of 36 died of uræmia. His left kidney was hydro-nephrotic and the ureter rather dilated, but no obstruction existed. Two large renal arteries existed on this side. On the right side the adrenal was in its usual position but there was no kidney or ureter or renal artery. (2) A man of 60 died of pontine hæmorrhage

[a] In a Monograph by H. W. Wilson and Hinds Howell (*Movable Kidney*, London, 1908) will be found a careful description of the fascia and peritoneal folds in relation with the kidney.

and great arterial sclerosis. On the right side there was neither ureter nor kidney. The left kidney was not apparently diseased and weighed 11 ounces. There were two left renal arteries. Microscopically there was marked fibrosis spreading from the arteries. (3) A man died of phthisis at 34 in whom the right kidney was absent. The ureter began on the side of the third lumbar vertebra, and ended in the vesicula seminalis of that side. The left kidney weighed 11 ounces and was natural. (4) In a girl of 11 the upper half of the left ureter was extremely small, and the kidney represented by a mere piece of connective tissue as big as a finger-nail. The right kidney was hypertrophied. She died of mitral stenosis. (5) A man of 28 died of dilatation of a hypertrophied heart. The right kidney was rudimentary, the left was the subject of chronic nephritis. (6) A similar case in a man who died at 50 of phthisis.

We have in the museum a specimen from a man aged 21 in whom not only the left kidney and ureter, but also the left vesicula seminalis, is entirely absent. The left suprarenal was natural and the opposite kidney was greatly hypertrophied.

A single horseshoe kidney is sometimes found. It is placed over the lumbar vertebræ or over the sacral promontory. Sometimes it is drained by two ureters (Fig. 25, p. 324).

Additional ureters, and additional renal arteries are not uncommon. The latter sometimes compress the ureter and lead to hydro-nephrosis.

Misshapen and misplaced kidneys are occasionally found. A man died at 25 of pneumonia. The case was remarkable clinically, in that the lung was so enlarged that it displaced the heart like a pleural effusion (*Proc. Roy. Soc. of Med.*, vol. iii, Clin. Section, p. 25). The right kidney was rudimentary, the ureter impermeable to a probe. The adrenal was absent. The left kidney (12½ oz.) was not on the left side, but was packed away above the rudimentary kidney in the right loin, with its own adrenal in natural relation

to it. Its ureter began in the front of the hilum and passed diagonally across the lumbar vertebræ to the left brim of the pelvis. It opened naturally on the left side of the bladder. There was also an abnormal sulcus in the brain owing to an accessory tentorium cerebelli on the right side.

3. Movable Kidney.

In a certain number of persons the right kidney is palpable on deep inspiration. During this action the liver tilts on a transverse axis, and presses the organ down. In a few the left kidney can be thus felt. This is not to be reckoned as morbid. In others the right kidney has altered its position. It may have rotated on either its vertical or its horizontal axis, or it may have become quite loose from its ordinary attachments and be found in the iliac fossa, in the hypogastrium, or even on the other side of the abdomen. This is much less frequently the case on the left side. The proportion found by Wilson and Hinds Howell was 74 on the right side to 16 on the left.

This condition is much commoner in women than in men. In the latter it is almost always the result of an injury, in the former it is generally spontaneous, and often unnoticed.

Statistics are deceptive, partly because authors hold different views of what is abnormal, and also because numbers based on post-mortem examination show much fewer cases than clinical records. In dead bodies the condition escapes notice. But excluding merely palpable kidneys and confining the term to those which have really altered their position, Wilson and Hinds Howell estimate the number as not more than 5 per cent. of female hospital patients. This is about the same number as Sir Henry Morris (7 per cent.) or Skorcewsky gives (less than 10 per cent.), but considerably less than Glénard (22 per cent.) or Kuttner and Lindner (20 per cent.). In men it is much rarer.

Various causes have been suggested to account for this preference. The first is pregnancy. It has been thought, on the one hand, that the contraction of the abdominal muscles may force the kidney out of place and, on the

other, that the diminution of abdominal pressure produced by the expulsion of the fœtus, removes the natural support of the viscera. Wilson and Howell, however, found no excess among women who had borne children. Of 76 cases, 39 occurred in multiparæ, 37 in nulliparæ. They also point out that the removal of large tumours, as in ovariotomy, has no such effect.

Another alleged cause is emaciation. The patient is not infrequently thin, and the pad of perinephric fat which lies below the kidney may very possibly give some support. But the condition also occurs in fat women.

Wilson and Howell lay special stress upon three factors. The first is that the renal fossæ in women are much shallower than in the male. The second is the greater frequency of chronic constipation in women. This acts by dragging on the hepatic flexure of the colon which is attached to the lower end of the right kidney. The third is tight-lacing.

Occasional causes are enlargement of the kidney itself by tumour, Glénard's disease, which again is most common in women, and injury, which is most common in men. A mesonephron has been found in some cases,[1] but it is doubtful whether this is not the result of the displacement.

The signs of a movable kidney are generally easy to discover, and only difficult of interpretation when the organ is in a very unusual position. The physician, standing on that side of the patient which he is intending to examine, must place his left hand under the patient's right loin, or his right under the left loin, and tell the patient to rest her whole weight upon it. When she is lying easily, the legs should be drawn up to more completely relax the abdominal walls. Then the opposite hand should be gently laid flat upon the front of the same part, and pressure made gradually so as to avoid muscular contraction. In ordinary cases a hard rounded tumour of a size that corresponds either to one end of the kidney or to its convex border will be felt near the front of the abdomen. At the same time a hollow or loss of solidity will be felt by the hand at

the back. Deep inspiration will cause the tumour to move. With the front hand steady, the thumb of the other can be brought to the front above the tumour, and squeezed in between it and the ribs or the lower border of the liver. The tumour can be pressed back by the front hand or forward by the back hand against the other. Pressure with the front hand will make it slip back into the loin, and the back hand will feel that the loin is now full and resistent. In many cases the patient can by straining force the tumour out again into the original place. This is not always so. I remember seeing a woman after she had come a journey by rail. The kidney was then well in the iliac fossa. I admitted her to the hospital, but I never, while she was lying in bed, could feel any displacement, nor could she produce it.

Sometimes the tumour is found at some distance from the proper position of the kidney, and may, as in the above case, lie in the iliac fossa. It may be quite loose in the front of the abdomen so that the hand can grasp it. In that case the whole shape including the hilum can be appreciated. The kidney has been found actually in the pelvis, or even, as above mentioned, on the opposite side.

I have on one occasion mistaken a retroperitoneal cyst for a movable kidney. The patient, a woman of 28, had during a fortnight had several attacks of sudden pain in the right hypochondrium, accompanied by vomiting, with persistent tenderness. When admitted, a tumour about the size of the kidney was felt on the left side but, though the right hypochondrium was tender and resistent, nothing abnormal could be found there. The tumour could be pushed up under the ribs, and was freely movable with respiration. There was a little pus in the urine. Though the contrast between the signs and the symptoms, the tumour being on the left side and the pain on the right, was puzzling, the diagnosis was that of movable kidney. Mr. Lockwood operated and found both kidneys in their natural position. The tumour was a thin-walled cyst lying behind the peritoneum and attached by a long pedicle. It

contained about 7 ounces of an albuminous fluid, which was surrounded by a fibrous capsule without any epithelial lining.

The symptoms vary greatly. There may be none at all, and the condition may only be discovered accidentally either by the patient or by the doctor. But commonly it gives rise to symptoms, which can be referred partly to the kidney itself, and partly to its effect upon other abdominal organs.

There is a feeling of weight or of dragging in the left loin. This is increased by the erect posture and especially by any active exertion. Sometimes patients know when the kidney slips out of its place. The discomfort may be increased to the pitch of pain. The kidney may be tender, and micturition may be more frequent than natural. Many cases go no further than this. But in others there appear attacks, first described by Dietl in 1869, of extreme pain and of violent associated symptoms. They resemble the gastric crises of tabes and attacks of biliary or renal colic, and as they are often accompanied by hæmaturia they are difficult to distinguish from the latter. Vomiting may be intense and prostration great. Sometimes there is suppression of urine. Such symptoms have even led to the diagnosis of perforative peritonitis.

It is probable that these attacks are due to some twisting of the pedicle formed by the renal vessels and the ureters. Such a condition has been observed at operation by Newman.[2]

The symptoms of an acute attack include violent vomiting. But it may also happen that severe gastric symptoms, either paroxysmal or continuous may be present apart from acute renal pain.

Bramwell's patient[3] was a lady of 49, who had been subject to attacks of acute indigestion with vomiting for twenty-nine years. In November 1899, she had an attack in which he found intermittent dilatation of the stomach and some induration about the pylorus. Operation was refused. She died in February by syncope from acute distension of the stomach with gas. At the autopsy the stomach was enormously dilated and its walls thinned.

The pylorus was surrounded by thickened and matted peritoneum, and was itself thickened and contracted by hypertrophy of the muscular coat without any trace of malignant disease there or elsewhere. Extending from it to the right kidney were three distinct cords of thickened peritoneum. When the kidney, which was very movable, was depressed these cords moved with it and dragged upon the pylorus. In Kendal Franks's case[4] similar bands ran to the duodenum, and on moving the kidney so dragged upon the gut that nothing could pass. The stomach was dilated. This patient had symptoms like those of the former, and was cured by nephrorrhaphy.

This clinical picture is not uncommon, but the physical conditions underlying it are seldom verified.

Occasionally attacks of jaundice occur which have been ascribed to similar pressure exerted upon the bile-duct.

The diagnosis between cancer of the pylorus and movable kidney is not always easy. They are both very movable, and when a patient has a history of severe gastric symptoms and a hard movable mass is discovered to the right of the middle line the idea of pyloric cancer is the first that occurs. I remember seeing such a case myself in a lady of about 30 years. Her symptoms were entirely gastric, and a hard tumour appeared in the pyloric region. Careful examination was, however, quite conclusive. It was the pole of the right kidney.

Girard has described a case in which the kidney obstructed the vena cava.

Cases in which attacks of dyspnœa were apparently due to displacement of the kidney have been described by Newman.

When the kidney moves downward the relations of the ureter are altered. It may come to lie at an acute angle with the kidney, or a fold of mucous membrane may be formed at its junction with the pelvis. Or it may be bent at the spot where it passes through the peri-renal fascia. Or if the kidney, as sometimes happens, makes a fold in the peritoneum, the edge of this may produce a similar effect.

In all these cases hydro-nephrosis is likely to follow. Such cases form the subject of an article by Terrier and Baudouin,[5] and are described by Newman. It must, however, be remembered that hydro-nephrosis may be the cause rather than the effect of displacement of the kidney.

It may further happen that such a kidney becomes infected with *B. Coli* and that a pyo-nephrosis results, or that as in some of Bruce Clarke's cases a secondary deposit of phosphatic gravel takes place.

For many patients a support to the kidney is sufficient. It is essential that the pressure should be upward, and therefore the belt should be fitted round the lower half of the abdomen. A pad can be fixed inside the belt just below the proper position of the kidney. The belts require very careful making, and must be put on while the patient is lying down, and the kidney in its right place. I have found these effectual in many cases. Another form which I have not used, but is highly recommended, is Ernst's truss. One of my patients found corsets made with steel springs better than either.

Where supports are not effectual, and in most cases where there are severe attacks of pain, the operation of nephrorrhaphy or nephropexy should be performed. It is usually successful if the kidney is healthy at the time. If the pelvis is dilated or the secreting substance largely destroyed, Bruce Clarke is of opinion that, provided the other kidney is known to be healthy, the wiser course is to remove the diseased one.

References.

1. Bruce Clarke, *Brit. Med. Journ.*, 1895, i. 575.
2. Newman, *Movable Kidney*, 1907, pp. 29–32.
3. Bramwell, *Brit. Med. Journ.*, 1901, ii. 1135.
4. Kendal Franks, ibid., 1895, ii. 895.
5. Terrier and Baudouin, *Rev. de Chirurgie*, 1891, xi. 719.

CHAPTER II

PHYSIOLOGY AND PHARMACOLOGY, DIABETES INSIPIDUS, AND ENURESIS

1. Physiology and Pharmacology.

I SUPPOSE no organ has been more closely examined in the last fifty or sixty years than the kidney. Yet even now we cannot say with certainty how far it is a simple pressure filter, how far it actively selects the substances it excretes, and how far it works by the laws of osmosis.

If it can be said that the laws of pressure can be applied to any living gland, the close connexion between the blood-flow through the kidney, and the amount of urinary water offers a good example. Yet the disease called diabetes insipidus shows that the excretion of water may increase enormously without any proportionate increase that we can appreciate, either of the rapidity of the general blood-flow or of the general blood-pressure. The laws of osmosis again seem to apply rather to the interchange between the blood and the tissue-fluids than to those between the blood and the urine. The urine is a more concentrated solution of salts than the blood. On the other hand, the selective action of the kidney is shown very clearly in its discrimination between the sugar and the urea of the blood. There is much more sugar than urea in the blood, yet the kidney of the normal man excretes urea, and does not excrete sugar. Our knowledge is still insufficient for any certain statement, but the opinion seems to be growing stronger that the activity of the renal cells is the main factor in the excretion of solids, and even that this activity may be found to be more special than was supposed. There are indications that the kidneys may be incompetent for one form of excretion, and yet competent for another. The

observations of Meyer on a case of diabetes insipidus quoted below seem, for instance, to show that a kidney which could not excrete salt except in extreme dilution, could excrete phosphates without any addition of water.

On the whole the general opinion now is that the blood reaching the glomerulus through the vas afferens is there drained of water, and perhaps of sodium chloride, while the other salts, urea, uric acid, and the like, are added to the urinary water on its way by the active excretion of the cells of the tubules. The urinary water is perhaps at the same time partly reabsorbed.

The excretion of urine can be varied experimentally.

a. If the general blood-pressure is lowered the urine diminishes, and if the aortic pressure falls below 40 mm. Hg. (the normal systolic pressure being somewhere between 120 and 220 mm.) the excretion stops entirely.

In man a similar condition is produced by shock and collapse.

b. By ligaturing several large arteries the area of the blood-vessels can be diminished without altering the total amount of blood. The pressure in the aorta then rises and the flow of urine increases.

In man a similar condition is produced by cold, which constricts the peripheral vessels and increases the flow of urine. Heat has the opposite effect.

Professor Michell Clarke related to the Association of Physicians of Great Britain and Ireland in 1908 a case of pontine hæmorrhage. The systolic pressure was 250 mm. and the bladder held two quarts ($2\frac{1}{4}$ litres) of urine. As the kidneys, though intensely congested, did not appear to be diseased, and the man had been in good health up to the time of the accident, the great secretion of urine was probably due in some way to the hæmorrhage. It is tempting to suppose that it was directly due to the high blood-pressure, and that this was due to stimulation of the bulbar vasomotor centre by the hæmorrhage. But the blood-pressure before the accident was of course unknown and therefore the proof is wanting.

High blood-pressure is a common symptom of chronic nephritis and is often, though by no means always, associated with increase of the urinary water. It is sometimes assumed that the increased flow is the result of the increased pressure. But other factors may be at work. For instance, if it be true that the renal epithelium reabsorbs water, the copious flow of dilute urine which is characteristic of these cases may be due to the loss of epithelial surface.

c. If the renal vessels are constricted more than the other arteries, as by stimulation of the splanchnics, the urine decreases, and if they are disproportionately dilated as by division of the renal nerves, it increases.

It is suggested that the curious changes which take place in hysteria, usually a great increase of the urinary water (hydruria), sometimes suppression (anuria), may be explained by some local paralysis or stimulation of the vasomotors. But this is a mere guess.

d. Ligature of the renal artery stops the secretion. Rose Bradford and Lawrence,[1] Griffith and I,[2] Lloyd of Melbourne,[3] and Klotz,[12] have recorded cases of general thrombosis of the renal vessels after parturition, in each of which there was total suppression of urine for many days.

It is fair to say, however, as Parkes Weber [4] points out, that both the anuria and the thrombosis may have been secondary to some toxic condition.

Ligature of the renal vein has the same effect. This is important because it shows that to produce secretion pressure alone is not sufficient ; it must be combined with movement of the blood.

The venous stasis of heart failure approaches the condition of this experiment. It is regularly accompanied by a diminished flow of urine.

e. Rose Bradford [5] removed portions of kidney tissue with surprising results. If a portion, even a small portion, of one kidney was removed the urinary water increased. A mere incision produced no such effect. If a portion of one kidney and the whole of the other was removed, the amount of urinary water increased greatly and permanently, and no

other effect was produced provided the amount of kidney left was about one-third of the original weight of both kidneys. If less than this was left there was great increase in the excretion of urea. The latter phenomenon has been explained by Bainbridge and Beddard [6] as the result of simple inanition. They are corroborated by Pearce.[7] The increase of water is as yet unexplained, unless it is due to a loss of the reabsorbing tubular tissue. Bradford inclines to think that the polyuria of chronic diffuse and interstitial nephritis may depend upon the diminution of the kidney tissue. But looking through fifteen consecutive such cases of polyuria in which records were kept of the blood-pressure measured by the sphygmo-manometer I cannot find one in which the pressure was below normal, and only one in which it was normal. We have therefore always to take into account an increase of blood-pressure as well. Bradford's experiments were undertaken in order to find out whether the kidney like the pancreas had an internal secretion affecting metabolism. They were at first thought to show that it had. But Bainbridge and Beddard appear to have disproved the value of the evidence.

f. Experimentally the urine can be increased by injecting into the circulation either (α) some of the neutral salts which we commonly call diuretics, such as sodium or potassium—acetate, citrate or tartrate, or (β) digitalis, or (γ) caffein or theobromin. Neutral salts injected into a vein attract water from the tissues. They thus lead to a state of hydræmic plethora. This increases the pressure in the renal vessels, and this as usual increases the flow of urine. But they may also stimulate the epithelium. Caffein has a selective action upon the renal vessels causing first a slight contraction and then a great expansion of them. As the general pressure is not decreased this causes a disproportionate flow of blood to the kidneys, and increases the urine in consequence. A stimulant action to the renal epithelium has also been ascribed to caffein, and it is likewise said to be a cardiac tonic. Digitalis has no such selective action. Experimentally used, it strengthens the cardiac systole, and

at the same time contracts the arterioles throughout. This raises the general pressure, and when in experiments with healthy animals the flow of urine is increased, which is not always, it is supposed that the general arterial pressure overcomes the contraction of the renal vessels. This does not much matter. The importance of digitalis as a diuretic for man is in cases where the heart is weak and the urine is scanty in consequence of venous congestion. It seems doubtful whether digitalis affects the arterioles in man. Squill, strophanthus, and convallaria act in the same way. The compound pill (pil. hydrarg., pulv. digitalis, pulv. scillæ, $\overline{aa}$ gr. j, ext. hyoscyami gr. ij) is an excellent preparation and often effectual. I do not know how the mercury helps, but I think it does.

Of late years several drugs which were originally derived from cocoa have been added. The alkaloid is theobromin. Diuretin is theobromin sodium salicylate (grs. x–xv). Theophyllin and theocin are closely allied to theobromin. Theocin sodium acetate is analogous to diuretin (grs. v–viii). These drugs are allied to the derivatives of coffee. Caffein is tri- and theobromin is di-methylxanthine. Both can be, and now usually are, made synthetically from xanthine. This connexion with the alloxur bases may explain the selective action of caffein upon the kidney. Probably the theobromin derivatives act like caffein.

Nitrate of pilocarpin (gr. $\frac{1}{20}$–$\frac{1}{2}$) used hypodermically is a powerful drug. It stimulates every secreting gland in the body including the kidney. I do not usually give it till I have tried other things. It is by some people considered unsafe in uræmia, because it has certain poisonous effects on the nervous system of lower animals. It is usually in uræmia that I have given it, and I have not seen any ill effect. It is supposed to act by stimulating the secretory nerves (Brunton), but secretory nerves to the kidney are not proved to exist. Its chief effect is to remove a great deal of fluid from the body by sweat, but it also increases the flow of urine for the time, and I have several times seen patients recover temporarily from uræmia under its use.

All these drugs have been used experimentally, and therefore I have mentioned them in speaking of renal physiology, for pharmacology is only that branch of experimental physiology in which drugs are used as the stimulants. There are one or two others. Apocynum has been a good deal puffed as a diuretic. I have given it often, and have never found it of the slightest use. Scoparium contains sparteine, and therefore I suppose acts through the heart if it has any effect at all. I have never found it of any good. Gin is a popular remedy for the dropsy. That is due to the juniper oil which it contains, which like turpentine is undoubtedly a stimulant not to say an irritant to the kidney. I have never used either as diuretics, and I do not think many now would think them safe, but they were given fifty years ago.

2. Diabetes Insipidus.

Here may be mentioned certain cases in which the urinary water undergoes a great increase. This may be a transient phenomenon as in some cases of heart disease, and of ascites. It may be of long duration in cases of granular kidney, in which it is not uncommon for 4 pints or even more of a dilute urine to be excreted daily.

There is another class of cases in which the polyuria is a phenomenon of long standing, but there is no sugar in the urine, nor any evidence of disease of the kidneys. The condition is called Diabetes Insipidus. Cases in which there is structural disease of the kidney are excluded by the definition, and of the cases reported by Roberts [8] Nos. 1, 2, and 4 would not now be admitted. Of genuine cases some are hereditary. Bulloch [9] has collected all the recorded examples. In one family the condition has been traced through five generations. Many of the persons recorded died at an advanced age though they had drunk and passed enormous quantities throughout life. In other instances the disease is acquired. In that case the symptom may appear quite suddenly as in a German officer when on the march. When it has once begun it is permanent. The quantities passed

are enormous, even up to 15 litres. The urine is of very low density, and contains neither albumen nor any other abnormal constituent. The total quantity of the various solids do not exceed the normal.

Bernard showed that by a particular puncture in the floor of the fourth ventricle the phenomenon might be produced, and in some instances polyuria has occurred in human patients in whom a tubercular or other form of tumour existed in this region. But for the majority of cases no such cause exists and the pathology of the condition is quite unknown. Erich Meyer[10] points out that we must distinguish between polydipsia and diabetes insipidus. In the former the polyuria is caused by the large quantity of fluid taken, and can be stopped without injuring the patient by cutting off the supply. But in the latter the reduction of water taken does not reduce the amount passed without producing severe symptoms. In the case of the officer just mentioned a diet without meat and salt greatly reduced the output of water. The patient who was a fine swimmer found that a long bathe mitigated his symptoms. While the quantity of water was greatly increased by the addition of salt to the diet, the addition of sodium phosphate did not have the same effect. From a long series of observations on this and other cases Meyer concludes that the kidney of such a patient is for some reason unable to excrete a urine of normal concentration, and is in consequence obliged to pass a large quantity of water in order to get rid of his waste products. Thirst is a mere consequence of the polyuria. To a less extent the same is true of the granular kidney, and the polyuria of this disease is therefore similar in kind to that of diabetes insipidus. Two or three of his cases had syphilis with nervous manifestations. Seiler[11] confirms his conclusions. The patients whom I have seen, in all of whom the disease was acquired, did not appear to have suffered much in health. Lassitude and the loss of sleep caused by frequent micturition were the chief symptoms of which they complained.

3. Enuresis.

This is very common in young children, and in some patients lasts till young adult life. I have never seen it after 20 years of age. It sometimes shows itself by day as well as by night, more often by night only.

When incontinence of urine exists the first step is to make sure that it does not depend upon any organic disease whether in the urinary tract, such as inflammation of the vulva, phimosis, balanitis, cystitis, tubercle, calculus, or new growth, or in the spinal column. Pott's disease produces it sometimes. Epilepsy has also to be excluded.

We are then left with what may be called pure reflexes. The first and simplest is cold. I was once consulted by the medical officer of a charitable school. He sent me under the charge of the matron one of his patients, a little girl. I could find nothing in the child herself to account for the enuresis, which I learnt from the matron was a perfect plague in the school; but I elicited from her that it was much more common in winter. I advised an extra blanket, and a hot-bottle for each such patient, which measures completely stopped the symptoms.

In some cases the urine is found to be unusually acid, in others it is cloudy from *B. Coli*, and treatment by alkalies is then often successful (see Pyelitis). In other cases threadworms are present, and the enuresis stops when they are cleared away.

Some such patients have adenoids, and when these are improved by regular breathing exercises, or if necessary removed by operation, the enuresis often stops.

There remain however a certain number of children in whom there is apparently no other cause than that the infant habit persists, and the presence of very little water is sufficient to cause contraction of the bladder. The incontinence is always in the forepart of the night or is worse at that time. Often before the child has been two hours asleep the bed is flooded, and then no more may be passed the whole of the rest of the night.

It is now generally recognized that punishment is of no use. The habit must be fought by other habits. The child must be woken up every hour for the first three hours after going to bed, and made to pass water. He must avoid all renal stimulants such as tea and coffee, and be very moderate in the use of sugar. He must drink very little with his last meal, and this must be taken at least an hour before bedtime. Some physicians forbid meat, but I never have done so myself. Certain drugs such as urotropin (gr. v–x in a wineglass of water thrice daily), or tinct. belladonnæ pushed till the pupil dilates and the throat is dry, are useful, and potass. bromide may be added at night. With these measures nearly all cases can be cured. If however they fail, the application of a galvanic current with the negative pole on the perinæum is sometimes successful. It is the tendency of a normal child to develop the unconscious or subconscious cerebral control which prevents the habit, even if he is without proper treatment, but it sometimes takes several years to do so.

References.

1. Bradford and Lawrence, *Journ. of Pathol. and Bacteriol.* 1898, v. 197.
2. Griffith and Herringham, ibid. 1906, xi. 237.
3. Lloyd, *Lancet*, 1906, i. 156.
4. Parkes Weber, ibid. 1909, i. 601.
5. Bradford, *Proc. Roy. Soc.* 1892, li. 25.
6. Bainbridge and Beddard, ibid. 1907.
7. Pearce, *Journ. of Experiment. Medicine*, 1908, x. 632.
8. Roberts, *Urinary and Renal Diseases.*
9. Bulloch, *Treasury of Human Inheritance*, 1909, Part I, p. 1.
10. Meyer, *Deutsch. Arch. f. Klin. Med.* 1905, lxxxiii. 1.
11. Seiler, *Zeitsch. f. Klin. Med.* 1907, lxi. 1.
12. Klotz, *Amer. Journ. of Obstetrics*, 1908, lviii. 619.

CHAPTER III

NORMAL CONSTITUENTS OF URINE

WHATEVER view is held of the mechanism of renal secretion, there is an agreement that the great function of the kidneys is to drain the body of waste products. We are beginning to believe that other organs, while extracting from the blood nourishment necessary for their own cells, are at the same time by those cells working up products required for the nourishment and activity of other parts. We know however that this is not the case with the carbonic acid gas of expiration, and with the solids of the urine. These are true waste products and nothing else. But the question still remains how far are they the result of metabolism necessary to life and action, and how much of what we call the 'normal' constituents is really useless, going in at one orifice and out at the other, but not needed for either the recreation of tissue or for energy ?

Urea.—It used to be thought that 30 g. of urea was the natural amount to excrete, and 120 g. of proteid the natural amount to take in. But Professor Chittenden by his experiments has shaken this belief. He claims that only about a third of these respective amounts is necessary for health even under the active life of an American college athlete. Professor McCay [1] in Calcutta finds that the average Bengali only excretes from 12 to 13 g. of urea, and therefore only metabolizes from 37 to 40 g. of proteid daily. McCay connects this with the slight frame, and low power of work of the Indian. It would be interesting to have similar analyses in the case of other races such for instance as the Soudanese who on a diet almost the same as the Indian work as hard as Englishmen.

This question is pursued with enthusiasm on various

grounds. Some seek to avoid taking animal life, others to preserve their own bodies in a state of greater purity, and others again to diminish the intake of the purin bodies or whatever other chemical compound is at the moment in disfavour. But it is also of great economic interest, and its further investigation is anxiously expected by all of us.

In some fascinating lectures given at Guy's, Gowland Hopkins [2] states his opinion that the N excretion is more or less of a by-product in the organism. It does not represent waste due to energy, for it hardly increases at all after work. And as tissue protein seems very stable it is not likely to be wanted in that amount for repair. He thinks it is the result of disintegrated protein food, of which the non-nitrogenous part is used for energy, and the nitrogenous elements, going to the liver as amino-acids, are there turned out as urea for excretion, without entering the tissues at all. This theory does not of course touch the question of the amount of proteid food required.

Uric Acid.—Not long ago uric acid was the pathological scapegoat. It was thought to be a result of deficient oxidation and a relic of a previous biological stage, in which excretion had not yet taken the soluble form of urea. It was stated that it should bear a definite ratio to urea, and that any departure from this standard which was fixed at 1 to 33 implied either a dangerous retention or a fortunate removal of surplus. This controversy is dead. No one now holds this position. Uric acid which is excreted in amount something less than a gramme daily, is derived chiefly from nuclein taken with the food, and partly from nuclein liberated in the body by cellular activity.

It is deposited from the urine in two forms, amorphous urates, which are quadriurates, and crystalline uric acid. These two forms are precipitated when the urine is acid, and interchange in the presence of phosphates until either equilibrium is established, or, if there is an excess of acid phosphates, all, or nearly all, the urates fall as crystals of uric acid. Sometimes deposits of quadriurates are found

in the kidneys of new-born infants, and for the first few days of life the uric acid excretion is very much higher than at any later age.

Creatinin is found in small quantities. It is closely allied to creatin, which is found in muscular tissue, and therefore creatinin was supposed to be related to muscular metabolism. Spriggs [3] investigated this question by comparing three classes of disease with the normal. On the constant diet containing—except in minute quantities—neither creatin, nor creatinin, nor purin bodies, he found that the amount of creatinin excreted in the urine was below the normal in primary myopathies, in amyotonia congenita, and in myasthenia gravis, but not in mere loss of tone as in tabes dorsalis. It was but slightly increased in tetanus and spastic paraplegia. It is probably therefore connected rather with the nutritional metabolism than with the functional activity of muscle. Mellanby [4] found creatin constantly present in the urine of a boy, aged 6, who was subject to periodic vomiting, and largely increased just before the attack.

Inorganic Salts.—The excretion of inorganic constituents depends ultimately upon the amount taken in with the food. But the connexion is not always direct. The bases can probably replace one another. Bunge showed that the ingestion of potassium might lead to the excretion of sodium, and explained thus the strong desire which herbivorous animals, whose diet is rich in potassium, have for sodium chloride. In open country wild animals travel long distances to salt-licks, and in England hares go down to the seaside under, I suppose, the same impulse.

Of the acids, the sulphates and phosphates are due to the oxidation of S and P in the proteid molecule. They generally vary pretty closely with the N excretion.

The total weight of sulphates excreted per diem is about 3 grammes. About nine-tenths of this is composed of inorganic sulphates. Certain aromatic substances, and indoxyl and skatoxyl, which are closely related to them, are excreted as sulphates. They are called ethereal or

conjugated sulphates. They are increased in amount when there is increased bacterial decomposition in the intestines.

The ordinary sulphates are precipitated from urine acidulated with acetic acid by barium chloride in the cold. If the filtrate containing excess of barium chloride is boiled with hydrochloric acid a fresh precipitation takes place. This represents the conjugated sulphates.

Sulphur to the amount of about 0·2 grammes is also excreted in a less oxydized form and is called the neutral sulphur. It does not vary with diet, and is therefore probably the result of some special line of metabolism. According to Mathison [5] phosphorus also is partly excreted as an organic compound.

Oxalic acid excreted as oxalate of lime is in small quantities a normal constituent (·05 g. per diem according to Gowland Hopkins). It is probably in most part derived from the vegetables in the diet, but can also apparently be formed by proteid metabolism, as in starvation, and increases greatly when carbohydrate metabolism is impaired, as in diabetes mellitus. A curious observation was published by Burkitt.[6] In the district round Chandkira, in Eastern Bengal, there are several races of Mongolian origin resembling each other in manners, customs, and appearance. Of these the Manipuris alone live on nothing but vegetables and fruit. They suffer badly from oxalate of lime gravel. Yet the water of the district is very deficient in calcium salts, which have to be actually supplied to imported horses, and often to man. The processes which lead to the formation of oxalic acid are however very little understood. The alternation of uric acid and calcium oxalate layers in some stones is unexplained.[7]

Much has been written of old on phosphaturia and oxaluria. They have each been connected with serious nervous conditions. No one now believes that hypochondriasis and other neuroses depend upon either phosphaturia or oxaluria.

The chlorides in health depend upon the amount ingested.

But they vary much more in disease than the other inorganic constituents. In fevers, especially in pneumonia, they may be for a few days completely retained.[8] The reason is unknown. They almost, sometimes entirely, disappear from the urine, when any large effusion occurs, as in pleurisy and ascites. This is more easily understood. The effusion takes up all the available chloride from the blood. Lastly, in some cases of renal disease without effusion, the excretion of chlorine falls very greatly. Instead of 6 or 8 grammes daily, it may go down to nil. Continental physicians, especially in France, lay great stress on this.[9] They look upon it as a failure of renal function, which is of grave omen, and requires to be actively treated by withdrawing salt from the diet. My own observations lead me to believe that this is often, but not always, true. Most of my cases in which the excretion of Cl reckoned as NaCl has sunk below a gramme in the twenty-four hours have died. Some however have recovered. I think that the excretion of Cl is of greater prognostic significance than that of urea.

It must be added that, as Garratt has pointed out, sodium and chlorine do not always vary together.

On a diet which though not by any means normal, for it included neither bread, vegetables, nor any kind of flesh, yet contained the three classes of food in the proportion of a standard diet, namely :

Protein	119 grammes.
Fat	148 grammes.
Carbohydrates	225 grammes.

Folin has shown the proportions of the various urinary constituents in healthy persons. He gives them as follows :

Total N.		*In per cent. of Total N.*					
		Urea.	*Ammonia.*	*Urea and ammonia.*	*Creatinin.*	*Uric Acid.*	*Undetermined.*
Average .	16·0	87·5	4·3	91·85	3·6	0·8	3·75
Minimum .	14·8	86·2	3·3	90·70	3·2	0·6	2·70
Maximum .	18·2	89·4	5·0	92·60	4·5	1·0	5·30

Total S as SO_3	*In per cent. of Total S.*			*Total P_2O_5.*	*Total Cl.*
	Inorganic.	*Ethereal.*	*Neutral.*		
Average . . 3·31	87·8	6·8	5·1	3·87	6·1
Minimum . 3·11	84·7	5·5	4·1	3·44	5·6
Maximum . 3·73	89·6	8·0	6·1	4·50	6·9

He found that when the amount of nitrogen in the diet was much reduced the proportion of N excreted as urea and of S excreted as inorganic sulphates fell. The creatinin excretion remained at about the same level whatever the diet, and therefore the proportion of N excreted as creatinin rose as the urea nitrogen fell. Uric acid excretion fell somewhat as the diet became less nitrogenous, but not in proportion to the diminution in the total N, and therefore the proportion of N excreted as uric acid also rose as the urea nitrogen fell.

This is exactly what we should expect if, as above said, the creatinin represents a regular product of the nutritional metabolism of muscle, which is likely to be unaffected by diet, and if uric acid represents partly the purin bodies of the food which would vary with the food, and partly the results of the nutritional metabolism of cells, which would not.

The same may be said of the variation which he found in the proportions of the sulphur excreted.

References.

1. McCay, *Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Govt. of India*, N.S., No. 34.

2. Gowland Hopkins, *Guy's Hospital Gazette*, 1907, p. 327.

3. Spriggs, *Quarterly Journ. of Med.* i. 63.

4. Mellanby, *Lancet*, 1911, ii. 8.

5. Mathison, *Bio-chemical Journ.*, 1909, iv. 233, 274.

6. Burkitt, *Brit. Med. Journ.*, 1909, i. 898.

7. For a table of the oxalic acid content of various foods see Minkowski, *Handb. der Ernährung's Therapie*, ii, Pt. II. 540.

8. See for a full discussion Garratt, 'Observations on Metabolism in the Febrile State in Man,' *Medico-Chirurg. Trans.* lxxxvii. 163.

9. See Mauté, *Chlorurie alimentaire expérimentale*, Paris, 1903, with bibliography.

CHAPTER IV

ABNORMAL CONSTITUENTS OF URINE

ALBUMINURIA, AMMONIA, DIACETIC ACID, ACETONE, GLUCOSE

1. Albuminuria.

In renal and many other diseases the urine contains certain proteid bodies. To show their presence the urine must, if turbid, first be filtered. A turbidity that cannot be removed by filtering is usually due to bacteria.

The best tests are the following :

1. Boil the urine. If a precipitate appears add a little dilute nitric acid. If the precipitate dissolves in the acid it is phosphates ; if it remains it is due to albumen. When the urine contains very little albumen it may be needful to compare two test-tubes, the one heated and the other not, in order to be sure ; or to heat only the upper part of a column of urine.

Resins and balsams such as turpentine or copaiba will, on boiling, produce a similar cloud which does not disappear on adding nitric acid. But it dissolves in alcohol, which coagulated albumen does not.

2. Put some strong nitric acid in a test-tube, slant it, and trickle urine through a pipette on to the surface. A white layer of acid albumen, which is insoluble in the excess of acid, forms on the lower surface of the urine (Heller's test).

Note that—

(*a*) A colour ring often forms in the acid. It is of no importance.

(*b*) Albumoses and resins give similar precipitates.

(*c*) A cloud often appears, not at the line of contact, but in the upper part of the urine. It may then extend downwards

to the line of contact. Such a precipitate is produced both by urates, and by mucinoid, or nucleo-albumen.

3. Add to the urine a few drops of a saturated solution of salicyl-sulphonic acid, or a few crystals of the solid acid, and shake it up. A flaky precipitate falls. This may be albumen or albumose. If the latter it disappears on heating. If both are present, it is possible, by filtering while hot, to obtain a clear filtrate which will deposit a precipitate of albumose on cooling. This reagent does not precipitate urates, resins, bile salts, or alkaloids, and is for this reason useful. But it has the slight disadvantage that the crystals are very hygroscopic, and cake, while the saturated solution is inclined to 'creep' and form a crust round the stopper.

4. Add to the urine a little dilute picric acid (1 per cent. is a good strength) and a little acetic acid. A precipitate forms. This test may be done in Heller's way, in which case the precipitate will form a layer at the point of contact.

The disadvantage of this test is that it precipitates many things besides albumen, such as albumose, mucinoid, uric acid, creatinin, and alkaloids.

I never use one test alone, and nearly always use all four tests together. To do so takes hardly any additional time, and adds greatly to certainty. I have seen a critic remark that an author ought to give the one best test and not trouble his readers with others. If any test were perfect no others would be necessary. But no test is so, and the boiling test, which is the least fallacious, is sometimes so extremely faint, that but for using other tests I should have passed it unnoticed.

These tests establish the existence of what is called albuminuria. It is a symptom common to many different conditions. It is found—

(1) In passive congestion of the kidney when the return of blood through the renal veins is blocked either by direct pressure, or by disease of the lungs or heart.

(2) In tonsillitis, in acute fevers, and in pregnancy.

(3) In some cases which show no other sign of disease—physiological albuminuria.

(4) In active congestion of the kidney such as that produced by turpentine or cantharides.

(5) In inflammation and other structural diseases of the kidney.

What we clinically call by the single name albumen is in most cases a combination of two different proteids. The first is serum albumen, the second globulin. Both are derived from the blood and the two usually occur together. But the proportion in which they occur is not that proper to the blood, it varies very much, and each body sometimes occurs alone. Many attempts have been made to discover the clinical significance of these variations. Senator [1] thought that in lardaceous disease globulin was usually abundant. Maguire [2] said the same of functional or physiological albuminuria. Noel Paton [3] denies both these statements. He found that the proportion varied greatly in the same patient during the course of the day. This was owing to variation in the albumen, the globulin remaining nearly constant, and the variation in albumen seemed to depend chiefly upon food. The amount was greatest after breakfast, and least during the night. It was increased by a rich nitrogen diet, and decreased as did also that of the globulin, on a milk diet. It is impossible to believe that the variations corresponded to changes in the blood. Csatary [4] made similar observations. He examined the total urine of over thirty patients, usually several times in each case. But he was unable to come to any satisfactory conclusions. He thought however that the proteid quotient $\frac{\text{albumen}}{\text{globulin}}$ was generally high

(*a*) in genuine contracted kidney ;

(*b*) in cases where there is much œdema ;

and that in any case a rise above the patient's usual level was of bad omen. Boyd [5] also made a large number of observations. It is evident from his results too that the proteid quotient varies greatly in different cases of the same class, and also, as he says, in each single patient. Gross [6] reaches the same conclusion. Sykes [7] believes that on standing a certain proportion of the albumen is converted

into globulin, which renders such an investigation still more uncertain and difficult.

Investigations by Freund and Joachim [8] and by Oswald [9] showed that the globulin of urine is a compound body which can be separated into three different species by fractional precipitation with ammonium sulphate.

In microscopic sections a substance, coagulated by the hardening agents employed, and therefore probably proteid, is often seen in the cavity of the glomerular capsule. This is probably the albumen afterwards found by the above tests in the urine. It is therefore exuded there first, but we have no means of knowing whether this escape occurs in the urinary tubes as well.

A third proteid also occurs in the urine.

1. It does not form a cloud or a precipitate on boiling.

2. With Heller's test it forms a ring at the point of junction, and also a cloud which appears a little above that level, sometimes a good way above it, and spreads downwards.

3. It is precipitated by picric acid and by salicyl-sulphonic acid.

4. It slowly forms a cloud, and this is its characteristic reaction, with acetic acid in the cold. If the urine is concentrated it should be diluted to avoid the precipitation of urates. That however the precipitate described is not urates may be recognized also by the facts that the cloud does not alter on heating, and takes a long time to precipitate. There is still some doubt what this precipitate really is. Mörner believes it to be an albuminate of some organic acid; most authorities ascribe it to nucleo-albumen derived from the waste of cells in the body, and I have used this name, but recent investigations appear to show it to be a globulin.[10]

What is generally called mucus in urine, the floating cloud that appears when the urine has stood for some time, gives the same reactions. It is derived from the epithelium of the bladder and passages. In cystitis it is much increased and forms a slimy mass.

Nucleo-albumen has been found in considerable quantity in cases of leucocythæmia.

It is often useful to make an estimation of the quantity of albumen passed. Like every other quantitative analysis it should be made on a specimen of the whole urine of twenty-four hours. The process commonly used was brought out by Esbach. The fluid used to precipitate the albumen from the urine is made thus—

Dissolve 10 grams of pure picric acid
and 20 ,, of pure citric acid
in 900 c.c. of water.

Allow to cool, and make up to 1,000 c.c.

The albuminometer in which the urine and the fluid are mixed is a tube marked and graduated for the purpose. It is filled with urine up to the mark *U* and the reagent added up to the mark *R*. Put a cork in the top and turn it topsy-turvy once or twice to mix it. Corks and little wooden stands are sold with the tubes. The numbers below the mark *U*, from 7 down to $\frac{1}{2}$ are to measure the precipitate. They give the proportion per litre (i. e. per mille, not per cent.). But the instrument, which is never very accurate, becomes untrustworthy above 4 per mille, and if there is more albumen than that, the urine should be diluted before the estimation is made.

A more exact method is that invented by Sir W. Roberts which depends upon the time in which nitric acid used by Heller's method produces a visible precipitate. This is so much more troublesome a process that it is hardly worth while for what is after all still only an approximate result.

If real accuracy is needed the albumen must be precipitated and coagulated, washed pure, and then properly dried to a constant weight on a weighed filter.

The amount of albumen passed in the urine varies both from day to day, and also at different times in the day.

I have made many observations on the former point without being able to arrive at any conclusion. The variation occurs when the patient is in bed, and on a constant diet. It does not correspond to any appreciable variation in his general or local condition, and although no doubt if a suf-

ficient period is taken the albumen decreases as the patient improves, the daily variation remains unaccountable.

In the following charts, two of which were taken from

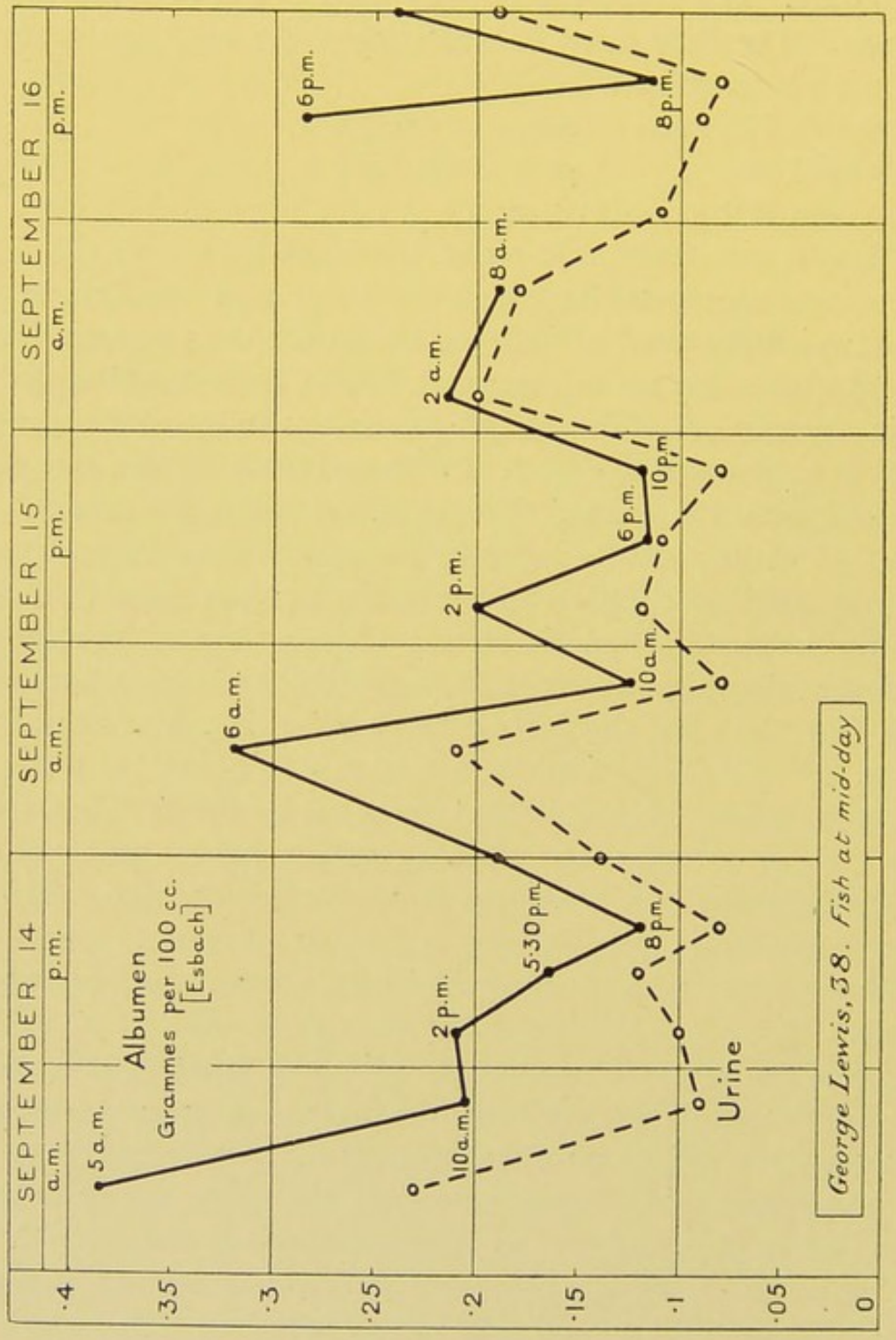

CHART A

the same patient, there is a tendency for the proportion of albumen to be greatest at two points in the twenty-four hours, namely about 6 a.m., and about 6 p.m. But at

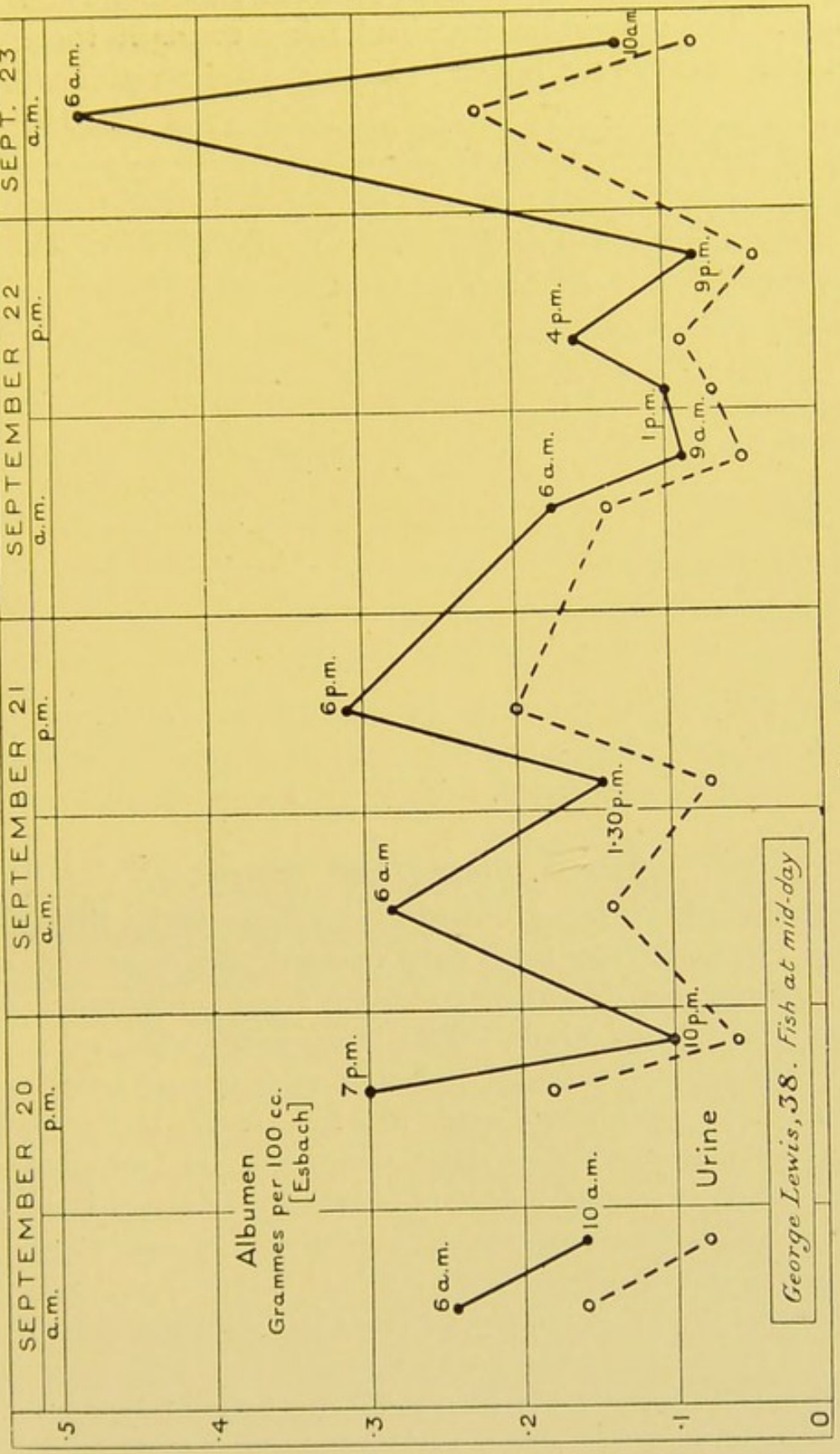
SEPTEMBER 20
SEPTEMBER 21
SEPTEMBER 22
SEPT. 23
a.m.
p.m.
Albumen
Grammes per 100 cc.
[Esbach]
Urine
George Lewis, 38. Fish at mid-day
6 a.m.
10 a.m.
7 p.m.
6 a.m
1·30 p.m.
6 p.m.
6 a.m.
1 p.m.
9 a.m.
4 p.m.
9 p.m.
10 a.m
10 p.m.
.5
.4
.3
.2
.1
0

CHART B

a later date in the same case, no such variation could be found. The proportion remained fairly constant throughout the twenty-four hours.

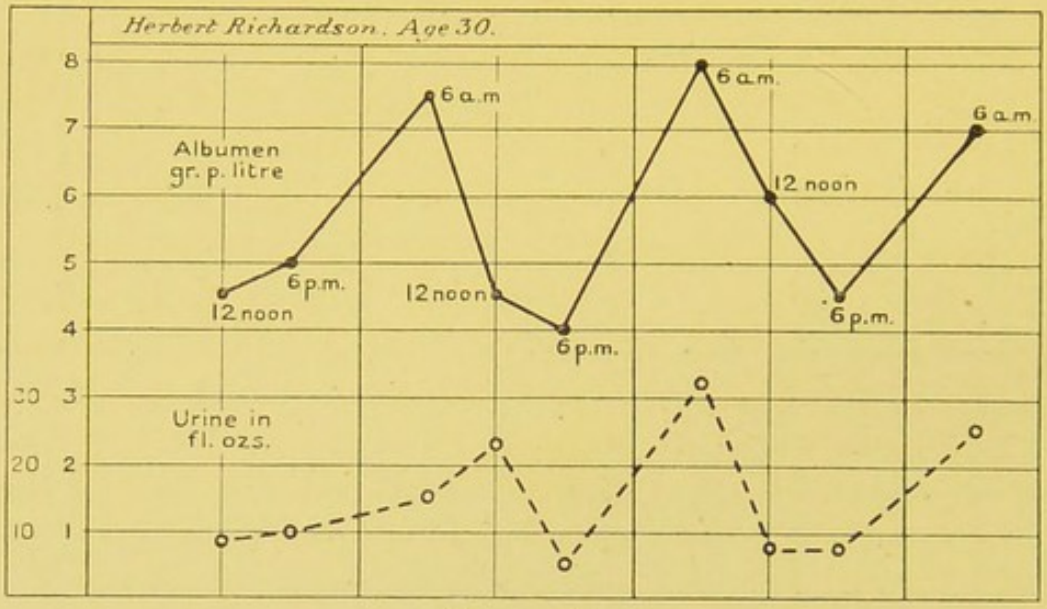

Chart C

The variation between the two constituents, albumen and globulin, may perhaps be at the bottom of these differences. But, as before mentioned, little is yet known on this point.

Ammonia, Diacetic Acid, Acetone.

Ammonia is always excreted in small quantities with the urine. In health the total daily amount may be as high as 1·2 grammes, and the nitrogen excreted as ammonia may be 5 per cent. of the whole. This is exceeded when mineral acids are ingested in large quantity, or inorganic bases are withheld, or the organic acids are increased. Under such circumstances man, like other carnivora, can utilize the amino-acids of proteid digestion in self defence, and instead of forming urea from them, uses them as ammonia to neutralize the surplus of acid.

The best known of these conditions is the acid intoxication (in the vulgar 'acidosis') which occurs in severe cases of diabetes mellitus. The breath smells sweet from the presence of acetone, and the urine contains acetone with diacetic and β-oxybutyric acids. The β-oxybutyric acid is probably

due to the incomplete oxidation of fats, but has also been ascribed to decomposition of proteids. Diacetic acid and acetone are derived from it by oxidation. There seems to be little doubt that the presence of β-oxybutyric acid in the blood is the cause of diabetic coma, and that the increase of ammonia in the urine shows the effort of the system to neutralize it. But the amount of ammonia is only a rough guide to the amount of the acid in the urine, and since a fall in the β-oxybutyric acid of the urine may, like a fall in glucose, coincide with an increase of coma, it is also probable that the amount of the acid in the urine may not correspond to that in the blood.

Diacetic acid may be found in the urine in many cases of starvation, especially in women and children. Almost every case of gastric ulcer in which food is withheld shows the presence of diacetic acid in two or three days. It is present also in cases of prolonged vomiting after anæsthesia, in the recurrent vomiting of children, and even on changing the diet in infants. In all these cases its presence is probably due to partial starvation, and it is doubtful whether it is itself the cause of any symptoms.

Lactic acid has been found in considerable quantities after convulsions, and in trichiniasis. Ammonia is produced in these cases also to neutralize the excess of acid.

Acid intoxication may be suspected where there is diacetic acid, acetone, or both in the urine. The test for the former is the deep red colour produced by adding a solution of perchloride of iron. The reagent throws down a whitish phosphate which at first obscures the colour. It can either be filtered off, or dissolved by a drop or two of dilute hydrochloric acid, or by adding more of the reagent. The colour must not be confused, as I have known to happen, with the purple colour produced by salicylic acid, and some other phenol compounds.

The best clinical test for acetone is modified from that described by Rothera.

Add to the urine in a test-tube an equal volume of a saturated solution of ammonium sulphate. Then add a few

drops of ammonia solution, and lastly a few drops of a fresh solution of sodium nitro-prusside. A purple violet colour indicates the presence of acetone. If no acetone be present the liquid remains yellow. If only traces be present the colour develops gradually.

A more exact test is to acidify half a litre of urine, preferably with phosphoric acid, in order to prevent it frothing, and then distil it. The distillate should not exceed 10–30 cc. To several cc. of the distillate add a few drops of caustic potash and of iodo-potassic iodide solution. Iodoform crystals are precipitated, and the smell of iodoform is perceptible.

The treatment both prophylactic and curative is to administer bicarbonate of soda in large amounts. If the patient is unable to swallow, it can be given by hypodermic irrigation. The effect of this is sometimes quite astonishing. I have seen a diabetic patient shrivelled with loss of water, and deeply comatose, who looked as if he would die any minute, become perfectly sensible on the hypodermic injection of between two and three pints of bicarbonate solution (10 grains to the ounce). The condition, however, always recurs.[11]

Although diabetes mellitus is not within the scope of this volume the tests for sugar in the urine must be mentioned.

Urines containing sugar are usually, but not always, of high specific gravity. I have found sugar in one case of diabetes when the specific gravity was only 1014. The tests are—

1. The precipitation of the yellow or red suboxide of copper from a solution of the sulphate in an alkali. This test may be performed

a. As Trommer's test. To an inch of urine in a test-tube add an equal part of caustic potash, and add drop by drop a dilute solution of cupric sulphate until it ceases to be dissolved. Heat.

b. With Fehling's solution in which copper sulphate is dissolved in a mixture of potassium-sodium tartrate and caustic soda. It must be freshly prepared, and should

always be boiled before the test is carried out to see that no reduction takes place spontaneously.

Note.—Other substances beside sugar reduce cupric sulphate slightly, among which are uric acid, creatinin, nucleo-albumen, and bile pigments; and also compounds formed with glycuronic acid after taking various drugs, such as phenol, chloral, chloroform, and others.

2. The fermentation test which may be performed in a test-tube over mercury, or more simply as we carry it out in the wards, by filling one bottle with the suspected urine, another with normal urine, adding a little yeast to each and setting aside in a warm place for twenty-four hours. The specific gravity of the suspected urine and of the control is taken before and after. Even the control will perhaps have lost a little. Urine with sugar in it will, however, lose much more by fermentation. The difference in degrees on the urinometer roughly corresponds to the number of grains of sugar per ounce which the urine contains.

This test is a reliable qualitative test for sugar. For quantitative testing it is not reliable. This should be carried out by titration with standardized Fehling's solution.

References.

1. Senator, *Virch. Archiv*, lx. 476, cxiv. 1.
2. Maguire, *Lancet*, 1886, i. 1062, 1106.
3. Noel Paton, *Brit. Med. Journ.*, 1890, ii. 196.
4. Csatary, *Deutsch. Arch. f. Klin. Med.*, 1891, xlvii. 159.
5. Boyd, *Edinb. Med. Journ.*, 1894, xxxix, pt. ii, 991.
6. Gross, *Deutsch. Arch. f. Klin. Med.*, 1906, lxxxvi. 578.
7. Sykes, *Journ. of Physiol.*, xxxiii. 101.
8. Freund and Joachim, *Zeitsch. f. Physiol. Chemie*, 1902, xxxvi. 407.
9. Oswald, *Beiträge zur Chemisch. Physiol. u. Pathol.*, v. 234.
10. See for chemical discussion Neubauer and Vogel's *Analyse des Harns.*
11. See for discussion of acid intoxication, Bainbridge, *Lancet*, 1908, i. 94; Spriggs, *Quarterly Journ. of Med.*, 1909, ii. 325.

CHAPTER V

CHRONIC INTERMITTENT ALBUMINURIA IN THE YOUNG

Cyclic, Physiological, Functional Albuminuria

In 1878 Moxon[1] published a paper on this subject. Next Dukes[2] described it in the boys at Rugby, and Pavy in several papers from 1885 onwards discussed it under the name of Cyclic Albuminuria. It has been the subject of careful study, and of much speculation ever since.

Any physician who examines a number of boys, young men, and girls, whose health is apparently good, will find that a certain proportion of them at times pass albumen. The circumstances under which this happens vary with the patient, though for him or her they are constant.

Form 1. *Orthostatic Albuminuria.*

The albumen is only to be found when the patient is up and about. So long as he remains in bed, or even lying down, it is absent. In some cases it appears in the first hour after rising, in some only after two or three hours. It gradually reaches a maximum, and then gradually decreases again. It may altogether disappear before the patient goes to bed. If he goes to bed in the middle of the day for two or three hours the albuminuria may stop altogether, to begin again when he gets up in the afternoon. An hour in bed is not usually enough to stop it completely, but will reduce the amount. The following table is taken from observations on two girls by Porges and Přibram[3]:

6– 7 a.m.,	in bed.	No albumen.
7– 8 ,,	up.	Albumen 1 per mille (Esbach).
8– 9 ,,	in bed.	,, a trace only.
9–10 ,,	up.	,, 1·5 per mille.
10–11 ,,	in bed.	,, a trace.
11–12 noon,	up.	,, 2 per mille.

It has often been noticed that when up the volume of urine passed and its content of salts are both less in proportion than while in bed. Sometimes to drink a pint or so of fluid on rising, and thereby increase the volume of urine, will lessen not only the percentage of albumen but also the total amount (Porges and Přibram). In this form albuminuria is not increased by taking food, or by exercise. On the contrary, these two factors tend to decrease it.

Jehle drew attention to the influence of lordosis and believed that these cases were all caused by it. He produced artificial lordosis by means of pillows, and albuminuria followed. Götzky,[4] however, though allowing that artificial lordosis, which he produces by turning the child on its face and then putting supports under the thorax and pelvis, will produce albuminuria even in healthy children, denies that lordotic and orthostatic albuminuria are the same, or even connected with one another. Many of his cases, carefully watched for long while standing, were not lordotic ; many lordotic children do not pass albumen ; and lastly the albuminous body is in the orthostatic form chiefly an acetic acid precipitate,[a] while in artificial lordosis it is ordinary albumen. He further states that to produce albuminuria by artificial lordosis the most projecting point must be above the third lumbar vertebra.

These patients, though in fair health, are not as a rule robust. If they are boys or girls under fourteen they are often nervous, excitable children who sleep badly, and have a weak digestion. If they are young men they are weedy, and unfit for the time to play fast games or to take any hard exercise.

There is now a general agreement that this, the orthostatic form of albuminuria, is due to some disturbance of the circulation. I do not think it possible to define exactly what the disturbance is. It is simple to suppose that it is a venous congestion due to the extra weight of the column of blood produced by standing up. But if that were the case

[a] My experience does not confirm this. My orthostatic cases have passed ordinary albumen.

we should expect the albumen to be increased after exercise, which it is not. In a case very accurately observed by Erlanger and Hooker [5] some curious facts were discovered. The albumen did not appear while sitting, but only when standing. But it did not appear if the patient stood in deep water, nor if he wore a pair of pneumatic trousers in which the lower part of the body and the legs were kept under a pressure of 50 mm. Hg. If he was fixed on a horizontal couch, and the whole was then tilted head upwards, albumen appeared when the body was at an angle of 40° with the horizontal. If it was tilted feet upwards it did not appear at all. The patient was a man of 27. This is an unusual age for the condition, and we cannot infer that every case would behave in the same way.

Most authorities, though recognizing the difficulties, have ascribed this form of albuminuria to venous pressure. Dr. Armstrong's observations on albuminuria after exercise referred to below make me inclined to think that orthostatic albuminuria is probably connected rather with a fall in the arterial than with a rise in the venous pressure. It is to be remembered that the albumen may disappear before evening, which shows that the body can after a time adapt itself to the upright position.

Several of these cases have been watched until recovery. A good example is recorded by Neukirch.[6] The patient was his own daughter. The affection began after diphtheria, when she was nine years old, and lasted till she was fifteen. Eight years had elapsed since the albumen had entirely disappeared, and the young lady was in excellent health, able to ride, and play lawn tennis with the best. Thrice during the period of albuminuria he and his daughter went to St. Moritz for a holiday. There, despite long walks, the albuminuria on each occasion almost entirely disappeared. He tried many remedies, including several weeks' rest in bed. None but the mountain holiday had any effect. Heubner[7] records several recoveries. I have seen three.

So far as I know, only one of these cases has been dissected. In this instance Heubner and Langstein could find no

abnormality whatever in the kidneys after the most minute examination.

Form 2. Albuminuria after hard exercise.

In 1888 Sir T. Grainger Stewart found that hard physical exercise produced albuminuria in a certain proportion of soldiers. The same observation was made by von Leube and other German physicians. The most important contribution, however, has been made by Dr. Collier,[8] of Oxford. He is himself an athlete, and during twenty years' practice in Oxford has had exceptional opportunities of examining athletic young men. In February 1906 he examined 156 healthy undergraduates who were training for boat races an hour or so after they had been rowing. He writes :

'My previous experience led me to anticipate that we should find numerous cases of albuminuria, but I was quite unprepared for what we did find. In some cases the urine of every member of the crew contained albumen, and sometimes the urine of two or three, or even four, members would contain very heavy clouds of albumen ; especially was this true of the head boats on the river. The better the crew, it seemed, the more cases of albuminuria, the probable explanation being, the harder the work the heavier the percentage of albumen.

'Later on we examined the urines of the crews competing in the Inter-University Boat Race. From the Oxford crew we obtained specimens from the eight members of the crew one hour after rowing the full course from Putney to Mortlake, and in every instance albumen was present, in 50 per cent. in large quantities.'

He found the same after running races, and was corroborated by several medical officers of public schools, who made similar observations at his request. He has been unable, except in a few cases, to follow the history of these patients after leaving Oxford ; but 'in the few cases I have been able to follow in later life the albumen has permanently disappeared'.

Professor Holst, of Christiania, tells me that in examining over 100 men after racing on snow-shoes he found albuminuria in every instance but one.

Dr. Collier points out that we know from Dr. Morgan's inquiry (*University Oars*, London, 1873) that the expectation of life among University oarsmen is exceptionally good, so that the albuminuria noticed cannot be of serious importance.

This matter was very fully discussed at the Medical Section of the Royal Society of Medicine in 1911.[9] Dr. Collier then added further observations. In 1907 he took the urines of five crews, forty men, soon after they had rowed the races at Oxford. Every one of the men passed albumen, and many of them casts, and oxalate crystals. He had also examined the urines of runners, and in all there was plenty of albumen after a race. He believed that albumen would always be found in the urine of any man who had the faculty of 'running himself out.' Dr. Armstrong, of Wellington College, stated that he frequently found albuminuria in his schoolboys after a cross-country run. He had taken systematic observations on the systolic blood-pressure, and found that in some boys the pressure was lowered, by even as much as 25 mm. of mercury, and that in these cases albumen was present; where the pressure was not lowered there was no albumen.

A case occurred to me which I may quote here, as it illustrates the difficulties that occur to us in practice. A lady, aged 42, of eccentric and excitable disposition, was sent to me. She married at 26. In the two following years she had miscarriages, the last with convulsions, but without any swelling of the legs. When 29 she was rather out of health. Albumen and a cast were then found in the urine. Four years later she again miscarried and again had convulsions. Albuminuria and slight œdema of the legs was found then. Since then she had twice been insane. No swelling of the legs had been noticed since the miscarriage. At the age of 41 a trace of albumen was again found. She also had had megrim. I saw her after a long railway journey: there was slight œdema of the legs, the urine passed on rising contained no albumen, that passed after breakfast and again that passed after dinner showed a haze only. There were no

other symptoms of renal disease. I made careful observations for six consecutive days on every specimen passed, both when up and when in bed, and on every kind of diet. Not a trace of albumen was present. But six months later, again after a railway journey, a trace of albumen was found. Dr. Gossage, in the discussion above quoted, noted the effect of railway journeys. I stated my opinion that this lady had not any condition of the kidneys that could be called disease, or would shorten life.

3. *Other forms.*

Beside these two established forms, albuminuria is known to occur temporarily in candidates for examination,[10] apparently as a result of mental strain. Dr. Armstrong mentioned in the discussion above quoted that albuminuria frequently occurred from fear, as when a boy was about to be flogged. A somewhat similar case happened to me. A young man consulted me one morning. He was in a state of extreme nervousness. I found no other disease in him, and he passed water in my room. To my surprise it contained a large quantity of albumen. There were no casts or other recognizable organic deposit. He sent me another specimen passed at bedtime that day, and another passed on rising. In neither was there a trace of albumen. Briefly, I made exhaustive analyses of all the specimens passed, during two consecutive days, and no albumen appeared again. There were no other symptoms of nephritis, and he had been passed for life insurance not long before. I have known paroxysmal hæmoglobinuria to occur under the same conditions.[11]

Lastly, transient albuminuria due to cold bathing has been described by George Johnson, by Mahomed, by Mason, and by Rem Picci, who observed several cases.

It will be found in Chapter X that these three conditions, violent exercise, mental strain, and cold, are also known to produce hæmoglobinuria. It is there recorded that occasionally the hæmoglobin is absent and albuminuria alone appears. It is in my opinion probable that these cases of transient albuminuria, which are quite different from the

orthostatic form, are analogous to paroxysmal hæmoglobinuria, and indeed may be slight forms of hæmoglobinuria.

In former days the existence of albuminuria was held to justify a diagnosis of organic renal disease. This opinion is no longer held. It is accepted on the one hand that by very delicate tests, on large quantities of urine, albuminuria may be detected, if not in all men, yet in the great majority. On the other, observations of the kind just quoted have been continued now for long enough to prove that albumen in sufficient quantity to react easily with ordinary tests may be passed by persons who show no other symptoms of renal disease and eventually cease to pass it.

Clinical diagnosis, however, remains difficult, and there is no one symptom on which we can rely alone.

Intermittence is by no means unknown in the albuminuria of chronic interstitial nephritis and the amount of albumen passed in this disease is often minute. In physiological albuminuria casts are generally absent. But hyaline casts can occasionally be found in this condition, and on the other hand casts are sometimes absent in genuine nephritis, even when albumen is copious. The history of the patient is of no avail. True organic nephritis often, I believe more often than not, begins insidiously, and on the other hand such a case as Neukirch's obliges us to conclude that a disease like diphtheria, which sometimes causes organic nephritis, may give rise to albuminuria which appears and disappears according to posture.

No case should be diagnosed as physiological until all possible evidence, both of renal disease and of cardio-vascular and retinal changes, has been examined. No case should so be diagnosed in persons over thirty years of age. But with those precautions I believe it is possible to distinguish between albuminuria which will, and albuminuria which will not, permanently affect the patient's health and shorten his life.

REFERENCES.

1. Moxon, *Guy's Hosp. Reports*, xxiii. 233.
2. Dukes, *Brit. Med. Journ.*, 1878, ii ; *Lancet*, 1891, ii.
3. Porges and Přibram, *Deutsch. Arch. f. Klin. Med.*, 1907, xc. 367.
4. Götzky, *Orthotische Albuminurie*, Berlin, 1910.
5. Erlanger and Hooker, *Johns Hopkins Hosp. Reports*, 1904, xii. 145.
6. Neukirch, *Deutsch. Arch. f. Klin. Med.*, 1905, lxxxiv. 165.
7. See also Sutherland, *Cyclic Albuminuria*, London, 1900 ; Heubner, *Ergebnisse der inn. Med. u. Kinderheilk.*, ii. 567, 1908, with a large bibliography.
8. Collier, *Brit. Med. Journ.*, 1907, i. 4.
9. Discussion, *Proc. Roy. Soc. of Med.*, vol. iv, Medical Section, p. 109, 1911.
10. *Trans. Clin. Soc.*, xvi, Presidential address by Sir Andrew Clark, 1883.
11. Herringham, *St. Barth. Hosp. Reports*, xxxii. 133.

CHAPTER VI

ABNORMAL CONSTITUENTS OF THE URINE (CONTINUED)

ALBUMOSURIA, CHYLURIA, PYURIA

Albumosuria.

In many cases of suppuration, such as empyema, suppurating hydatid, or internal abscess, in cases of resolving pneumonia, and in some other forms of disease, a body appears in the urine which is not coagulated by boiling with the addition of acetic or nitric acid, but is precipitated by salicyl sulphonic acid, either alone, or when the urine has been mixed with two or three times its volume of a saturated solution of ammonium sulphate. It gives a pink colour on adding caustic alkali and sulphate of copper. Lee Dickinson and Fyffe [1] recommended to treat the urine with an equal volume of 20 per cent. soda solution and then to add a little very dilute solution of copper sulphate. This body, which was thought to be peptone, is an albumose. Its appearance is at present of scientific rather than of clinical interest.

Much greater importance attaches to the presence of that particular form of albumose which was first discovered by Bence Jones, and called after him. It has lately been named 'myelopathic' by Bradshaw of Liverpool, and 'myelopathic albumosuria' is the term now in general use.

In the great majority of cases it is diagnostic of tumour formation in bones, chiefly in the red, but partly also in the yellow marrow. These tumours are of various kinds. Most of them are cases of multiple myeloma, an overgrowth, that is, of elements natural in marrow, without metastasis in other organs. The cells forming this overgrowth may be (*a*) lymphocytes, (*b*) large lymphoid cells, (*c*) myelocytes, (*d*) plasma cells, and (*e*) even erythrocytes.

But albumosuria has also been found in other bone

tumours, in multiple small-celled sarcoma of bone with metastasis in other organs, in multiple chondro-sarcoma, in multiple endothelioma, and once in a case of carcinoma with metastasis in bones.

Besides these it has been found rarely in cases of lymphatic leuchæmia.

The following is a case of diffuse myeloma with unusual appearances in the blood:

Thomas S., 64, was admitted to my wards in St. Bartholomew's on September 8th, 1909. He was very pale, very ill, and very emaciated. He had been losing weight for a year. For five months he had suffered much pain over the lower ribs on each side. It was much aggravated by pressure. For the last seven weeks he had been short of breath, and his strength had rapidly failed. He had had occasional attacks of shivering, and had begun to cough up foul sputum containing blood.

The urine was found to contain albumose of the Bence Jones type. There were no tumours to be felt in any of the bones.

The other striking abnormality was found in the blood, which contained red cells, 995,000 per cmm.; Hb., 24 per cent.; colour index, 1·26; leucocytes, 9,500 per cmm.

The differential count was at first returned as

Polymorphonuclears	9 per cent.
Small lymphocytes	19 per cent.
Large ,, ...	72 per cent.

But these last were subsequently found, when Pappenheim's stain was used, to be chiefly large plasma cells. No nucleated red cells were seen.

The patient died a few days later.

Post Mortem. The only important changes were found in the bones. In the vertebræ the marrow was unduly pale, salmon-pink in colour. In the patellæ and ribs the marrow was like that in the vertebræ. In the head and upper end of the shaft of the humerus it was like red currant jelly, and much the same in the clavicles.

Under the microscope the cells in the marrow were all of an indifferent type, lymphocytic or megaloblastic in character. There were no plasma cells. It was much like the marrow of acute lymphatic leuchæmia.

The blood and organs were examined by Dr. F. W. Andrewes.

This albumose precipitates on heating between 50° C. and 56° C. and also with all ordinary precipitants of albumen (mineral acids, salicyl sulphonic acid, acetic acid and potassium ferrocyanide, gallic and picric acids), but its characteristic is that the copious precipitate formed at about 50° C. gradually redissolves with further heating, until at boiling-point it is wholly or almost wholly dissolved. On cooling it reappears again. It appears that the body is really an albumen, not an albumose, since it gives up proto- and hetero-albumose on digestion with pepsin.[2]

Chyluria.

Instead of being transparent and yellow, the urine is opaque, and either white like milk, yellowish white, or slightly pink from admixture with blood. It sets into a thin jelly, or else deposits small jelly-like masses. Sometimes this coagulation takes place in the bladder. This causes difficulty and pain in micturition, and long clots may have to be pulled out of the urethra.

The opacity and whiteness can be removed by shaking it up with ether. The urine that is left may be clear and yellow. But it always contains some albumen. The ether when evaporated leaves oil.

When it is left to stand for twelve hours or more the urine separates into three layers. On the top is a white layer just like milk. Oil globules may be seen floating on it. Below this the urine is clear like ordinary urine, save that in it floats a gelatinous coagulum. At the bottom is a sediment containing blood-clots, and a brownish deposit containing blood-cells.

It is an almost universal rule that no precipitate takes place on adding acetic acid. This enables the physician to

say that the fluid is not merely a mixture of milk and urine, for acetic acid curdles milk. Salkowski [3] had known cases in which hysterical girls had actually injected milk into the bladder. When therefore a milky urine was sent him to test, he added acetic acid and was not surprised to see a precipitate like casein appear. To confirm the evidence he tested for sugar of milk, but was astonished to find that Trommer's test was negative. In the next sample that he could obtain from the case no precipitation took place with acetic acid, and the condition turned out to be chyluria. This is, as far as I know, the only instance of precipitation like that of casein taking place, and Salkowski himself was unable to explain it.

The coagulum, when, either by simple draining or by squeezing, the fluid has been removed from it, becomes almost colourless, shrinks very much, and gives the reactions of fibrin.

The presence of albumen, of fibrin, and of fat, are the characteristics of chyluria.

Occasionally there is no fat, but only albumen and fibrin, produced by an admixture of mere lymph. The condition is called *lymphuria* or *fibrinuria*.

Chylous urine usually contains blood, sometimes only just enough to colour it a faint pink, sometimes in larger quantities when it is bright red.

Besides these abnormal constituents it also contains the normal constituents of healthy urine.

Chyluria is seldom seen in England. At St. Bartholomew's we had a case in 1898, and no other until 1910.

But it is endemic in other parts of the world, China, India, Egypt, Zanzibar, Mauritius, certain parts of Australia, Brazil, the Southern States of North America, and Bermuda.

There it is one of a group of diseases, of which other members are varicose inguinal lymphatics, lymph scrotum, chylocele, and elephantiasis. They have long been known to be caused by the presence of parasites in the lymph vessels.

The *Filaria bancrofti*, first discovered by Bancroft of Brisbane, is like a piece of white horsehair, the female about

three inches, the male about half as long, with a curly tail. They live in the lymph vessels. In 1881 Sir Patrick Manson [4] showed a scrotum with a worm visible in a dilated lymphatic which had been cut across at the operation.

The embryos (*Microfilaria nocturna*) are found in the blood, but only at night. If, however, the habits of life are reversed, and the patient goes to bed by day and sits up at night, the embryos appear in the blood by day and disappear at night. Mackenzie [5] gives an elaborate chart extending over two months and a half, during which the blood was drawn and the embryos counted eight times daily. They appeared regularly at 6 p.m., and had usually all gone by 9 a.m., the maximum being invariably at midnight. When the patient sat up at night the embryos appeared at 3 a.m. and the maximum was at noon. The appearance of the embryos is therefore related not to the sun, but to the unknown changes in the body which coincide with sleep. The paper contains very good microphotographs of the embryos.

In all these diseases the lymphatics in some one or more parts of the body are greatly distended and filled with chyle. When these lymphatic varices reach the surface of the body, as in lymph scrotum, they often burst and discharge a surprising amount of the fluid. In one case four pints a day could be collected, in another (Roberts) the flow was at the rate of 8 ounces per hour.

The explanation generally given is that the parent worms in some way obstruct the thoracic duct, and that the lymphatics below the obstruction dilate in consequence. Mackenzie's paper contains a drawing by Mr. Hurry Fenwick, showing the extraordinary degree to which this dilatation has progressed. The lymphatic vessels are much slighter than veins, and in consequence dilate much more. Otherwise the process is the same as that by which obstruction causes varicose veins.

Sir Patrick Manson [6] thinks that this dilatation below the obstruction, which may affect the lumbar, the pelvic, the genital, and the femoral lymphatics, and those of the abdominal wall, is a step in the formation of a collateral circulation.

These parasitic cases include the majority of the patients. But sporadic cases occur from time to time in which there is no likelihood of infection. The patient has not been abroad, and the embryos are not to be found in the blood. There have been very few dissections of such cases. Sir William Roberts examined one case which in life had been the subject not of chyluria but of chylous weeping from the abdominal wall. He found local dilatation of the lymphatic vessels, but says distinctly, 'no enlargement or unnatural condition of the thoracic duct or of the lymphatic vessels or glands could be detected.' Port [7] relates another in a man of 63 who had had chyluria intermittently for three years. It ceased entirely for two days while he was under observation, and then began again. He died of prostatic abscess. There was old tubercle in the lungs, and the thoracic duct ran into a mass of bronchial glands through which it would not be traced. Below this it was a little dilated. There was the scar of a tuberculous ulcer in the small intestine, and in the upper part of the gut the lacteals were injected. The mesenteric glands were caseous, and there was a milky fluid in the pelves of the kidneys. He thought this was probably the point of entry of the chyle, but could not prove it in his microscopical sections.

In a case recorded by Havelburg [8] the place of communication was in the wall of the bladder. The dilated lymphatics formed a large loculated sac in which the bladder was partly embedded, and the milky fluid could be pressed through openings in the bladder wall.

In another case the thoracic duct and lymphatics were found by Ponfick [9] to be much enlarged, but no direct communication with the kidney was discovered.

The anatomical evidence is certainly on the whole in favour of such a mechanical explanation as that given above, and perhaps such a negative case as Ponfick's need not be allowed much weight. It must always be difficult to follow the connexion of the lymphatics with the kidney. Roberts's case, however, is different. It remains unexplained.

The physiological evidence is rather more doubtful.

Fat is known to occur in the urine (lipuria) in certain cases of diabetes, and the blood after death looks quite milky from the presence of fat in it (lipæmia). In such cases the lipæmia is undoubtedly due to a failure of assimilation, together with a great increase of fat in the diet, and the lipuria, as I have myself observed, can be stopped by decreasing the amount of fat taken. The fat in the urine is evidently derived from the blood. This is the explanation which Eggel (*Diss. inaug.*, Tübingen, 1869, quoted by Grimm, not seen by me) gave of his case of chyluria, and he stated that he found the blood filled with droplets of fat. I am not aware that this observation has been corroborated.

Eggel's hypothesis does not explain the presence of albumen and fibrin along with the fat. It is admitted that ordinary organic disease of the kidneys does not exist in these cases.

If chyle were being poured directly into the urine, lipuria might be expected to increase rapidly after meals that were rich in fat. Brieger [10] did not find that it did so. But on the other hand, Grimm [11] observed that both the amount and the composition of the fat in the urine of a filarial patient depended upon the fat taken with the food, and Salkowski [12] in a non-filarial case has confirmed his conclusions. Manson says 'a single tumbler full of milk will at once give ocular proof of the patency or closure of the rupture in the varix'.

Senator raises another question. Chyle contains sugar, about the same amount as blood serum, namely 0·1 per cent. But sugar has not been found as a rule in the urine of chyluria, though Morison [13] and Ralfe [14] have detected it. The exclusion of sugar from normal urine, though it exists in the blood, is generally held to be evidence of the selective action of the renal cells. But such an explanation would not hold good for chyluria. Leaking from ruptured lymphatics would hardly give any opportunity for the cells to act.

In considering the course of chyluria those cases must

first be set aside in which the symptom is transient and accidental. Hunt [15] saw a young man who had fallen from a height, and who had chyluria after the accident which shortly disappeared. Wehlan [16] saw another case in an elderly woman. Chyluria lasted a few weeks and then entirely disappeared. In neither were any filaria to be found.

When chyluria is of long standing the symptoms are extremely irregular. The alteration in the urine usually appears suddenly, as might be expected if it is due to rupture of a lymphatic varix. From that time the chyle is found regularly at some time or under some conditions. In some patients the urina noctis is clear, the urina cibi alone contains the chyle. In most it can be greatly diminished by a meagre diet. In others chyle is excreted chiefly after exertion. In a case under Ackermann [17] it could be stopped by lying on the right side. In another (Francotte, quoted by Senator) it came on only when the patient stood up.

Huber's patient,[18] a Swiss who had not been abroad when the chyluria began, and whose blood contained no filaria, passed milky urine after lying in bed, but not during the rest of the day.

Sometimes after lasting a long while it ceases suddenly, as in a lady of 64 after sea-bathing, and in other patients, for no known cause. While Port's patient was in hospital a period of two days occurred during which the chyle quite disappeared. But it reappears as capriciously.

While it lasts the patients sometimes complain of bodily pains of a dragging character, or of a feeling of weight, in the loins and legs. They occasionally lose flesh. Some of them become very depressed. But in others there are no such symptoms and the condition appears to do no harm.

When coagulation takes place within the bladder, as sometimes happens, the passage of clots causes considerable pain and sometimes retention.

Chyluria does not lead to death. It has been known to last for more than fifty years.

Since the condition sometimes ceases abruptly of itself it is not safe to lay too much stress on reported cases. Mangrove bark is said to have cured one case, and Bence Jones thought he had cured one case with gallic acid. He gave the patient towards the end as much as ℥ij daily. In another case gallic acid failed, and tannic acid could not be taken, so he gave tannate of alumina (ac. tannici ℥j, alum ℥j, aquæ ad ℥iij) in doses of about gr. xx, with a successful result. His success does not appear to have been repeated. Ackermann found that tonic treatment was the best he could do for his patient. Methylene blue, thymol, salicylate of sodium, and picronitrite of potassium in ¾-grain doses have been recommended. Atoxyl and the arylarsonates will no doubt be tried in the future. But it must be remembered that the disease is not due to the mere presence of either the adult filaria or the embryo (*Microfilaria nocturna*). Manson says that in Amoy about 10 per cent. of the whole population have the embryo in the blood, and that the great majority are not a bit the worse for it. It is a harmless parasite. When it causes symptoms it is by what we may call an accident. Ackermann's patient, for instance, had left Brazil, where we may safely suppose he became infected, eighteen years before chyluria occurred, and many other patients have often shown no symptoms till long after their return from the tropics. The way in which the accident occurs, the process by which the thoracic duct is blocked, is still unknown. In Mackenzie's case the thoracic duct was apparently blocked by inflammatory tissue, but the worms were nowhere found. No anti-parasitic remedies would have removed the inflammatory tissue which caused the chyluria.

Pyuria.

When pus is present to any considerable amount it settles as a cream-coloured mass at the bottom of the urine glass. Pus cells can often be seen with the microscope when no such deposit exists.

Examination with the microscope is the only satisfactory test for pus.

The following chemical tests can be employed :—

On adding an equal amount of caustic alkali to the urine the fluid becomes slightly viscid and stringy masses gradually form in it.

On adding ozonic ether to the urine bubbles of gas form in the fluid.

Pus cells appear in the urine whenever there is inflammation of any part of the urinary tract from the renal pelvis downwards. The urethra and vagina should always be examined. If they are healthy the source of the pus may be the bladder, the renal pelvis, or some external abscess. Cystitis is a frequent cause. It occasionally occurs as a sequela of typhoid fever. Tuberculous ulcer is another cause that is not uncommon. The largest amounts of pus, however, are seen in cases of pyo-nephrosis. When the pus comes from the kidney the urine is usually acid. It is sometimes acid when cystitis or ulceration of the bladder is present, but in the majority of cases of cystitis it is alkaline.

It should be an invariable rule in any case of pyuria to make an examination by the microscope, by test-tube cultivation, and, if necessary, by inoculation, in order to discover the infective agent. I remember a case of tubercular disease of the bladder which had long remained unsuspected because this precaution had not been taken.

References.

1. Lee Dickinson and Fyffe, *Clin. Soc. Trans.*, xxv. 64.
2. Chief papers on myelopathic albumosuria : Bradshaw, *Trans. Roy. Medico-Chirurg. Soc.*, 1898, lxxxi. 259 ; and with Warrington, ibid., 1899, lxxxii. 251 ; Parkes Weber, ibid., 1903, lxxxvi. 397 ; De Castello, *Zeitsch. f. Klin. Med.*, 1909, lxvii. 319. The two last are exhaustive accounts with good bibliographies.
3. Salkowski, *Berl. Klin. Woch.*, 1907, xliv. 51.
4. Manson, *Trans. Path. Soc. Lond.*, 1881, xxxii. 285.
5. Mackenzie, ibid., 1882, xxxiii. 394.
6. Manson, *Allbutt's System*, second edition, ii, Pt. II. 944.
7. Port, *Zeitsch. f. Klin. Med.*, 1906, lix. 455.
8. Havelburg, *Virch. Arch.*, 1882, lxxxix. 365.
9. Ponfick, *Deutsch. Med. Woch.*, 1881, 624.

10. Brieger, *Zeitsch. f. Physiol. Chemie*, 1880, iv. 414.
11. Grimm, *Virch. Arch.*, 1888, cxi. 341.
12. Salkowski, *Berl. Klin. Woch.*, 1907, xliv. 51.
13. Morison, *Trans. Path. Soc. Lond.*, 1878, xxix. 395.
14. Ralfe, ibid., p. 388.
15. Hunt, *Brit. Med. Journ.*, 1889, i. 421.
16. Wehlan, *Med. Rec. N.Y.*, 1890, xxxvii. 184.
17. Ackermann, *Deutsche Klinik*, 1863, xv. 221.
18. Huber, *Virch. Arch.*, 1886, cvi. 126.

CHAPTER VII

ABNORMAL CONSTITUENTS OF THE URINE (CONTINUED)

ABNORMAL PIGMENTS, ERRORS OF METABOLISM— ALKAPTONURIA, CYSTINURIA

Abnormal Pigments.

THE usual yellow colour of the urine is due to a pigment called Urochrome.

Urobilin is often added, and, when it is present in large quantities, changes the colour to a warm *orange*. This is common both in hepatic disease, and where hæmolysis is going on, as for instance, in pernicious anæmia, and during absorption of large hæmorrhages. Urobilin is formed in the intestine out of the bile-pigment. It gives a single band in the green of the spectrum towards the blue. If a chloroform extract of the urine be treated with solution of iodine and caustic potash added, a green fluorescence develops.

Urine is sometimes *red, claret-coloured, or purple,* without the presence of blood or even of hæmoglobin. Such urines usually contain an excess of *Hæmato-porphyrin,* which in small quantities is a normal constituent. The colour, however, is not due to the hæmato-porphyrin, but to some as yet unknown purple pigment. All hæmato-porphyrin can be removed and yet the purple colour remain. The commonest cause of this curious phenomenon is sulphonal poisoning. Such cases are often fatal. Most of them have occurred in lunatic asylums where patients have been given sulphonal regularly over long periods to cure sleeplessness. The change in the urine is generally the first indication, and is followed by abdominal pain, diarrhœa, and severe nervous symptoms. Hæmato-porphyrin gives a characteristic spectrum, but it cannot be seen in normal urine until it has

been acidulated with acetic acid, and shaken with amylic alcohol. The amylic extract gives the alkaline spectrum of hæmato-porphyrin, a narrow band between *C* and *D*, two broad ones between *D* and *E*, and one near *F*. In the red urines the spectrum may be this, or may consist of two bands like those of oxyhæmoglobin. This might be puzzling, but these urines do not give a blue colour with tincture of guaiacum and ozonic ether, and there is usually no albuminuria, which tests prove the absence of hæmoglobin.[1] Rhubarb and senna in large doses may produce a purple colour in the urine.

Bile-pigment in the urine colours it *green* or *brown* or even *black* when jaundice is intense. The tests are a green ring formed at the line of juncture when urine is poured gently on to the surface of nitric acid in a tube, or a green colour when tincture of iodine is dropped into the urine. When the urine is shaken up the foam has a green tinge.

Aniline dye taken in sweets may colour the urine *red*, *green*, or *blue*.

Urine may look *black* from containing a large amount of bile-pigment or of blood, or of hæmoglobin. Hæmato-porphyrinuria may also occur with very dark urine. Urine that is either black when passed or turns black on standing is seen in certain other conditions.

1. *Melanuria* due to melanin occurs with melanotic sarcoma when the internal viscera are attacked. The urine is usually normal in colour or brown when passed, and in that state contains only melanogen. Nitric acid in the cold turns it black at once. Ferric chloride does the same, and gives a grey precipitate which is dissolved in excess of the reagent.

2. *Indicanuria* is commoner. It does not give the ferric chloride reaction, and does not immediately blacken with nitric acid in the cold. These tests distinguish it from melanuria. But if warmed with nitric acid it blackens. To the dark urine add an equal volume of strong HCl and a few drops of nitric acid, and boil. After cooling shake it up with chloroform, which takes up indigo blue and forms

a blue layer on separating out. Or to the urine and HCl add first a little chloroform, and then drop by drop, shaking after each drop, a dilute solution of bleaching powder. Indigo blue is formed and taken up by the chloroform as before. Excess of bleaching powder destroys the colour. Indican is indoxyl-sulphuric acid and indoxyl is the oxidized form of indol, which is a product of proteid decomposition. It is formed in the intestines in constipation, or obstruction, or putrefaction from bacterial activity, and sometimes from the putrefaction of collections of pus, as in empyema and bronchiectasis.

3. *Carboluria* gives a green colour which may turn black on standing. The same may happen with similar drugs such as salol, naphthalin, and creosote. It may be noted that carboluria may occur from the use of antitoxic serum put up for preservation with small amounts of carbolic acid. A boy in my wards had a streptococcal empyema, and 50 c.c. of polyvalent anti-streptococcic serum was injected into the pleural cavity. The next day the urine was faintly green. It did not react with ferric chloride, but gave the characteristic yellow precipitate with bromine solution.

4. Hale White described [2] the blackening of certain urines from *phthisical patients* after long keeping. Garrod suggests it may be due to phenol, like the preceding.

5. In the disease called *Ochronosis*, and in certain other rare cases, the urine blackens on standing.

6. And lastly in *Alkaptonuria*.

In alkaptonuria the urine when passed is of a natural colour, but quickly becomes dark-brown or black on exposure to the air. This change is intensified on adding alkalies. Any linen wetted with the urine becomes deeply stained when exposed to the air. The urine reduces Fehling's solution with the aid of heat. But it does not give the bismuth reaction, it does not rotate either to right or left with the polariscope, and it does not ferment with yeast. It reduces ammoniacal silver nitrate solution in the cold.

This is a rare abnormality. Garrod [3] has collected 40 instances, 29 in males and 11 in females. In most cases

the condition is congenital and lifelong, and does not affect the health. In a few it has occurred as a temporary condition, and in one or two of these it appeared shortly before death. It is remarkable that of 32 congenital cases no less than 19 have occurred in seven families, and Garrod finds that in far more than the natural proportion the patients are the offspring of first cousins. He believes that the condition is a 'sport', and that it conforms to the Mendelian laws of inheritance, being of a 'recessive' character, and only becoming manifest when the strain exists in both parents.

The chemical characteristic of the urine is that it contains homogentisic acid, which is a member of the aromatic group and can be derived from tyrosin and phenyl alanin. These are aromatic products formed in the breaking down of the protein molecule, and whereas in ordinary persons this process continues until the benzene ring present in these bodies is in its turn broken up, in alkaptonurics there appears to be an inherent inability to break it up. It is excreted whole in homogentisic acid.

The actual amount of homogentisic acid excreted depends upon the proteid food taken. The proportionate analyses which have been made by Langstein, E. Meyer, Falta, Garrod, and Hele show that the acid bears a very regular relation to the nitrogen excreted, and that the variations depend upon the amount of tyrosin and phenyl alanin in the food rather than upon the individual. Falta and Garrod are of opinion, therefore, that where the defect exists at all, at any rate in the usual congenital cases, it is total. In other words, it may be said that in the particular branch of the metabolic factory which is devoted to the aromatic (benzene) products of proteid decomposition, these bodies are carried through certain stages just as they are in a normal man, but that the machinery for making what are usually the final products is absent, and consequently the process stops short at what in the normal man is an intermediate body.

Cystinuria [4] is another metabolic abnormality, which I

place here, though it does not colour the urine, because of its analogy with alkaptonuria. Cystin occurs in symmetrical hexagonal tables, insoluble in acetic acid and by heat, but readily soluble in ammonia. If the deposit is dissolved in caustic ammonia, and evaporated in a watch-glass, the crystals are easily obtained. Until lately cystinuria was of interest merely as a rare clinical cause of gravel and calculus. It is now known to be a symptom of an error of metabolism, which may be congenital and hereditary, and is then usually permanent throughout life. Cystin contains sulphur, and is a product of protein decomposition, of which, in normal persons, some goes to form the taurocholic acid of the bile, some is perhaps taken up by the tissues, and the rest appears as sulphates in the urine. In cystinurics these processes do not take place in the normal manner, but in different instances they vary in different ways, and are also accompanied by other abnormalities in nitrogenous decomposition, so that both S and N metabolism may be affected. Thus it happens that cases of cystinuria differ widely among themselves.

References.

1. Garrod and Hopkins, *Journ. of Pathol. and Bacteriol.*, 1896, iii. 434.
2. Hale White, *Brit. Med. Journ.*, 1892, i. 1070.
3. Garrod, *Medico-Chirurg. Trans.*, 1899, lxxxii. 367 ; idem, *Lancet*, 1902, ii. 1616.
4. Idem, 'Inborn Errors of Metabolism ; the Croonian Lectures for 1908,' *Lancet*, 1908, ii. 142, 173, 214, with full reff.

CHAPTER VIII

METHODS OF EXAMINATION OF THE RENAL FUNCTION

THERE are several methods by which the capacity of the kidneys to perform their proper functions can be carried out.

1. The first is that of chemical analysis of the urine. In clinical practice this is usually confined to the abnormal constituents. If albumen or sugar is present the evidence is, with certain exceptions, conclusive for disease. This will always remain the most important division of chemical analysis, and it is not easy in ordinary practice to go beyond it. But where special knowledge is desired, more must be done, and the excretion of some at least of the normal constituents must be estimated. The most important are urea, the phosphates, the chlorides, and the sulphates. It is not necessary for me to describe the process necessary in each case. There are many excellent books already written on the subject. But I shall point out certain precautions that must be observed and certain fallacies that must be remembered in all these cases.

In the first place, it is of no use whatever to estimate anything but the total amount passed in a complete daily cycle. The patient should pass water the last thing before breakfast, so that the bladder may be empty, and from that time all the urine should be collected until and including that passed just before breakfast the next day. In that way, under conditions of health, no food is taken for the last ten hours of the cycle. This interval is usually long enough to estimate the products of all food previously taken. The total daily excretion will then fairly represent the total daily intake. But in cases of kidney disease, at any rate, one day by itself is often unreliable. From many causes, some connected with the kidney, some with the other organs,

the excretion of the day's intake may not be completed in the twenty-four hours, or it may contain some solids left over from the previous day. It is therefore always desirable, and in any estimation that is meant to be exact it is necessary, to extend the analysis to several, say six, consecutive days.

Secondly, it is of no use to estimate the totals excreted unless we can in some measure estimate the total intake. Physiologists, who can experiment with healthy animals or men, are able to reach a high degree of accuracy by using a diet composed of substances whose exact composition is known. We are under greater disadvantages. Persons who are sick refuse to take such artificial diets, and if they try are often unable to assimilate them. Milk is of course the staple which lies to hand. But it is generally impossible to put a patient on milk and nothing else. Such a diet is disliked and upsets digestion. It produces an unnatural state which gives us little information as to the natural power of excretion. It is therefore desirable to approach as nearly to an ordinary diet as we can. Every ordinary diet, however, is mixed, and with each fresh ingredient we complicate the calculation and introduce a source of error.

A third difficulty is caused by that portion of the intake which passes out with the fæces. In all observations which attempt to be exact the contents of the fæces must be estimated. This is usually done with the help of some coloured substance such as charcoal, of which one dose is given at the beginning and another at the end of the experiment. The black stools which result mark off the fæces which correspond to the ingesta with which the estimations are concerned.

It is evident that we must not expect too high a degree of accuracy in such results, and must be prepared to rely only upon broad variations from the normal as evidence of disease.

2. A second method is that called cryoscopy. It consists in comparing by means of Beckmann's apparatus the freezing-point of urine with that of distilled water or other fluids. Its value depends upon the law that the freezing-

point of any fluid tends to sink proportionately to the number of molecules which the fluid contains. The freezing-point of the healthy urine of Europeans varies between −1·0° C. and −2·7° C. This is a wide range. That of the urine in Bright's disease is said to vary from −0·1° C. to −1° C. This is only true of those cases in which the disease is so far advanced as to have greatly damaged the renal structure. Still, in these cases, if proper allowance could be made for the increase of water, which is often a marked feature, the method would afford a useful indication.

The specific gravity gives quite a different indication. It depends upon the weight of the total molecules. A molecule of albumen contains a vastly greater number of atoms than a molecule of salt, and adds much more to the density of a fluid. But each affects the freezing-point equally. They may be compared to a hundred-pound note and a halfpenny, and the chlorides have accordingly been called by the French ' the small change of the circulation '. The chlorides, which are the most abundant salts of the urine, affect the freezing-point more than any other factor.

The following uses have been made of the estimation of the freezing-point.

(1) Its depression (usually denoted by Δ) in the urine has been compared with that in the blood, which is normally 0·56° C., and the relation between the two has been used as a gauge of the amount of work done by the kidney.

Since, however, the urine in some cases has a Δ of less than 0·56, the kidneys would then have done work that was actually negative. Which may be taken as absurd. The same objection applies to the comparison of the electrical resistance of the blood and the urine.

(2) It has been found that as the urine becomes more concentrated the proportion of NaCl to other salts tends to fall. This has been brought forward in support of the theory that the filtrate from the glomeruli represents the chloride content of the blood, but that in the passage down the tubules the chlorides are exchanged against other salts, and are themselves, along with water, reabsorbed into the blood.

A comparison, therefore, of Δ of urine and Δ of blood has been used to gauge the rapidity of the blood-flow in the kidney.

It may be remarked that if the theory were correct, urine, however dilute, should never contain a lesser percentage of NaCl than that present in the blood. This, however, is not the case.

(3) Calculations have been made of the excretion per unit of weight. If V is the volume of the urine and P the weight of the body, then $\frac{\Delta V}{P}$ is the formula for the excretion per unit of weight.

(4) Let p be the percentage of NaCl found in the urine by chemical analysis. Then, since 1 per cent. of NaCl depresses the freezing-point by 0·613° C., that part of the total depression in any urine which is produced by the NaCl which it contains can be calculated as follows: $a = p \times 0{\cdot}613$, where a expresses the depression due to the chlorides.

Then the part taken in the same depression by the non-chlorides, that is, roughly, the organic elements together with phosphates and sulphates which are chiefly derived from organic sources, will be expressed by $\Delta - a$, which is usually denoted by δ and $\frac{\delta V}{P}$ will represent the excretion of the organic elements per unit of weight.

There is a certain fascination about the use of algebraical formulæ, but, to speak plainly, no subject has less pretence to the exactness which the use of such formulæ requires than medicine. We may safely neglect any rules based upon them.

In the above case the whole of the elaborate structure is based upon the estimation of NaCl, or, as is generally the case, upon the estimation of Cl alone. The importance of the other formulæ rests upon that, and upon the interpretation given to it. The latter is, however, so uncertain that the remainder falls to the ground.

3. Another method was devised by Sir Almroth Wright.[1]

One volume of blood is mixed in a capillary test-tube with two volumes of salt solution, of varying strengths, until that particular salt solution is reached with which hæmolysis takes place. The strength of the salt solution is known.

One volume of blood is mixed in a similar way with two volumes of blood serum. The dilution of serum at which hæmolysis takes place is reckoned to contain the equivalent of the hæmolysing salt solution, and by finding the proportion between the two, the NaCl content of the serum is calculated and called its hæmosozic value.

The same procedure is then carried out with two volumes of urine.

Then the fraction formed by the degree of dilution of the urine, divided by that of the serum, gives the proportion of concentration of the urine as compared with the serum. This is supposed to represent the work of the kidneys, and is called the excretory quotient.

In health Wright found that this quotient did not fall below 2, but in renal disease was much below 2, and he claimed that albuminuria not due to renal lesions, e. g. physiological albuminuria, could thus be diagnosed from that due to organic change in the kidneys.[2]

McCay, however, showed that in Bengal the excretory quotient was always much less than 2, and also that low excretory quotients resembling those of nephritis were found in various forms of anæmia.

This must depend on the state of the blood, for the kidneys were considered to be healthy, and consequently the low quotient of nephritis may equally be due not to the incompetence of the kidney, but to some tendency in the blood or tissues to retain chlorides. This destroys the value of the method.

4. Another method is to estimate the toxicity of the urine by injecting it into rabbits. This, which is based on most uncertain premises, is also liable to vary with every variation in the quantity of water excreted. It is entirely useless for any clinical purpose.

5. Lastly there remains the administration of some body whose detection in the urine is easy. The time at which excretion begins, its duration, and the amount of the substance which is excreted are all noted and compared with the normal. The substances employed have been dyes such as rosanilin, fuchsin, and methylene blue, drugs such as iodide of potassium and sodium salicylate, or natural ingredients such as common salt in unnatural quantities.

The dyes such as methylene blue, which is best given in one dose of 1 c.c. of a sterilized 5 per cent. solution, injected subcutaneously, usually appear in one hour, and disappear in from thirty-six to sixty hours, but they are subject to many variations.

The method has been elaborated in several ways. The estimation has been made quantitative by preparing a series of known solutions and comparing the colour of the urine passed from the first faint tinge to the time of complete disappearance. This must be done on each occasion that the patient micturates, and the quantity passed each time must also be taken into account. The first appearance of the colour is usually delayed in chronic nephritis with fibrosis. Sometimes in the early stages it appears more quickly than natural. Sometimes its excretion does not run a regular course, but is intermittent. This may occur in the sound kidney in cases of one-sided disease such as calculus or tubercle, while the diseased kidney excretes regularly. The elimination is usually prolonged in cases of fibrosis. It sometimes lasts for a shorter time than usual in early stages. But these variations occur also in normal kidneys. Lastly it has been found that the colouring matter is liable to be decomposed, and to pass through the kidney in a form which is colourless when passed, but when boiled in an acid solution gives the blue colour [3].

I have seen a remarkable delay in the excretion of phenol in a case in which no symptoms of nephritis existed. A girl with diabetes complained of muscular pains, for which she was given salicylate of soda. The characteristic reaction did not appear in the urine until four days later. The same

patient was on another occasion given 5 grains of phenacetin. The phenol reaction appeared two days later.

The method of experimenting with common salt is to put the patient on a pure milk diet for five days and on the third day to give 10 to 20 grammes of common salt in water, or after calculating the amount of salt in a fixed diet to add on one of a series of days 10 grammes of salt, and to estimate the output on each day of the series. The amount excreted, and the rapidity with which it passes, furnishes a measure of the permeability of the kidney.

As a test of the glandular activity phloridzin has been much employed. It is said that renal disease greatly diminishes or retards the production of sugar.

It must, however, be confessed that these methods of testing the action of the kidney are subject to the drawback that the kidney does not react alike for all substances. The methylene blue reaction may not vary with the chloride test, and either or both may react differently to urea. Thus it is not safe to argue that a good reaction with any one of them means a good excretion of the natural products. Yet this is, after all, the point at which the whole process aims.

We owe, however, to Schlayer[4] an interesting development of this line of research. From experiments on rabbits he believes that the powers of excreting water and salts vary independently. He thinks that this function test (*Funktionsprüfung*) is of equal importance with, or even more important than, anatomical investigation, and founds on it a distinction between 'vascular' and 'tubular' nephritis. It is too early yet to say that the theory has been established. His method has been used clinically by v. Monakow.[5] At present, however, there is nothing better or more reliable, probably it would be safe to say that there is nothing so reliable, as an ordinary chemical analysis of the excretion carried out with the precautions mentioned above.

For ordinary medical purposes the excretion of both kidneys together is all that is necessary for examination. A nephritis confined to one side is practically never seen.

Occasionally one kidney is considerably more shrunken than the other. But I have never seen a case in which one kidney was natural and the other diseased.

In cases, however, of pyelitis, pyelonephritis, calculus, cancer of the kidney, and so on, it is often of great importance to establish the condition of each kidney separately.

One method of doing this is by a Luys separator. If care be taken to keep the base of the instrument upon the fundus of the bladder it is reliable.

Of late years, however, the catheterization of the ureters has taken the place of separation in the bladder, and, though it occasionally gives rise to unpleasant symptoms, its results are so much more certain that it will certainly supplant the other method.

References.

1. Wright, *Lancet*, 1904, i. 921.
2. Idem, *Lancet*, 1905, ii. 1164.
3. For an account of all these methods see Albarran, *Exploration des fonctions rénales*, Paris, 1905.
4. Schlayer u. Hedinger, *Deutsch. Arch. f. Klin. Med.*, 1907, xc. 1; idem u. Takayasu, ibid., 1911, ci. 333.
5. v. Monakow, ibid., 1911, cii. 248.

CHAPTER IX

HÆMATURIA, FAMILY HÆMATURIA, AND ESSENTIAL HÆMATURIA

Hæmaturia.

The passage of blood with the urine is recognized by the naked eye, by the spectroscope, by certain chemical reactions, and lastly with the aid of the microscope.

The colour of the urine changes to red, brown, smoke or mahogany colour, or becomes as dark as porter. The variation depends partly upon the quantity of blood and partly upon the form in which its colouring matter is present. The greater the amount of blood lost, the deeper will in any case be the colour. But whereas blood effused in the bladder or urethra is red and gives a spectrum of hæmoglobin, that which is effused in the kidneys usually tinges the urine rather brown or greyish brown, than red, and gives the spectrum of methæmoglobin. This change is due to a long contact and intimate mixture with the acid urine, such as usually occurs in renal hæmorrhage, but there are cases in which the blood, though effused in the kidneys, is still red when passed. Urine brown from methæmoglobin can be made red by adding an alkali, and then gives the spectrum of alkaline hæmatin. Such urine sometimes turns red spontaneously on standing, I suppose from the formation of ammonia in it.

The colours given by blood are imitated to a certain extent by senna and rhubarb. I have seen a double dose of mist. sennæ co. give a remarkably vivid colour to the urine. It was like a brown sherry. The red colouring of lollipops, an aniline die, is sometimes excreted in the urine. In one such case that I saw, the colour was too brilliant for blood, and of course the urine did not give the other reactions

immediately to be described. The child had been eating sweets coloured with red aniline dye.

The pink of uroerythrin, and the curious orange colour of urobilin must be also distinguished.

Lastly, all the black or dark colours (see Chapter VII) which arise from other sources may for the moment deceive the eye.

The chemical reactions, like the spectroscopical, depend upon the hæmoglobin.

Put a drop of tincture of guaiacum in a test-tube, dissolve it in an inch of ozonic ether, and trickle the solution on to the surface of the urine in another test-tube, or add the guaiac to the urine, shake up, and then add the ozonic ether. A blue ring forms at the line of contact. If the ether be poured in roughly so that it mixes with the urine the blue colour forms throughout the mixture, and gradually narrows to a ring as the fluids separate. This is a very delicate test. The only source of error is that iodide of potassium also gives the blue colour. But the iodide must be in large quantities to produce this reaction.

In Heller's test, which is often used in Germany, caustic potash is added to the urine, which is then boiled. Earthy phosphates are precipitated, and, by carrying down the alkaline hæmatin formed, are tinged red. But other substances, such as urobilin, hæmatoporphyrin, and melanin are said to produce the same result. The former test is the more delicate.

All the above phenomena, colour, spectrum, and reactions, depend upon the hæmoglobin of the blood cells and are therefore common to hæmaturia and hæmoglobinuria. The two can be distinguished only by the microscope. The red cells are often crenate, but otherwise offer no difficulty. They are often collected in casts.

Blood enters the urinary passages at various places, and for purposes of diagnosis there are several points which deserve attention.

When it comes from the urethra in front of the triangular ligament it drips from the meatus continually, and if urine

is passed a little blood precedes the urine, while the last part of the urine is clear. Bleeding from the urethra may be due to external injury, such as a kick, or to the passage of a catheter, or to calculus. Or again it may come from some nævoid growth or from a urethral chancre, and it occurs also in the urethritis of gonorrhœa. Lastly coitus or chordee sometimes ruptures the corpus spongiosum and gives rise to hæmorrhage.

When bleeding takes place in the bladder or prostate the blood tends to sink and clot. Thus the urine, itself tinged with blood, is succeeded by pure blood in clots which often cause great pain in their passage. The blood is usually bright red, unless very copious, when it may be very dark. It has not as a rule undergone the chocolate modification which betokens methæmoglobin.

There are many causes for hæmorrhage in the bladder or prostate.

Injury may cause it, whether from without or from within, as from a catheter, or a calculus, or from the sharp spine of the ovum of Bilharzia ; or it may arise from cystitis or prostatitis ; or from tubercular ulceration, or from new growth, whether villous or malignant. The eggs of Bilharzia, large, oval bodies 0·1 mm. long, are easily detected with the microscope.

Bleeding sometimes takes place from the ureter, as, for instance, during the passage of a calculus. I once saw a case of granular kidney with repeated hæmaturia, in which the mucous membrane of the ureter was full of dilated veins. They seemed to have been the source of hæmorrhage.

In the pelvis of the kidney, beside the above causes, hæmorrhage occurs as a symptom of chyluria. Blows over the kidney are frequently followed by hæmaturia, and it may even be produced by mere muscular action (Morris), but in medical practice the commonest cause of hæmorrhage from the parenchyma of the kidney is nephritis. It is common in the acute form, and has been seen as the initial symptom of enteric fever.[1] In chronic nephritis recurrent hæmorrhages are frequent.[2] Bowlby[3] relates two cases of granular kidney

secondary to disease of the lower passages, in which fatal hæmaturia occurred, and a third of very severe bleeding in primary chronic nephritis. In the two former, which died, a post-mortem examination was made. In the second, blood was found in the pelvis of the kidneys. In the first, the whole parenchyma, both cortical and medullary, was infiltrated with blood. Infarction and tubercle produce it occasionally. Sometimes the first symptom of renal tuberculosis is sudden and profuse hæmaturia, just as a large hæmoptysis may be the first indication of phthisis.[4] In some cases hæmaturia comes on without any other symptoms, oxalate crystals in considerable numbers are seen in the urine, and it is found that the patient has been taking stewed rhubarb. Asparagus sometimes causes it[5] and so do strawberries. But neither asparagus nor strawberries contain more than a very little oxalic acid. In some little children uric acid crystals appear to cause it. In these cases of lithuria, or oxaluria, the source of the hæmorrhage may be the pelvis or ureter.

Renal calculus and new growth of the kidney also produce hæmaturia.

Hæmorrhagic diseases such as scurvy or purpura often cause hæmaturia. It is not infrequent in the forms called rheumatic purpura and Henoch's purpura.

In 1909 a little girl of 9 was admitted into my ward under Dr. Drysdale with this combination. For a month her arms above the elbow had swelled, for three weeks her legs and ankles had hurt her so much that she could hardly walk. Ten days ago a hæmorrhagic rash had appeared on the skin and she had had severe abdominal pain since then. She had often had similar rashes, and occasionally they had been accompanied by pains in the joints. On October 1st, eighteen days after admission, a trace of blood and albumen first appeared in the urine. On November 25th she had tonsillitis, her temperature rose from subnormal to 101·2° F. and remained irregularly raised for a week. The next day profuse hæmaturia occurred, joint pains the following day. By December 28th all symptoms had disappeared. Both the urine and the

blood were cultivated, the latter three times. No organism was obtained from either.

There are, however, other cases of hæmaturia in which none of these recognized causes appear to exist. I remember two cases in which, after severe exertion in walking, men for a time passed blood. Both occurred in Switzerland, and from the symptoms it seemed that the bladder was the part affected. I must add, however, that the urine could not be examined by the microscope. Both these men many years later suffered with enlarged prostate.

Family Hæmaturia.

Some remarkable groups of cases have been recorded by Attlee [6] and Neave,[7] by Guthrie [8] and by Aitken.[9]

Attlee saw in 1901 three sisters aged $5\frac{1}{2}$, $4\frac{1}{2}$, and $2\frac{1}{3}$ years, who were all admitted for recurrent hæmaturia. The eldest was feverish, during the attack, and had some bronchitis, but except for hæmaturia was healthy in other respects. The blood disappeared in two weeks, but the urine contained a trace of albumen five months later. The second had had one previous attack of hæmaturia, and had been subject to fits since eleven months old. There were granular casts but no crystals visible. The child seemed healthy in other respects. A third attack occurred four months later, and a fourth six weeks after that. The younger had a feverish attack ushered in by a fit and by frequent vomiting. Four years later, in 1905, the same children were seen by Neave. Their general health remained good, but albumen and blood seemed to have increased. The father of these children had died, at the age of 30, from uræmia.

Guthrie described a family in which hæmaturia seemed to be hereditary. It was known to have occurred in two generations, and of a total of fifteen individuals twelve were affected. Both males and females were subject to the disease. The individuals known to Guthrie were a mother aged 40, her daughter aged 15, and her son aged 6 years. The general health was not involved. The mother had

ceased to be affected. The children were under observation for three years. The urine always contained blood which at times was greatly increased. As blood casts were seen, the blood presumably came from the renal cortex. Dr. Guthrie tells me that now, 1908, both children have outgrown the disease and no longer pass any blood.

Aitken traced the disease through four generations. The family through these generations contained seventeen members, of whom ten were affected. Seven of the family were known to Aitken. All were subject to recurrent febrile attacks, for which no cause could be assigned, in which the hæmaturia was much increased. But it was constant in the intervals also whenever he examined it, though it was so slight as not to be noticed by the mother. One of the children, aged 5 years, died in an acute attack with symptoms of uræmia.

These cases are probably in a class by themselves. They are free from the usual symptoms of renal disease, retinitis, cardiac hypertrophy, arterial sclerosis, and dropsy. Aitken mentions that the six children seem to have had excellent health. The mother, aged 40, and the two children known to Guthrie have outgrown the conditions. On the other hand, Attlee and Aitken each report a case of uræmia. It seems, therefore, that though not of the usual type these cases are liable to be affected by the same fatal symptoms. Calculus, tubercle, and sarcoma can certainly be excluded. Further observations are much wanted. No autopsy has yet been made on such a case. It must be remembered that true nephritis also occasionally shows a marked tendency to be inherited.

Essential Hæmaturia.

There occasionally occur cases of hæmaturia from one kidney alone of an unusual nature. Sometimes the bleeding has begun suddenly and is accompanied by no other symptom. Sometimes it has recurred over a period of several years. When discontinuous, the attacks of hæmorrhage are often accompanied by pain in one loin, sometimes radiating to the

groin or thigh. The cystoscope shows the blood to be coming from one ureter only. Usually the bleeding is thought to be due to calculus, or tubercle, or new growth. Sometimes the severity of the hæmorrhage renders an operation necessary as a last resort, even when the diagnosis is doubtful. The kidney is exposed, and either carefully examined by palpation and needling, or incised and laid freely open. No obvious disease is discovered. Small pieces of the organ have been sometimes removed for microscopical examination. The organ is then sewn up and put back. In other cases nephrectomy is performed. Whatever is done usually, but not always, stops the hæmorrhage within a few days. In one or two cases nephrotomy was unsuccessful, and nephrectomy was performed later. The cure after nephrotomy is sometimes permanent; occasionally the bleeding has recurred from the same side, and more rarely from the other. In many instances the cases are reported too soon after operation for this point to be settled.

Recently I saw a case which appeared to me to belong to this group. A gentleman, aged 59, was seized at the age of 32 with hæmaturia for which he could assign no cause. He had been up to that time a healthy athletic man. The first attack lasted six weeks and gradually ceased. He has had frequent attacks since. They are not brought on by cold, or diet, or by any other cause known to him, unless perhaps fatigue predisposes to them. He has played cricket all through such attacks, and, speaking generally, has not altered his life in any way because of them. He has been examined by two of the first surgeons of the day with a cystoscope, and has been by each informed that the bladder is perfectly normal.

So far as symptoms go he has never had any real pain. He has had a little dull aching in the left loin, never on the right. There has never been any swelling of the face or of the legs. He sometimes passes clots. He is a temperate man, usually drinking barley water, and as a rule micturates only once during the night.

I saw him in the middle of such an attack. The urine

was almost like blood, sp. gr. 1020, neutral reaction. The deposit consisted of nothing but blood cells and a few crystals of uric acid. The heart was not hypertrophied; the radial was not thick, the systolic pressure was 120 mm. Hg. The fundus was natural. There was no œdema of the legs. There was no abdominal tumour, and no tenderness.

He did not wish again to undergo cystoscopy, so that I was unable to discover whether the blood was coming from one kidney alone. Disease of the bladder, new growth, calculus, and nephritis seem to be excluded.

Cases with a history like this are of more than one class.

Some of them are due to a nævus of a renal papilla. Fenwick,[10] Whitney,[11] and Cabot [12] have described such cases.

Some of them are due to torsion of the pedicle of a movable kidney compressing the renal vein.

But after eliminating cases with a definite causation, there remains a large number in which either no lesion is discovered at all, or those which are discovered seem insufficient to account for the bleeding. Eshner [13] has collected and compared 48 such cases, of which 31 were in female and 16 in male patients. Twenty-seven of them were between 20 and 40 years of age. They are equally divided between the two kidneys. Kretschmer [14] gives a still larger bibliography, and Hale White [15] completes it up to date.

In the great majority of cases in which the kidney has been carefully examined evidence of some degree of chronic nephritis has been found. Of Eshner's collection only two cases out of about a dozen which were thoroughly examined were pronounced normal. But even when this is the case the explanation of the hæmorrhage is not easy. As above remarked, some of the cases are accompanied by great pain. These cannot, I think, be separated from those with hæmorrhage alone, but they are even more difficult to understand. Mansell Moullin [16] relates a case in which, beside hæmaturia, there was severe and repeated renal colic on the right side. He operated, but the symptoms did not improve and the patient died. There was no calculus and both kidneys were granular. In the same volume Howard Marsh describes

a case in which after removal of the left kidney violent paroxysms of pain in the right loin, with hæmaturia, occurred. At death the remaining kidney appeared pale but healthy, and no explanation of the symptoms could be given. In many of the cases the changes described are so slight as to make the diagnosis of chronic nephritis uncertain.

But there is a considerable number in which either microscopical examination has proved negative (Klemperer, Schede, Rovsing, Morris, Hale White), or at least to the naked eye the kidney has appeared healthy, or the subsequent history is sufficient to prove that chronic nephritis, which is practically never confined to one kidney, was not the cause. Some of them have recovered and remained well without operation (Harris, Spitzer), and others have remained well for several years after an operation. Hale White gives one or two cases of this kind and I remember a case of my own.

A healthy looking man, aged 25, was training for a long walk, when in August 1903 he had sudden acute pain in the left loin and passed bloody urine. A few days later the pain was again repeated and passed downwards to the left testicle, while again there was hæmaturia. These attacks recurred several times. He was more liable to them when standing long, or walking about. He had also a continual dragging pain, and for the last two months almost continually a dull aching in the loin.

He had had no previous illness, was moderate in alcohol, and denied syphilis. There was no gout or phthisis in the family.

When he came with this story to the hospital, my house physician sent him for a ride on an omnibus. The urine passed on his return contained blood, and he was admitted as a case of renal calculus. The viscera and the blood-pressure were natural. There was no œdema. There was some tenderness in the left loin, but the abdomen was otherwise natural. The kidney could not be felt. A skiagram gave no evidence of calculus. The urine averaged 1,700 c.c. with sp. gr. 1015–1035, and an acid reaction. Occasionally

there was a faint cloud of albumen, and once a granular cast was seen. The urea averaged 1·4 per cent. Methylene blue appeared one hour after being taken by the mouth. But still, though so little could be found, the aching pain continued even when lying in bed. I, in my turn, made a diagnosis of renal calculus, and Mr. Lockwood performed nephrotomy. There was much adhesion to the peri-nephric tissue and the kidney felt rather hard, but there was no stone in it or in the ureter. The capsule was stripped back, coming away easily, and the kidney was returned.

I saw the man again four months later. He had had no return of pain, but had had three attacks of hæmaturia, lasting only for one micturition, and each time after lifting a heavy weight. The specimen passed when he saw me was acid, sp. gr. 1021, albumen 0·15 per cent., blood cells, no casts, no crystals. Six years later, September 1910, I saw him again. He was in excellent health and had 'done a lot of sprinting' each year without any bad effect.

Klemperer described his case frankly as 'bleeding from healthy kidneys'. Senator, in relating a case of his own, ascribed it to renal hæmophilia. But with all respect to a great physician I do not see how such a hypothesis can be maintained in the absence of any other evidence of the diathesis, and in face of the fact that a severe operation such as nephrectomy was carried out safely. It is better to adopt the name now commonly used 'essential hæmaturia', remembering that there is only one thing essential about it, and that is our own ignorance. Hale White suggests that there may be some unknown toxin in the blood, and cites the instances of splenic anæmia, the purpuras, and hæmorrhagic fevers.

The treatment of such cases is conducted in the dark. If we knew the diagnosis an operation would seldom be necessary, for the cases when the hæmorrhage endangers life are very rare, and, as many instances prove, patients may live for many years with such attacks. But it is nearly always supposed that the patient is suffering from calculus, or renal tumour, and the operation is performed in that

belief. If operation shows that no gross lesion is present we can now tell the patient with confidence that he has not a progressive or fatal disease.

References.

1. Pissavy and Gauchery, *Bull. et Mém. Soc. Méd. d. Hôp. de Paris*, 1910, xxx. 633.
2. West, *Granular Kidney*, London, 1900.
3. Bowlby, *Clin. Soc. Trans.*, xx. 147.
4. Newman, *Renal Cases*, p. 134.
5. Bruce Porter, *Medical Soc. Trans.*, 1905, xxviii. 146.
6 Attlee, *St. Barth. Hosp. Journ.*, 1902, ix. 41.
7. Sheffield Neave, ibid., 1906, xiii. 123.
8. Guthrie, *Lancet*, 1902, i. 1243.
9. Aitken, ibid., 1909, ii. 444.
10. Hurry Fenwick, *Clinical Cystoscopy*, London, 1904.
11. Whitney, *Boston Med. and Surg. Journ.*, 1908, clviii. 797.
12. Cabot, *Amer. Journ. of Med. Sci.*, 1909, cxxxvii. 98.
13. Eshner, ibid., 1903, cxxv. 636.
14. Kretschmer, *Zeitschr. f. Urologie*, 1907, i. 490.
15. Hale White, *Quarterly Journ. of Med.*, 1911, iv. 509.
16. Mansell Moullin, *Clin. Soc. Trans.*, xxv.

CHAPTER X

HÆMOGLOBINURIA AND PAROXYSMAL HÆMOGLOBINURIA

Hæmoglobinuria signifies the passage in the urine of the colouring matter of the blood free from corpuscles. It does not imply that no corpuscles are passed at all, for sometimes in the fresh urine a few are visible. But they bear no proportion to the amount of hæmoglobin.

In these cases the urine may be black and opaque like porter, red and translucent like port wine, or of any shade and degree of transparency between the two. It gives the reactions of albumen. Sometimes the proteid has been found to be chiefly globulin. On standing, a brown precipitate falls.

The urine gives the colour reaction of hæmoglobin with guaiac and ozonic ether, and the spectrum of hæmoglobin or methæmoglobin. As in ordinary hæmaturia methæmoglobin is the form commonly observed.

With the microscope casts are sometimes to be seen. They are often so delicate and transparent that they are hardly visible until a little methylene blue or carmine is added. Roberts figures granular casts from one of his cases. Sometimes they are set thick with yellow masses of hæmoglobin. A few red corpuscles can sometimes be recognized if the urine is quite fresh. Oxalate crystals have been observed. The pigment is sometimes deposited in rounded masses, and hæmatin crystals occur occasionally.

The diagnosis from hæmaturia depends upon the fact that the red cells are entirely or almost entirely absent, while their colouring matter is present in large quantity. It can be made easily, but only, with the microscope.

Hæmoglobinuria occurs under several conditions.

1. It is seen after transfusion with the blood of another

species. According to a general law now well established, the recipient's serum develops an 'intermediary body' or 'amboceptor' which, combining with the natural 'complement', dissolves the blood cells of the foreign species. Hæmoglobin is let loose into the serum and is excreted by the kidney.

2. Occasionally in the course of some acute disease the urine is heavily coloured with hæmoglobin, but contains no blood cells. I have seen a few cases of this kind. A boy, aged 5, was admitted to my ward on May 9th, 1908, because he was thought to have hæmaturia. He had had measles in 1907, 'pneumonia' in January 1908, sore throat and pains in his legs in March. On April 10th he had malaise, and was sent to bed, but soon recovered. On April 19th he passed red urine, but the colour went off again. He was indoors until May 4th, when he went out. On May 6th he again passed red urine, and continued to do so till admission. When admitted he had some fever, for which no cause was discovered. His urine was smoky, turbid, acid, sp. gr. 1009, contained much albumen and gave a strong guaiac reaction. Under the microscope were seen numerous epithelial cells, and some casts, but no blood cells. On May 12th signs of pneumonia appeared for the first time. The urine was now less smoky, sp. gr. 1008, but still gave a strong guaiac reaction. It contained fewer epithelial cells, several epithelial casts, and a very few blood cells. The blood contained red cells, 3,950,000; white, 31,000; Hgb. 58 per cent.; colour index 0·73. (Polymorphonuclears 38 per cent.) The pneumonia ran an ordinary course.

On May 15th double otitis media supervened with perforation of both tympana. On May 21st the urine contained still a trace of albumen, but gave no guaiac reaction, and contained no casts or other organized deposit. On June 5th blood from the ear was tested by Eason's method of freezing followed by incubation at 38° C. No hæmolysis occurred.

Garrod [1] refers to a case of rheumatism under Sir Dyce Duckworth in which oxyhæmoglobin appeared in the urine for one day only. Cardiac lesions and pneumonia were

present at the time. Hayem [2] relates a similar case. A woman, aged 37, had had rheumatic fever in 1886. On December 20th a second attack began. On December 21st she passed red urine containing methæmoglobin, oxyhæmoglobin, and urobilin, white cells and granular epithelial casts, but no red cells. The serum of the blood was not coloured. On December 30th œdema of legs and forearms was noticed. On January 2nd pneumonia (rheumatic) and pericarditis supervened. On January 16th resolution took place. The albuminuria and tube-casts were present for several days after all trace of hæmoglobin had gone.

My patient had, as will have been seen, an attack during the previous month which was probably rheumatism. But his heart was normal. These cases are all connected, curiously enough, with both rheumatism (for my boy had rheumatic symptoms at first) and pneumonia. Other cases have a different connexion.

Hood [3] had a case in which the patient, a boy of 14, recovering from an attack of acute nephritis with true hæmaturia, suffered from a series of chills followed by hæmoglobinuria. No red cells could now be found in the urine.

Camus and Pagniez [4] record a somewhat similar case. A man was in the hospital for chronic nephritis. On December 2nd he passed red urine, which gave the spectrum of oxyhæmoglobin. No red cells, however, were visible. The next day the urine was still coloured, and the spectrum was as before. A few red cells only were visible. The serum of the patient's blood was not tinted. To the urine some of the patient's blood was added. The red cells were quickly destroyed. The same happened when blood from a healthy man was added to the urine.

Evidently, therefore, this urine had at the time cytolytic properties.

Cnopf [5] relates a case of a different kind. A boy, $4\frac{1}{2}$ years old, was seized with measles on May 11th. This was followed by broncho-pneumonia. On the fifteenth day he was apparently convalescing, and his urine was natural. Next day he caught scarlatina, and seven days later very

acute nephritis came on. For six days he passed very little urine, but gradually improved and after a few weeks passed about 1,400 c.c. The albumen, which had been as much as 11·5 per mille, sank to 0·2. But on July 21st the urine again became brownish red, and gave a red precipitate of hæmatin when boiled with caustic soda (Heller's test). Microscopically no blood cells were visible, but hyaline casts, leucocytes, and yellow granules of hæmoglobin. After seven days both the red colour and the albumen had disappeared. Four days later boiling produced only a slight opalescence. In this relapse, therefore, he had not hæmaturia but hæmoglobinuria.

He quotes a similar case, also after scarlatina, from Heubner, in a little girl aged 4¾ years. In this case there was no antecedent nephritis, but on the twentieth day, when the patient was up and apparently well, a trace of albumen was found in the urine. The same day sudden vomiting, collapse, and dyspnœa came on, with fever and a very rapid pulse. The urine now became black brown and gave the spectrum of hæmoglobin, but contained no red cells. In the blood nothing abnormal was found. She died on the fourth day. In the kidneys there were changes characteristic of acute nephritis, and the collecting tubes from the papillæ right up into the rays of Ferrein were plugged with yellow masses of hæmoglobin. The spleen was swollen, and there was a bloodstained serum in the pleuræ. Heubner believed the whole process to be some acute poisoning which had destroyed the blood cells.

Sharp and Summerskill[6] have related the case of a little girl 8 years old. The symptoms, œdema of the face, dyspnœa, and almost complete suppression of urine, were those of acute nephritis, but there were very few red cells though abundant hæmoglobin in the urine. She quickly recovered, and no cause could be found for the attack except perhaps sewer-gas. This group of cases is connected with nephritis.

A third class is represented by two cases that were in my wards.

A little girl, aged 11, had previously been in the hospital in December 1908 for what was at the time considered an attack

of nephritis with hæmaturia. There was, however, no œdema, and no casts could be seen, though the blood was very persistent. There is, moreover, no note whether blood cells were present at that time. No further attack occurred until January 1910, when one evening after her tea she was seized with pain across the abdomen and liver. Two days later the urine was dark. She was admitted next day into my ward, under Dr. Drysdale, when it was found that though hæmoglobin was present there were no red cells. With the cystoscope a dark urine was seen by Mr. Gask issuing from the left ureter, that from the right was normal. The symptoms completely disappeared and the urine became normal in a fortnight, and so remained. No casts or other symptoms of nephritis were seen. The cultures made from the urine were sterile. The first attack in 1908 began with an attack of abdominal pain just as did the second.

A woman, aged 35, had in November a sudden attack of abdominal pain in which she vomited. Micturition was painful and the urine scanty. In February she had a similar attack, and again on March 18th. She was admitted that day, and the urine was found to be thick with hæmoglobin, but it contained hardly any blood cells. Under the microscope a few hyaline casts and many casts of brown pigment, presumably hæmoglobin, were seen. Three days later she had severe pain in the right loin and down the right leg, and also in the left arm. At the same time the temperature ran up to 102° F. and she vomited. The next day the loin was very tender, and retching frequent. No blood cells could be found in the urine, though it was still highly coloured with hæmoglobin. This condition continued, slowly improving, until April 14th, when hæmoglobin finally disappeared. The urine was sterile. On April 15th the urine of the two kidneys was separated. In fifteen minutes :

Right kidney 22 c.c.	Urea 0·46 per cent.	Cl 0·12 per cent.
Left kidney 28 c.c.	,, 0·4 ,,	,, 0·13 ,,	,,

When the urine was mixed with the patient's blood and incubated at blood heat no hæmolysis took place.

These cases remind us of cases of essential hæmaturia, but I know of no explanation for the dissolution of the corpuscles.

3. A separate form of hæmoglobinuria is that described by Winckel.[7] During March and April twenty-four new-born children in a lying-in hospital were attacked with an unknown form of disease whose symptoms were cyanosis, jaundice, convulsions, and hæmoglobinuria. The temperature was usually subnormal. The blood was very black and viscid, and would not run out of the veins.

All but one of the children died; the earliest death was in nine hours, the latest in 4½ days from onset.

Dissection showed redness and swelling of the mucosa throughout the alimentary canal, great enlargement of the mesenteric glands, enlargement of the liver and of the spleen. There were cortical hæmorrhages in the kidneys and hæmoglobin infarcts in the papillæ. There were occasionally hæmorrhages in the pericardium, pleuræ, and peritoneum.

No cause could be found. The mothers were all healthy.

It is generally acknowledged that Winckel's disease represents some form of infection. I therefore class with it a case related by Klemperer.[8] The patient was a strong labourer of 28, and the symptoms came on after eating black pudding (*Blutwurst*).

4. Hæmoglobinuria is known also as an effect of several poisons, such as potassium chlorate,[9] arseniuretted hydrogen,[10] carbolic acid,[11, 12] pyrogallic acid,[13] and naphthol. Hydrochloric acid, sulphuric acid, and nitrobenzol are also said to have caused it.

In Neisser's case of poisoning by pyrogallic acid the man died, and the post mortem showed the large veins to be full of chocolate-coloured altered blood. The kidneys were bluish black in colour, and the tubules were full of the pigment.

The symptoms in cases of poisoning are restlessness, shivering, fever, and collapse.

5. Hæmoglobinuric fever (Blackwater fever) is another cause. This is a complication of malaria produced by

quinine. Accounts of it belong rather to text-books of general medicine or of infectious fevers than to such a book as this.

6. Hæmoglobinuria occurs in animals. One form of it is known as Texas fever, tick fever, East African and bilious fever. It is due to piroplasmosis, and in it the piroplasma living in the erythrocyte destroys it, and sets hæmoglobin free. Another form, the hæmoglobinuria of horses, occurs in England when a horse has been for several days without exercise. On taking him out he is suddenly seized with spasm of the hind-quarters, and passes dark urine, which contains hæmoglobinuria alone. How this is caused is doubtful. Professor Sir John Macfadyean has made the remarkable discovery that the red cells of the blood are greatly increased in the attack, instead of, as might be expected, diminished. A case published by Meyer-Betz,[26] which occurred in a boy aged 13, was accompanied by extreme muscular weakness, and was not connected with chill; it is classed by him with horse hæmoglobinuria. It is quite unlike any other case known to me. The hæmoglobinuria of cattle in Roumania is probably again different. It has been ascribed by Babés to a hæmatococcus.

7. Lastly, it occurs as a well-marked recurrent affection, called Paroxysmal Hæmoglobinuria, from at least three causes :—

(1) Mental anxiety. One of my friends used to get an attack just before going in for an examination. Dr. Druitt, himself a sufferer, wrote :[14] 'The most efficient cause is mental worry or exertion ; an annoying letter or a game of chess might bring on an attack in a quarter of an hour.' Druitt was also subject to it from cold, but my friend was quite impervious to cold. He was a great strong man, and an excellent football-player.

(2) Hard exercise. It was found by Fleischer [15] in a young soldier after marching. Strubing and Kast have published similar cases. In these patients neither cold nor any other exertion but walking could produce it. Robin [16] had a patient, a lad of sixteen, in whom at one time even a short walk produced hæmoglobinuria. He treated him by several

months' complete rest and milk diet, and cured him. Bastianelli had a similar case, and Lee Dickinson [17] describes two cases in long-distance runners, and one which followed a hard game of lawn tennis.

(3) A unique case has been published by Enson and Barratt [18] in which hæmoglobinuria was produced by blows. The patient, a lunatic, had attacks in which he used for hours together to thump his forehead and his thigh violently with his hands. These were followed by hæmoglobinuria. They thought that the blows produced hæmatomata, and the absorption of the effusion produced anauto-hæmolysin in the blood. A similar explanation was suggested by Michaelis [19] for the following case. He saw a woman, aged 41, suffering from severe internal hæmorrhage due to an extra-uterine pregnancy. When first seen, three days after the onset, the urine was nearly black with hæmoglobin. It became clear in a few days, and no albuminuria remained. No red cells were visible throughout. He thought that a rapid absorption from the peritoneum had produced an auto-hæmolysin in the blood which led to hæmoglobinæmia and hæmoglobinuria.

Injury has sometimes been alleged to have started the series of hæmoglobinuric attacks, which have, after the first, been due to cold. But such statements are liable to error. For instance, a man was admitted twice into St. Bartholomew's with paroxysmal hæmoglobinuria. In 1900 he said the disease began after a very cold drive, but in 1904 he said that he had had a fall off the carriage, and did not mention the cold drive. There is no doubt, however, that injury may produce a single attack of hæmoglobinuria.[20]

(4) But the commonest and best-known cause is cold. This is the classical form of the disease, and from it the description of an attack may be drawn.

A patient is exposed to cold. He does not, perhaps, even notice it at the time, or, on the contrary, he may feel that he has had a chill, and his hands, nose, and ears may turn blue. After an hour or two, perhaps longer, be begins to feel uncomfortable. He yawns, stretches himself, perhaps feels

sick or has a slight headache, and feels an aching in the loins or abdomen. These symptoms get worse. He at length has a severe shivering fit, sometimes followed by a regular sweating stage. His skin is hot and dry, and his face flushed. The headache by this time is severe, and he probably vomits. The temperature, at any rate in attacks artificially provoked, usually falls at first to subnormal, then rises again, and may reach during the rigor a level of 104° F. (40° C.). The pulse and respiration quicken at the same time, and the man feels very ill. Soon after this he passes urine of the character above described. If he has been in a warm place or in bed he will now soon begin to mend, the symptoms will gradually pass off, the temperature will fall, the next urine is not so deeply stained, and after a few hours he is restored to health.

That is the typical attack, and it is remarkable that it occurs in the same form from many causes. Eitner's patient, Professor X., poisoned by arseniuretted hydrogen, and my friend on the night of anxiety preceding his examinations, each had the symptoms typical of an attack from cold. The shivering, therefore, and the fever are probably not due to the cold even in hæmoglobinuria *e frigore*, but are coincident with and, I suppose, consequent on, the changes taking place in the blood.

The severity of the attack may vary whatever the cause may be. The patient may feel no general symptoms at all, and may only know from the colour of the urine that he has been through an attack, or he may be ill for two or three days.

Now to take some of the points separately.

The degree of cold necessary to produce an attack varies extremely. One patient gets an attack simply from getting out of bed for a few minutes; another only when exposed to severe frost. Usually the patient becomes more susceptible as time goes on.

No age is exempt. I have had two patients, sisters aged 3 and 4 years respectively, and two cases at least are known to have begun at two years old. It has been known

to begin as late as fifty-one, and one of our patients at St. Bartholomew's was still subject to it at 64 years of age.

The local cyanosis resembles that seen in Raynaud's disease. Yet in undoubted cases of Raynaud's disease, both of the cyanotic and of the gangrenous forms, no hæmoglobinuria has been seen, though in many it has occurred.

In several cases (e. g. Copeman's) albuminuria has preceded hæmoglobinuria, and in slight attacks albuminuria has occurred alone. Albuminuria generally persists for some time after the hæmoglobinuria has disappeared.

In some cases urticaria is a marked feature.

The immediate antecedent of hæmoglobinuria is probably in all cases hæmoglobinæmia. The blood-cells are broken up, and their colouring matter let loose in the blood. Serum tinged with red has been obtained during an attack from a blister, and from the blood itself when drawn and left to coagulate in a test-tube. The jaundice frequently noticed in these patients is almost certainly due to the presence of free hæmoglobin in the tissues. This evidence is not always to be found. Even with 50 c.c. of blood, Robin could not see any coloration of the serum. But with slight cases, such as his was, this is not surprising.

The exact site of the blood destruction is not certainly known. It was found by Boas to take place locally. He ligatured one finger, chilled it in iced water, drew a drop of blood, and saw the cells altered, while in the next finger the blood was natural. A spontaneous attack probably affects a much larger area, but it is at any rate natural to suppose that it is at the surface of the body that the process starts.

What is the process by which hæmolysis takes place? It is not mere cold. I have taken the blood of hæmoglobinuric patients and exposed it on a microscope slide, covered and sealed, to a freezing temperature for a considerable time, without being able to find any alteration in the cells. Many observers have received the blood in a test-tube kept on ice, and seen it clot without any coloration of the serum.

Ehrlich suggested that a hæmolysin might be developed

during an attack. Mannaberg and Donath [21] proved that this was so. They took the blood from their patient during a free interval, centrifugalized it, and obtained clear serum. Into this they put about ten volumes of the blood of a healthy person, and on centrifugalization the mixed serum remained clear. But when the same experiment was repeated during an attack the mixed serum was heavily stained. It is true the patient's own serum was slightly stained, but the colour of the mixed serum was much darker. The patient's serum was therefore able to dissolve the healthy man's blood-corpuscles. It contained a hæmolysin valid against healthy blood.

These indications were carried further by J. Eason,[22] who established that such a hæmolysis could be produced by cooling and subsequently warming the blood *in vitro*, that such hæmolysis was due to the activity of an intermediary body peculiar to hæmoglobinuric blood, and that this was valid against healthy blood. Eason was also able to produce an antitoxin valid *in vitro* against this intermediary body.

The pathology of paroxysmal hæmoglobinuria is therefore probably this : The patients have from one cause or another a peculiar intermediary body in their serum. To make this actively hæmolytic the blood has first to be cooled, to a different degree in different patients, and then again raised to blood heat. The cooling is aided by some reflex vasomotor mechanism of a peculiar kind common to this and Raynaud's disease, and shown by local coldness, local syncope, or local cyanosis. As a result of this stage the red cells combine with the intermediary body in the local areas of coldness and stagnation. The cooled blood passes to warmer parts, and there the 'complement' which is present in all human serum whether hæmoglobinuric or healthy, joins the combined pair. Its addition causes hæmolysis and hæmoglobinæmia, which process gives rise to general symptoms of fever.

When the number of blood-cells that are dissolved is small the liver and spleen can deal with the free hæmoglobin, and turn it into the usual pigments. In that case a transient albuminuria is all the evidence that we obtain.

And it is to be remarked that such transient albuminuria is a known result of cold, as after bathing; of emotion, as during examinations; and of walking, as in soldiers on the march. It is probable, therefore, that paroxysmal hæmoglobinuria is not an isolated condition, but that in many men under certain stimuli the blood is thus destroyed in small quantities, and that hæmoglobinuria occurs only in those in whom the process is carried to excess.

This agrees with the experimental facts. Mannaberg and Donath found that the red cells of their patients dissolved to a considerable extent when the blood was shaken. But so, to a less extent, did the cells of other persons who were not hæmoglobinuric. The behaviour of the blood when persufflated with CO_2 was only an exaggeration of that of ordinary blood.

There are certain factors which predispose to hæmoglobinuria. One is undoubtedly syphilis. This was maintained by Murri;[23] Stempel[24] found it in 29·8 per cent. I may mention that the seven cases that I have seen myself have all been syphilitic. Copeman says the same. Malaria has generally been allowed as another. This agrees very well with the view that blackwater or hæmoglobinuric fever is a paroxysm of hæmoglobinuria produced by quinine in a person predisposed by malaria. It has been shown that blood which is specially sensitive to cold is also specially sensitive to other stimuli. It is not hard to believe that malaria makes some blood specially sensitive to quinine.

The diagnosis of the condition is easy with the help of the microscope and the spectroscope. Hæmoglobinuria has to be distinguished from true hæmaturia on the one hand, and on the other from certain other colorations of the urine which do not give the spectrum of hæmoglobin, and are in many cases due to pigments as yet unknown.

In one case Pal[25] found paroxysmal attacks like those under discussion accompanied by hæmatoporphyrinuria without any blood or hæmoglobin.

The treatment of the individual attack is to make the patient warm as quickly as possible. Several patients have

been able to stave off attacks by hot drinks, hot blankets, and similar measures.

When a patient is subject to the attacks, his prospects, as in many other cases, depend upon his income. During the warm weather such a man can usually live like other people. But as the cold weather comes on he must either shut himself up in a warm house or he must go to a warm climate, if he wishes to avoid an attack. In some cases the patient is so sensitive that he is perforce an invalid throughout the winter. But there are all degrees, and in some persons an attack does not come as often as once a year.

In a few cases antisyphilitic treatment has cured the patient. But it seldom succeeds. I have tried it in cases of congenital syphilis, and of acquired, with no effect. Quinine has been recommended, and when taking it as a prophylactic in 5-grain doses thrice a day all through the winter, two of my patients escaped attacks which had been frequent before. Another, a medical man, tells me that he is sure that the quinine, which he took in large doses, stopped his attacks. Arsenic has also been recommended, but I have had no experience of it.

The repetition of attacks certainly makes the patient more susceptible. It is of great importance to prevent recurrence.

There is no doubt that some people cease to be susceptible. I knew a man of 40 who, from the account of his family doctor, had evidently had the disease in youth. His father, according to the same witness, had had syphilis. My patient had long outgrown it when I knew him. He was a rich man, and had when young travelled much in search of health. Hæmoglobinuria *e frigore* may, I think, be said never to be fatal, though it may make a patient very ill. Cases which are quoted as fatal have all been complicated with other conditions.

References.

1. Garrod, *Treatise on Rheumatism*, p. 172.
2. Hayem, *Du Sang*, p. 985.
3. Hood, *Lancet*, 1890, ii. 708.

4. Camus and Pagniez, *Bull. et Mém. Soc. Méd. d. Hôp.*, 1901, 3 S., xviii. 406.

5. Cnopf, *Münch. Med. Woch.*, 1895, xlii. 448.

6. Sharp and Summerskill, *Lancet*, 1893, ii. 1440.

7 Winckel, *Deutsch. Med. Woch.*, 1879, v. 301.

8. Klemperer, *Charité-Annalen*, 1895, xx. 130.

9. Marchand, *Virch. Archiv*, 1879, lxxvii. 455.

10. Eitner, *Berl. Klin. Woch.*, 1880, xvii. 256.

11. zur Nieden, ibid., 1881, xviii. 705.

12. Krukenberg, *Zeitschr. f. Geburtsh. u. Gynäkol.*, 1891, xxi. 167.

13. Neisser, *Zeitschr. f. Klin. Med.*, 1880, i. 88; *Centralbl. f. die med. Wissenschaften*, 1881, xix. 545.

14. Druitt, *Med. Times and Gaz.*, 1879, i. 215.

15. Fleischer, *Berl. Klin. Woch.*, 1881, 691.

16. Robin, *Bull. et Mém. Soc. Méd. d. Hôp.*, 1888, 3 S., v. 181; see also Garrod, *Encyclop. of Med.*, Edinburgh, 1900.

17. Lee Dickinson, *Clin. Soc. Trans.*, 1894, xxvii. 230.

18. Enson and Barratt, *Medico-Chirurg. Trans.*, 1903, lxxxvi. 165.

19. Michaelis, *Deutsch. Med. Woch.*, 1901, xxvii. 51.

20. Gull, *Guy's Hosp. Reports*, 3 S., xii. 381.

21. Mannaberg and Donath, *Deutsch. Arch. f. Klin. Med.*, 1900, lxv. 285.

22. John Eason, *Journ. of Pathol. and Bacteriol.*, xi. 167, and previous papers.

23. Murri, *Emoglobinuria aed Sifilide*, Bologna, 1885.

24. Stempel, *Centralbl. f. d. Grenzgebiete d. Med. u. Chir.*, 1902, v. 184.

25. Pal, *Centralbl. f. Innere Med.*, 1903, xxiv. 601.

26. Meyer-Betz, *Deutsch. Arch. f. Klin. Med.*, 1911, ci. 85.

CHAPTER XI

DROPSY, ESSENTIAL DROPSY, AND URÆMIA

Dropsy.

If we look back upon cases of renal disease in which dropsy has been present they will group themselves into two classes of which the picture is very different. Many of them are like cases of cardiac dropsy ; the œdema occurs at the parts which are most dependent or most distant from the circulation, and the face is not swollen. But in others the face and sometimes the upper limbs are swollen as soon as, or even before, the legs, at the very beginning of the attack of nephritis, while the heart is acting forcibly, the blood-pressure is as high as, or higher than, the normal, and no sign of cardiac failure is present.

These two groups stand apart, and though they are linked by many intermediate gradations, yet, as in other parts of the study of nephritis, we learn more by the difference than by the likeness.

It is the latter which is the true renal dropsy, but it occurs, though very rarely, in cardiac cases also. A man aged 35 was admitted under me with œdema, which had begun in the face, and was more marked in the arms than in the legs. He had a little albuminuria at first, but it quickly disappeared, and he had been admitted a year or two before as a simple case of heart disease. The amount of œdema may be guessed from the fact that he lost 42 lb. in weight when it disappeared.

It is evident that the cardiac form of œdema depends largely upon physical forces. It occurs chiefly where the venous current is at its weakest, and the capillary blood-pressure therefore at its highest. But it has long been known that more is required to produce excessive transudation into the

tissues than an increased capillary pressure. So long as the capillary walls are healthy they can keep transudation within the limits in which, for the nourishment of the tissues, it is always taking place. It is allowed, therefore, that even in cardiac dropsy there is some damage to the capillary walls.

This cardiac form of dropsy occurs as a late event in the chronic nephritis of elderly people, and coincides usually with the gradual failure of a previously hypertrophied heart, and with a fall of arterial blood-pressure.

But the true renal form occurs sometimes as the earliest symptom of acute nephritis in the young, and is seen at its worst, first when such an acute attack is at its height, and secondly at the much later time when the large white kidney has evolved. Even if cardiac failure plays some part in the fatal end of this form, yet the general white dropsy here seen is something quite different from anything that usually occurs in the course of heart disease.

It is probable that the factors above mentioned, a heightened capillary pressure and damage to the capillary walls, exist here also, but it is clear they must be in different proportion, and under special conditions, since both the distribution and the degree of the œdema vary from the cardiac type.

These conditions may include the presence of substances in the blood having a special action in increasing the flow of lymph. Heidenhain found that several substances had this power. Some were organic, such as leech extract, muscle extract, and peptone; others, such as sugar and salt, were inorganic.

French physicians have laid stress upon chlorides in this connexion. According to them, nephritis lessens the power of the kidney to excrete chlorides, and the retention of chlorides eventually leads to the retention of water. Schlayer believes the excretion of Cl to be a function of the tubes.

In one or two instances dropsy, which apparently depended upon an excessive ingestion of salt, has occurred in persons whose kidneys were healthy. Bryant relates the case of a doctor, aged 40, who consulted him for œdema of the feet

and legs. He ate enormous quantities of salt, and 'it was no unusual occurrence for him to empty the salt-cellar, both at luncheon and dinner'. 'His urine contained 1·86 per cent. of chlorides, i.e. nearly three times the usual amount.' Moderation in taking salt cured the dropsy. A case was lately recorded of an œdematous baby to whom the nurse was giving an excessive amount of salt with its milk. The salt was stopped and the dropsy disappeared. Hamburger[17] relates a similar case.

Widal with Lemierre,[1] and with Javal,[2] was able, in some cases of subacute and chronic nephritis with œdema, to remove the œdema and reproduce it again by giving a milk diet alone, and with the addition of 10 grammes of NaCl, respectively.

How this is brought about is disputed. Widal ascribed it to a special defect in elimination, due to the condition of the kidneys. But retention of Cl is a feature of many morbid states, in some of which, pneumonia for instance, there is no tendency to œdema. In these there is probably some process going on in the tissues which causes them to seize on the Cl and retain it.[3] In nephritis both renal impermeability and tissue-hunger may be at work. Mauté[4] states that it is of great importance for prognosis to determine whether the kidneys retain their power of eliminating Cl, by estimating the amount excreted after fixed doses of sodium chloride.

Strauss[5] allows full weight to these views, and gives many analyses, showing that, while both the blood and the œdema fluid contain about the normal percentage of NaCl, the total amount of chlorides in the body must, from the increase in both fluids, be very much increased. He points out, however, that while it is easy to say that the retention of salt is the first thing, and that the water is merely retained in order to dilute it to its proper proportion in the blood, it is very difficult to prove. An equally possible view is that the blood is diluted by the failure of the kidneys to excrete water, and the salt retained in order to raise it to its normal osmotic pressure. This latter view is to a certain extent supported

by Bence's experiments,[6] in which a relative retention of water followed regularly on lesions of the kidneys. He found that starving animals, in which the kidneys were extirpated or damaged, lost weight less rapidly than those in which the kidneys were intact. This means that they retain water. Bence found also that œdema occurred regularly in the former animals, even when no water was given. Œdema, therefore, is not a mere question of retention of fluid ingested, but depends upon some changes in the tissues which alter the usual distribution of fluids.

A case in my wards bears on this point.

William Batten, aged 8, was admitted for chronic nephritis and dropsy, which came and went spontaneously while he remained in bed on a constant diet and treatment. The upper line in Chart D shows the fluctuation in weight which corresponded to the œdema. At his normal weight, 3 st. 12 lb., there was no dropsy ; all excess above this represented dropsical fluid. The lowest line shows the daily output of urinary water ; the middle line estimations of Cl output. It will be seen that on November 14th–17th there was a large excretion of water which removed the dropsy. A great excretion of Cl took place on November 20th, when there had been no dropsy for four days. A second great excretion of Cl took place on December 3rd, during a period of œdema. But the water was very scanty then, and the œdema remained.

The attention paid to chlorides has, I think, been excessive. It has been forgotten that Heidenhain described another class of lymphagogues, which are extracts from organic tissues. Acute œdema is occasionally the first symptom of nephritis in a child who has been on restricted diet throughout an attack of scarlatina. It does not seem reasonable to ascribe this to Cl retention. It may be that some organic poison derived from the desquamating and disintegrating epithelium is concerned in many cases of œdema, or that the poison which damages the kidney is an active lymphagogue.

Fischer[18] has made important contributions to the subject of œdema. He found that colloids, fibrin and gelatin, placed in dilute solutions of acid or of alkali, took up large

proportions of water; that this imbibition was much reduced by the addition of a salt to the solution; that the salts could be arranged in a definite series according to their effect. He found that muscular tissue behaved like the simple colloids. Relying on observations which show that

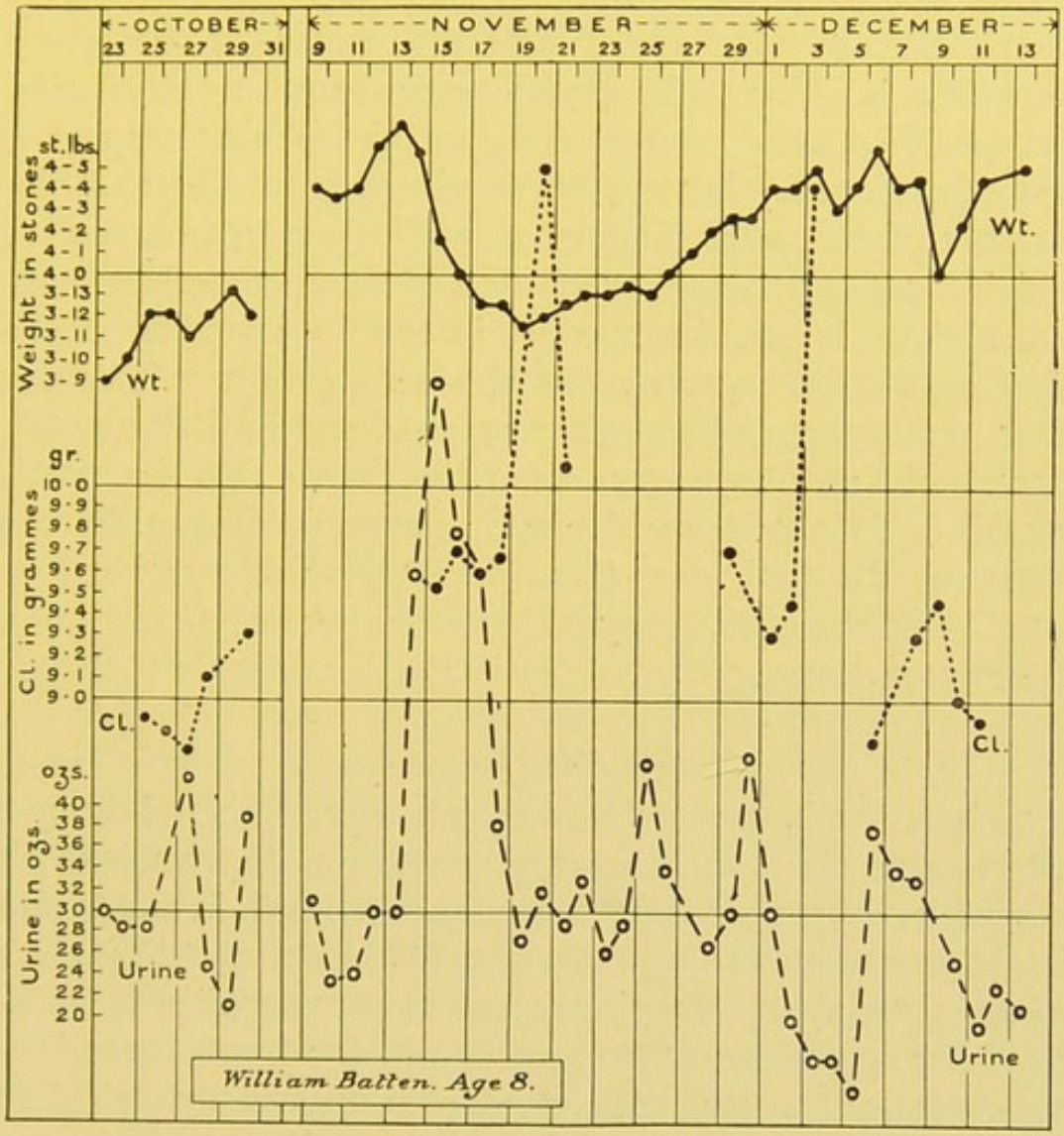

CHART D

the alkalinity of the blood is reduced in nephritis, he thinks that renal œdema is an example of imbibition by the colloids of the tissues under the above laws. It does not, however, appear to me to be a valid explanation. The tissues are normally bathed in an alkaline medium. If the alkalinity of the blood is reduced in nephritis, which is by no means certain, the tissues will lie in a medium which, though less

alkaline than natural, is still alkaline, and contains added salts. This is not a condition on which he has recorded direct experiments; but from the observations published we should expect imbibition to be rather diminished than increased by it.

But whatever the ultimate cause may be, the events of the process apparently begin with the increase of the watery element of the blood. This was long ago shown by estimating the specific gravity, and by weighing the albumen of serum from these cases. Later observers have found also that the number of red cells diminishes, and the refraction index, which depends upon the proportion of albumen in the serum, sinks. This implies an increase in the total volume of the blood and consequently a rise in blood-pressure. It occurs even in starving and waterless animals, and in that case the stream of fluid must come from the tissues into the blood-vessels. To produce œdema, however, a stream in the contrary direction must take place. Probably this occurs later when the capillary walls have been damaged, either by the high pressure, or by poisons in the blood, or by both.

Essential Dropsy.

This is the best place to mention other forms of dropsy, which though resembling the renal, are independent of nephritis. Wagner [7] related several cases, both in adults and in children, with two necropsies. Rilliet and Barthez speak of dropsy without albuminuria as a disease peculiar to childhood. They collected 78 cases, of which 25 were secondary to scarlatina, as had been previously noticed by Quincke,[8] 18 to some other disease, and in 35 no predisposing or exciting cause could be found. Fourteen cases out of sixty-three died, and they record a few necropsies. Donkin speaks of it as not infrequent, especially in cases of anæmia, and records two necropsies. Many text-books pass it over unnoticed (Baginsky, Starr and Westcott, Meigs and Pepper). Henoch mentions it, but adds that while some cases of general anasarca without albuminuria are found to be quite free from renal disease, there are others in which nephritis is

found after death; such a case is recorded by Litten[9] and another by myself.[10] Staehelin[11] and Wichern[12] relate each a single adult case, the former with an autopsy. Both papers contain observations on the blood and are very interesting.

There is besides an epidemic form of dropsy without albuminuria, of which outbreaks have been often observed in India and Mauritius. Its clinical features are similar to the sporadic form seen in Europe.[13]

As we see it here, the disease begins in some cases insidiously, in others rapidly, or even acutely. In adults there has sometimes been noticed a prodromal period, in which malaise and general pains were complained of. These pains persist after the œdema has appeared. Usually, however, the first thing noticed is œdema, beginning either in the face or in the feet, and spreading over the whole body. It has in several cases involved the mucosa of the pharynx and larynx. Serous effusions in the pleuræ, pericardium, and peritoneum are frequent. The patients are markedly anæmic and exactly resemble cases with large white kidneys. The urine is scanty, but contains no albumen, and no formed elements can be seen under the microscope. The temperature and pulse are usually natural throughout. Some cases recover in a few days, others last for several weeks, or even months, unchanged, and a few die. The post-mortems hitherto recorded throw no light upon the causation.

As already mentioned, scarlatina is a recognized cause, and in many cases the patients have ascribed the condition to a chill or a wetting. But that statement is not worth much. In the great majority no cause can be discovered. Tchirkoff thought his cases were syphilitic, but has not been corroborated by later observers. Wichern gives some interesting observations on the intake and output of fluid. During the first five days, his patient, a law-student, aged 27, who had been drinking beer to excess and taking little food, had great retention of fluid. Taking an average of 1700 c.c. daily, he only passed 2500 c.c. in the whole period. After that he began to pass large quantities, and the œdema had

entirely disappeared in eleven days. Both he and Staehelin found that the specific gravity and the dry residue of the blood were below the normal. It would be interesting to know the Cl exchange in these cases, for, as already stated, retention of Cl is one of the recognized causes of œdema. As I cannot find any records of this point I subjoin a case of my own.

A boy, aged 6, got wet on September 7th. A cough followed. A week after the wetting his face swelled, he had a headache, and vomited. On September 27th he was admitted with general œdema and slight ascites. Beyond a little bronchitis there was no evidence of any visceral disease. The urine at first was 690 c.c. in amount, sp. gr. 1023, was acid, and contained no albumen or sugar. There were no casts in it. Its Cl content was not then noted. On October 9th I removed all cooking and table salt from the diet. He was given saltless bread and saltless butter. On the 11th hot baths were begun, which were followed by considerable perspiration. On the 12th, though taking no salt, he passed over 800 c.c. of urine and over 2·169 g. of Cl. On the 20th he passed 930 c.c. of urine and 1·6 g. of Cl. On the 27th he passed 960 c.c. of urine and 0·864 g. of Cl. There was a trace of puffiness left in the face only.

It has always seemed to me that these cases are a natural experiment. It is not the actual lesion of the epithelium which is the immediate cause of renal dropsy. The lesion works through some other process. Perhaps in essential dropsy that process is started by some other cause. Unluckily it is a rare disease except in children, who owing to their incontinence of urine are unsuitable for such observations. But any adult case is of the greatest importance for the study of the pathology of dropsy.

Uræmia.

In renal diseases symptoms vary as much as in any. Yet in nearly all of them, whether acute or chronic, there is a group of symptoms, chiefly of the nervous system, which can be recognized as characteristic. They are of such a

nature that they recall the effects of poison, and irresistibly suggest the presence of some poisonous substance or substances in the blood. This belief has given rise to the term uræmia. Every physician holds this belief, no one has proved it, and few have a clear idea what they mean by it.

The first tendency was to ascribe uræmic symptoms to the retention in the blood of some substance or substances, which normal kidneys excrete. Urea, which was the first selected, gave rise to the word uræmia. It was soon, however, found that urea was very slightly toxic, and could be injected in large doses into the circulation without causing any disturbance. Urea was succeeded by carbonate of ammonia, but this again was displaced when it was found that uræmic symptoms occurred without the presence of carbonate of ammonia in the blood. In one way or another the same has happened in the case of each known organic constituent of normal urine.

But experiments with a fistula between the portal vein and the inferior cava [14] produced in dogs a series of symptoms so closely resembling those of uræmia in men as to suggest a similar origin. In these dogs large quantities of carbamic acid was found in the urine, and alkaline carbamates injected into the circulation produced similar results. Urea can easily be made from carbamate of ammonia, and the probable explanation of the phenomena is that the operation had the effect of stopping the transmutation of amido-acids at an intermediate stage. For a time these facts aroused great interest. But their direct application to uræmia is not allowable, for carbamic acid is not found in uræmic urine.

In the exhaustive work of Ascoli [15] will be found tables of all the chemical analyses of the urine, blood, lymph, and tissues, carried out up to that date, which could be used for the purpose of settling this question. In addition to those quoted by him, French and Butler [16] have published a similar analysis extending over a longer period than any hitherto attempted.

These cases show great irregularities. 'We have renal patients whose N metabolism is carried on in a perfectly regular way ; others again in whom the excretion is markedly above the intake ; lastly, those who show a considerable N retention. Uræmic symptoms appear chiefly in the last class ; but even this is no regular relationship, for they may be absent with the most marked N retention, and present when it is relatively less ; nay more, they are observable even with N equilibrium ' (Ascoli).

When the research is carried into the blood itself, the result is still the same. There is no regular relation between the N content of the blood, after it has been freed from its albumen, and the presence of uræmia. The same is true of the lymph and of the solid tissues.

While, therefore, it is found that cases of uræmia occur most frequently in that group of cases which show N retention, we are forbidden to believe that the connexion between the two is direct. The facts are better explained on the theory that both are consequences of renal disease, and may occur independently of one another.

The same must be said of researches into the saline contents of the urine and of the blood. To establish an exact account between the intake and output of salts is from the nature of the case extremely difficult and laborious. Yet without such accuracy it is impossible to infer in ordinary cases a retention of salts within the system. Ascoli tabulates cases in which both the food and the urine have been analysed. They are of doubtful import, and no law bearing upon the occurrence of uræmia can be deduced from them.

Quantitative analysis of the blood and serum are equally indefinite. Uræmia occurs with and without increase of the saline constituents, and the blood or serum examined by direct chemical method or by cryoscopy may contain an excess of these bodies, both when uræmia is present and when it is not.

In 1881 Feltz and Ritter started a new method of investigation by injecting urine into the circulation of animals. The operation produces certain nervous symptoms, myosis,

drowsiness, and convulsions, which occur in uræmia. Feltz and Ritter believed them to be due to the potash salts of the urine. Bouchard thought the symptoms were produced by the organic constituents. He believed the latter to be numerous, and specific in action, one convulsant, another soporific, another myotic. He even founded a theory of sleep on the results of his experiments. He further formulated a law of toxicity of human urine, and stated that the urine of chronic renal disease was less, that of certain other diseases more toxic, than the natural. He led a school in France which for a time sought an explanation of almost all morbid phenomena in terms of urinary toxicity. The theory was attractive; its weakness lay in the method. Of the supposed poisons none was ever isolated or analysed. Many who repeated the experiments found that the results were variable. It was seen that the excretion in man varies so much that no standard can be based upon animal experiment unsupported by chemical analysis.

The theory that uræmia is caused by the retention of some normal urinary products, has not, therefore, been supported by direct experiment.

The same conclusion must be drawn from clinical observation. Obstructive suppression, by closure of the ureters, does not produce uræmia, though a patient may live for over a week without passing any urine at all. This condition is different from that occurring in nephritis, since the kidney tissue may be itself healthy, and may therefore be producing a normal internal secretion, if there is such a thing, though it is unable to excrete. But there are instances which render it improbable that uræmia is due to the suppression of a normal internal secretion.

As above mentioned (see p. 12), cases have been recorded in which entire necrosis of the cortex occurred, and anuria lasted over a week without uræmic symptoms appearing. The necrotic condition of the cells seemed incompatible with any functional activity, and in three of the cases there was a stoppage of the circulation owing to universal thrombosis in the arteries of the renal cortex. It seems,

therefore, impossible that any internal secretion can have been formed.

Later researches have added two important facts. It is proved that a watery extract of the kidney tissue contains a substance which when injected into the circulation greatly raises blood-pressure (Tigerstedt), and it has been also shown (Lindemann, Pearce) that serum taken from dogs suffering from either spontaneous or artificial nephritis can produce renal lesions in healthy dogs. These results will be further discussed in connexion with chronic nephritis and the changes in the circulation which are common therein. They do not bear immediately upon the causation of uræmia. Yet general pathology has made so many discoveries in this direction that they cannot help affecting our ideas.

Innumerable instances are known in which the injection of an organic foreign body produces in the blood a substance which counteracts the effect of the first and tends to destroy it. Such are the antitoxins produced by injecting specific microbes, and such are the lysins produced by injecting various cells, or cellular extracts. We know further that in such experiments there is on the one hand a limit to the power of an antitoxin, and on the other that in the condition known as anaphylaxis, in which the system becomes abnormally sensitive to the poison injected, extraordinary nervous phenomena occasionally occur. The idea arises in the mind that possibly the symptoms of uræmia may be connected with the absorption of dying cells, and that the astonishing length to which degeneration of the kidneys may go before death takes place—we have all seen kidneys weighing less than three ounces—may be the result of some form of immunity produced by such absorption. This, however, is at present pure guesswork.

Clinical observation can add yet another contribution to the pathology of uræmia. Uræmic symptoms rarely occur in lardaceous disease, or in the large white fatty kidney, which is one of the terminal events of diffuse nephritis. They are chiefly seen in those forms of the disease which are accompanied with fibrosis, and as Samuel West has

remarked, there is a family resemblance between the poisoning of this condition and that which occurs (cholæmia) at the end of some cases of hepatic cirrhosis, in which a similar fibrosis takes place.

References.

1. Widal and Lemierre, *Bull. Soc. Méd. d. Hôp.*, 1903, 3e sér., xx. 678, 733.
2. Widal and Javal, ibid., p. 990.
3. Achard, ibid., p. 980.
4. Mauté, *La Chlorurie alimentaire expérimentale*, Paris, 1903.
5. Strauss, *Chronische Nierenentzündungen*, Berlin, 1902.
6. Bence, *Zeitschr. f. Klin. Med.*, 1909, lxvii. 69.
7. Wagner, *Deutsch. Arch. f. Klin. Med.*, 1887, xli. 509.
8. Quincke, *Berl. Klin. Wochenschr.*, 1882, xix. 409.
9. Litten, *Charité-Annalen*, vii. 109.
10. Herringham, *Clin. Soc. Trans.*, 1901, xxxiv. 34.
11. Staehelin, *Zeitsch. f. Klin. Med.*, 1903, xlix. 461.
12. Wichern, *Deutsch. Arch. f. Klin. Med.*, 1907, lxxxix. 631.
13. Macleod, *Allbutt's System*, ed. 2, ii, Pt. II. 643; and for later outbreaks, *Indian Med. Gaz.*, Calcutta, 1908, xliii.
14. Hahn, Masser, Nencki, and Pawlow, *Arch. f. Exp. Pathol. u. Pharmakol.*, xxxii. 161.
15. Ascoli, *Vorlesungen über Urämie*, Jena, 1903.
16. French and Butler, *Trans. Path. Soc. Lond.*, 1902, liii. 236.
17. Hamburger, *Münch. Med. Woch.*, 1911, lviii. 2500.
18. Martin Fischer, *Œdema*, New York, 1910.

CHAPTER XII

NEPHRITIS

Some general term is needed to include not only inflammatory diseases, whether acute or chronic, which attack the parenchyma of the kidney, but also that slow increase of the fibrous structures within it which resembles cirrhosis of the liver, and sclerosis of the nervous centres. There has always been a dispute whether this form of fibrosis is to be called an inflammation or not. When fibrosis occurs together with, and as an integral part of, parenchymatous nephritis we feel no doubt. We can watch the process from its first stage to its last, and can assure ourselves not only that it follows the ordinary lines of inflammation in connective tissues, but also that it is produced by a cause which is at the same time inflaming the epithelial structures. But the slow thickening of the matrix, which is the principal and may be the only change in other cases, certainly does not fulfil the ordinary idea of inflammation, and is even rather opposed to it. Some see in it merely a process of replacement by which lower tissues increase when the nobler structures atrophy and perish. Others view it as part of a change in the vascular structures, and others again think it a part of senile degeneration, like the loss of elasticity in skin.

Still, for all that, some general term is wanted, and nephritis has so long been used that no other can well take its place.

Nephritis may, like other inflammations, be acute or chronic. There are some poisons, such as those of scarlet fever, and of septic diseases, which either by their virulence or by their mass inflict such a damage on the kidney as produces an acute inflammation. But these same poisons may

in other instances do less harm. We may believe, if we like, either that the poison is less virulent, or that its mass —for instance, the number of pathogenic organisms—is less, or that the native power of resistance is greater. For all these hypotheses there is plenty of analogy though little direct evidence. In a much larger number of cases these particular poisons are not present, and we must look for others as the cause. These form the great group of subacute and chronic nephritis which are linked both to one another and to the group of acute cases by a number of intermediate forms. There is no definite line of division here any more than in other regions of biology.

Every one will agree with this view when applied, as I have so far applied it, merely to the degree of inflammation and the acuteness of the attack. But I shall try to prove that the same principle obtains also when we observe how the different structures which compose the kidney are affected. We have been taught that the large white kidney and the cirrhotic kidney are different, and again that the large white kidney may become contracted and form the small white kidney which will differ from the cirrhotic kidney. Some pathologists have set up glomerulo-nephritis as a separate form. Others think that every nephritis begins in the epithelium. I believe that all these divisions are artificial, and I shall try to prove that both clinically and anatomically we may represent chronic nephritis by some figure like a fan. Starting from a common centre, some cases will, when they come to die, show much epithelial disease and little alteration of the matrix, while at the other end are cases which show extreme increase of the connective tissue, and between the two every degree of variation. These differences in histology correspond, I think, to differences in clinical symptoms. But such difference could, if I am right, only show itself clearly in the extreme forms. Intermediate forms would show combined symptoms. And if, again, histological changes vary at different times in the same kidney—for instance, by fresh attacks of epithelial inflammation, or by the gradual contraction of the connective tissue—then the same patient

might at different periods present symptoms corresponding to the histological condition at the time.

I need not say that there is nothing new in this. On the pathological side, at any rate, Ziegler has stated the same view now for many years. I hope, however, that I shall be able to combine the clinical symptoms with the anatomical changes a little more fully than has been done till now. In accordance with these views I shall speak of diffuse nephritis, acute and chronic, and shall include under the latter both the large white and the contracting kidney.

But I must carry this same principle still further. At the one end of the scale, or, to use the previous figure, in the last ray of the fan, lie the cases in which fibrosis has played the greatest part. I shall try to show that in these cases the secondary cardio-vascular changes have also been very great. But by the side of these cases I shall place another group in which the same connexion occurs, but with, I believe, a reversed causation, the kidneys of arterial sclerosis. It would not be difficult to maintain this distinction if patients with arterial sclerosis did not also in large numbers suffer with ordinary nephritis. But they do. The result, unfortunately for classification, is that in a large number of cases both causes are at work. This affects both the physician and the pathologist. As a physician I meet with a certain number of cases of arterial sclerosis in which I can find no evidence of renal disease, as a pathologist I find a certain number of kidneys in which I believe I can show the results of arterial sclerosis uncomplicated by true inflammation. But the great majority of elderly patients show both groups of symptoms to the physician, while on the post-mortem table I defy any one to say whether certain kidneys with a granular surface will, when they are microscopically examined, show parenchymatous changes or not. These points I shall argue in detail later on. But the result is that it is impossible, for purposes of statistics, to separate the two. When, as I now will, I bring forward certain statistics of chronic nephritis, I know that some few of the cases on which they are founded are cases of arterial sclerosis alone.

DEATHS *FROM* RENAL DISEASE

Age.	*Uræmia.*		*Cerebral Hæmorrhage.*						*Cardiac Failure.*					
	M.	*F.*	*M.*			*F.*			*M.*			*F.*		
	No. of cases.	*No. of cases.*	*No. of cases.*	*Av. wt. of heart in oz.*	*Av. wt. of kidneys in oz.*	*No. of cases.*	*Av. wt. of heart in oz.*	*Av. wt. of kidneys in oz.*	*No. of cases.*	*Av. wt. of heart in oz.*	*Av. wt. of kidneys in oz.*	*No. of cases.*	*Av. wt. of heart in oz.*	*Av. wt. of kidneys in oz.*
–20	3	3	0	—	—	0	—	—	1	—	—	3	—	—
20–30	2	3	1	—	—	0	—	—	6	16·5	14·0	3	11·0	10·3
30–40	4	0	2	—	—	2	—	—	10	17·7	11·4	8	13·3	11·1
40–50	5	3	7	17·1	12·0	6	13·4	9·8	13	21·1	12·5	6	15·6	12·6
50–60	0	3	31	16·4	10·5	5	12·0	9·6	20	20·2	12·5	7	16·5	12·5
60–	2	0	21	17·5	10·0	7	12·8	9·0	8	19·1	13·2	5	16·4	12·2
Totals.	16	12	62			20			58			32		
Totals.	28		82						90					

In the eight years 1900 to 1907 we have dissected 2,547 bodies dying in the medical wards at St. Bartholomew's. Of these, 565 showed distinct evidence of renal disease. The incidence, therefore, of all forms of renal disease upon the patients who die in our medical wards is about 22 per cent. Of these 2,547 patients 576 were between 20 and 40 years old, of whom 135 or 23·4 per cent. had renal disease; 722 were over 40 years old, of whom 396 or 54·8 per cent. had renal disease. The majority, however, of these patients died of intercurrent diseases. It is difficult to estimate how many died *from* as well as *with* renal disease, because it is difficult to say how many of the conditions which led to death were consequences of renal disease, and how many were independent of it. I have included as deaths *from* renal disease:

Cases dying suddenly without any other sufficient cause	9
Cases dying in uræmia	28
Cases with renal disease dying of cerebral hæmorrhage	82
Cases with renal disease dying with various results of cardiac failure	90

The last two are indirect results of renal disease, but so commonly associated with it that these cases may well be included among renal deaths.

There is a remarkable difference in the age-distribution of the two largest groups of deaths from renal disease. Hardly any cases of cerebral hæmorrhage occur under 50, whereas more than half the cases of heart failure die before that age. The weight both of the heart and of the kidneys is considerably higher in the cases of heart failure than in the other group. The uræmic group differs again in its age-distribution, but its numbers are too small to give reliable statistics. Of the cases who died suddenly, four were between 40 and 50 years of age, and the remaining five were all over 60 years.

It is impossible, as I have before remarked, to separate renal disease into true interstitial nephritis and diffuse nephritis from these statistics, since microscopic examination was in a large number of cases not carried out. In the absence of this separation, statistics of the weight of the

kidneys are not of much interest. Still it is worth while to point out cases of extreme variation from the normal.

In a man of 26, who died of asthenia, the kidneys weighed 4 ounces only. The heart weighed 15 ounces.

In a man of 35, who died with anasarca and pericarditis, the kidneys weighed 3 ounces, the heart 24 ounces.

In a man of 40, who died with hydrothorax and œdema of the lungs, the kidneys weighed 5 ounces, the heart 24 ounces.

These are the smallest weights recorded in patients over 20 years of age. It will be noticed that they all occurred among the deaths by cardiac failure. Among the deaths by uræmia the lowest weight for the pair of kidneys was 7 ounces in a man of 40 with a heart weighing 22 ounces. Among the deaths by cerebral hæmorrhage there is one case in which the weight of the kidneys was 5 ounces, a man of 54, with a heart weighing 16 ounces, and two cases in which the kidneys weighed 7 ounces.

Excluding cases of polycystic disease, the highest weights recorded for the kidneys are :

26	ounces	in	a	man	of	28	who	died of cardiac failure
24	,,	,,	,,	41	,,	,,	,,	,,
24	,,	,,	,,	41	,,	,,	uræmia	
24	,,	,,	,,	60	,,	,,	cardiac	failure
20	,,	,,	,,	36	,,	,,	uræmia.	

The impression usually given by text-books is that chronic nephritis reduces the size of the kidney, and that it is common to find small shrunken kidneys. That is not really the case. In 142 male cases, the weights for the pair of kidneys are distributed thus :—

Under	9	ounces								27	cases
9	and	10	ounces							30	,,
11	,,	12	,,							30	,,
13	,,	14	,,							26	,,
15	,,	16	,,							18	,,
17	,,	18	,,							5	,,
19	ounces	and	over							6	,,

Little more than a third are under 11 ounces in weight.

The standard for females is considerably lower than that for males, and therefore I have excluded them from the above table. To add females to males and then take an average is misleading.

The additional lesions found in these cases varied somewhat with the method of death.

Among the 28 uræmic cases there were two cases of polycystic disease which will be referred to in the chapter on that affection. In two cases there was concomitant diabetes. Four cases had cirrhosis of the liver. Two cases occurred in stunted, ill-developed boys, in one of whom the testicles were undescended.

Among the 82 cases of cerebral hæmorrhage, there were 17 cases of emphysema, 2 cases of cirrhosis, 2 cases of dissecting aneurysm of the aorta, 4 cases of ulcer of the intestine, 1 case of ulcerative colitis, 2 cases of gastric and 1 case of duodenal ulcer.

Among the 90 cases of cardiac failure, there were 42 which showed effusions in various parts, 14 cases of cirrhosis, 3 cases of submucous hæmorrhages in the intestines, 1 case of intestinal ulcer, and 1 case of multiple ulcer of the stomach. There were also 7 cases of thrombosis of various veins, including 4 cases of cerebral softening. One case had purulent peritonitis without obvious cause.

The remainder of the total of 565 cases, 356 in number, includes those who died of intercurrent diseases, and not from the renal disease which, in most cases after death, but sometimes during life, they were found to possess.

Of these a large number, 99 in all, were cases of valvular disease of the heart. It has been maintained that with mitral stenosis there is more than a chance connexion, and as this is still a debated point I will give some statistics from our post-mortem records. There are, however, many points to be considered before such evidence is of much value.

1. Mitral stenosis may be a primary lesion, but there are many cases in which the valve does not admit two fingers, yet the condition is merely part of a general

cardio-vascular degeneration. I have, therefore, classed separately cases in which the mitral valve was either affected alone, or so severely that it was evidently a primary endocarditis.

2. The surface of a kidney may be made irregular not only by general fibrosis, but also by the scarring of infarcts. Unless carefully observed, the one may be mistaken for the other. These cases have been so observed, and infarction or infarction scars are noted. The records are the work of Drs. Garrod, Calvert, Morley Fletcher, Hartley, Horder, and Langdon Brown.

TABLE SHOWING CONNEXION OF HEART DISEASE WITH RENAL DISEASE.

Age at Death.	*Total Cases of Mitral Stenosis.*	*Ditto with Renal Disease.*	*Per Cent.*	*Total Cases of Aortic Regurgitation.*	*Ditto with Renal Disease.*	*Per Cent.*	*Total Cases of other forms of Heart Disease.*	*Ditto with Renal Disease.*	*Per Cent.*
0–10	5	0		0	0		6	0	
10–20	34	2		3	0		13	1	
20–30	27	9	37·5	8	2	38·8	12	3	32·1
30–40	29	12		10	5		16	6	
40–50	14	9	70·0	14	2	42·8	26	13	58·5
50–	16	12		7	7		15	11	
Total.	125	44		42	16		88	34	

For aortic regurgitation, and for the other forms of valvular disease, chiefly mitral regurgitation, I do not think any such connexion can be traced. Though the incidence of renal disease is higher than normal before 40 years of age, the numbers are small, and the proportion does not remain appreciably above the average after 40 years of age.

During 8 years, of 122 persons who died in our medical wards with mitral stenosis, 56 were male, 66 were female.

They are classified in the following tables:

TABLE I.

Males.

Age.	*Mitral Stenosis.*		*State of Kidneys.*				
	Severe or Solitary.	*Combined.*	*Natural or only congested.*	*Congested with adh. capsule.*	*Infarcts.*	*Granular.*	*Other forms.*
–20	13	11	18	2	3	0	1
20–	4	8	6	1	2	3	0
30–	6	4	5	2	2	0	1
40–	4	0	1	0	0	2	1
50–	3	3	1	0	1	4	0
	30	26	31	5	8	9	3

Females.

–20	6	7	8	0	5	0	0
20–	7	6	4	2	3	4	0
30–	11	7	6	1	2	7	2
40–	8	2	3	1	1	5	1
50–	4	8	2	0	2	7	0
	36	30	23	4	13	23	3

TABLE II. CASES WITH SEVERE OR SOLITARY MITRAL STENOSIS.

Sex.	*Total at all ages.*	*State of Kidneys.*				
		Natural or only congested.	*Congested with adh. capsule.*	*Infarcts.*	*Granular.*	*Other forms*
Male . . .	30	17	2	2	7	2
Female . .	36	16	2	2	14	2

These tables show :

1. That under 20 years of age mitral stenosis, whether primary or combined, is more frequent in males than in females, while above that age it is more frequent in females than in males.

2. That in neither sex under 20 years of age is there any connexion between mitral stenosis and granular kidney.

3. That over 20 years of age there is a coincidence of mitral stenosis of all forms and granular kidney, which is insignificant in males (32:9) but is significant in females (53:23).

4. That if cases of 'primary' mitral stenosis are taken alone the coincidence over 20 years of age is in males as 17:7, in females as 30:14, which is probably significant. If the combined form of mitral stenosis is taken alone the coincidence is probably insignificant in either sex (males 15:2, females 23:9), but is yet considerably greater in the females.

The relationship was noticed by Goodhart and by Newton Pitt.[1] Gibson[2] explains it as a form of cardio-vascular sclerosis, and gives an instance which bears out his view. It is well known that mitral obstruction is more frequent in women than in adult men, and that in a large proportion of them there is no rheumatic history to be obtained. It is possible that it is these cases which increase the coincidence of granular kidney.

I have tried by referring to our records to distinguish between the rheumatic cases and the rest. But I have found, as usual, that unless notes are taken with a particular question in view they are useless for that question afterwards. The cases in which it is definitely stated that the patient had or had not had rheumatic fever are too few to afford reliable conclusions.

Another point that may be remarked is the connexion of septic endocarditis with renal disease. This occurred in 49 cases. The result of septic endocarditis upon a normal kidney is an acute or subacute nephritis rendering the kidney large, with a pale or mottled cortex and congested pyramids. This condition was found in 18 cases. In many cases infarcts were found. In 26 cases the kidneys were merely described as granular or as the subject of chronic interstitial nephritis. One was a case of polycystic disease.

There was old heart disease in 22 of these septic cases, two cases were pneumococcal and occurred in pneumonia, and two were infected from the uterus. The great majority of the cases of old heart disease showed kidneys which were the

subjects of chronic rather than acute change, and the evidence points to the conclusion that the nephritis predisposed to septic infection of the heart.

The connexion between renal disease and cirrhosis of the liver has already been touched upon. It may be again examined from another point of view. In these eight years there have been 131 autopsies on cases of cirrhosis of the liver. Of these, 71 had renal disease, 60 had not. As far as could be made out, 21 out of the 71 died of their kidneys, the remaining 50 died of their liver disease, or of some other disease not consequent upon nephritis.

There does not seem to be a close connexion between cirrhosis of the liver and any special form of renal disease. Among those that died of renal disease, there were found both large and small kidneys, and they are variously described. It is the same with the remaining 50. The majority in both groups are described as chronic interstitial nephritis; but this, as before remarked, means little except that fibrosis was present.

Of these 50, 16 cases died directly from the effects of hepatic cirrhosis, 8 cases died of heart disease, 6 cases died of tuberculosis, and the remainder of various causes.

The connexion with renal disease seldom occurs early in life. In the whole 131 cases :

3	cases	died	under	10	years	of age,	of which	0	had	renal disease.
6	,,	,,	between	10	and	20 yrs.	,,	0	,,	,, ,,
9	,,	,,	,,	20	,,	30	,,	,,	3	,, ,, ,,
18	,,	,,	,,	30	,,	40	,,	,,	8	,, ,, ,,
41	,,	,	,,	40	,,	50	,,	,,	22	,, ,, ,,
40	,,	,,	,,	50	,,	60	,,	,,	27	,, ,, ,,
12	,,	,,	over	60	years	of age	,,	9	,,	,, ,,

And in two the age is not stated.

References.

1. Newton Pitt, *Brit. Med. Journ.*, 1887, i. 108.
2. Gibson, *Allbutt's System*, ed. 2, vi. 373.

CHAPTER XIII

ACUTE NEPHRITIS

Acute nephritis is not a common disease. At St. Bartholomew's, with an average of 7,000 medical cases a year, we have only had 166 cases, 120 males and 46 females, in the last nine years.

It is, however, practically impossible to obtain accurate statistics, either of the incidence or of the causation of acute nephritis, there, because no patients with scarlatina are knowingly admitted to the general hospitals. In consequence, we cannot compare the frequency of scarlatina with that of other causes.

Looking through the 20 cases of which I have detailed notes, I find that 7 were connected with sore throat, 2 were due to exposure, 2 came on during acute fever, and for the remainder no cause could be discovered.

I have often seen albuminuria with tonsillitis, but I was not prepared to find so many cases of acute nephritis preceded by it. In two cases, each in a boy 15 years old, there was tonsillar abscess, and nephritis supervened during its course. In one boy, aged 6, the symptoms began one week after the onset of a very severe sore throat with swelling of the cervical glands, which was present when he was admitted. In four other patients, the first symptom, facial œdema in each case, did not appear until three or four weeks after the tonsillitis, and when all symptoms of that had passed. The last case, a boy aged 11, had never had scarlatina, and presented no symptoms of it during his stay in the hospital, though he was examined very carefully and repeatedly. But scarlatina was rife in the neighbourhood. In the other cases no evidence of scarlatina could be obtained, and diphtheria was, so far as possible, excluded.

Among the infectious fevers scarlatina is far the commonest cause of nephritis. The latter may begin during the acute stage, but is more common in the third or fourth week. A slight case of scarlatina is quite as likely to produce nephritis as a severe case, and one of the difficulties of such a case as that last described is that nephritis is well known to occur in patients who are exposed to scarlatinal infection, but never show a rash. Diphtheria comes next in the order of frequency. Measles occasionally produces nephritis. This we see sometimes in the hospital, but I remember a little boy who was admitted for albuminuria catching measles in the hospital, and recovering from the measles and the albuminuria at the same time. It was probably an acute nephritis which happened to clear up at the same time as the measles.

Two of my cases arose in the course of other fevers. One, a man of 51, of drunken habits, was admitted for an irregular pneumonia. The fever was never above 101° F. and fell by lysis. On the sixth day he began to pass blood, albumen, and casts, and was discharged with albuminuria still remaining.

Another patient, aged 26, was in the fourth week of typhoid fever when blood and casts first appeared. The *B. typhosus* was found in the urine. Geier [1] records similar cases in children.

In another case it seemed as if *B. Coli* might perhaps have caused nephritis. A man of 21 had headache on October 9th, and next day his face swelled. He had been in good health till then, and had had no renal symptoms at any time. On October 10th he was admitted with albuminuria. On October 20th the albumen was 0·13 per cent. (Esbach) and the urine was found to be swarming with *B. Coli*; October 22nd, albumen 0·01 per cent.; October 23rd, no albumen, but a few *B. Coli* were still visible. Albumen did not reappear and he was discharged well.

Nephritis sometimes, but rarely, occurs in the secondary and tertiary stages of syphilis. No such case is included in my series.

The two cases of nephritis from exposure were both in men. One, a lad of 18, got wet through from rain, the other, a man aged 26, a river constable, fell off a wharf in a fog.

In each the first indication of renal disease began two days later.

In the remaining cases, whose ages ran from 4 to 29, no cause whatever could be found for the attack.

There can be little doubt that when nephritis arises in the course of an infectious fever, it is due either to the specific microbe or to its toxin. In typhoid fever we know that the microbe itself is excreted in the urine, and nephritis is probably caused by it. In scarlatina and in diphtheria nephritis may come on later, and it is then likely that it is rather a toxin produced by the microbe than the microbe itself which causes it. The nephritis which occurs with tonsillitis is no doubt due to a similar cause.

In all these diseases, and in many other fevers, transient albuminuria is often observed. This appears, for instance, to occur in 75 per cent. of cases of diphtheria. It seems certain that this must be due to slighter damage, but of the same nature, as that which leads to undoubted nephritis.

So is it, I imagine, with nephritis from a chill. A chill, by which we mean not mere exposure to cold, but exposure at a time when the body is unprepared, and the skin full of blood, has the effect of lowering the natural resistance. A man so weakened is liable to be attacked by any pathogenic organisms present, and in his weakest part. Both factors are important. Some organisms, such as the pneumococcus, have places of predilection, and it may be that some tend naturally to attack the kidney. They are, however, with the possible exception of *B. Coli* and its congeners, as yet unrecognized.

On the other hand, the man may be especially vulnerable in one spot. After a chill one man gets a cold in his head, another bronchitis, a third diarrhœa, and a fourth nephritis. In each case he is probably suffering from the invasion of some organism, but as yet we have not recovered or isolated it in enough cases to formulate the pathological laws involved.

A third hypothesis which the pathology of hæmoglobinuria raises in the mind is that chill may produce some substance in the blood which damages the kidneys.

None of the cases above mentioned were due to chemical

irritants. There is no doubt, however, that such cases occur. Copaiba, cantharides, perchloride of mercury, carbolic acid, and phosphorus are all known to cause acute nephritis when taken internally. The same effect will follow their absorption through the skin. Chlorate of potash, which is hæmolytic, first causes hæmoglobinæmia, and then a profuse hæmoglobinuria, which may lead subsequently to nephritis.

It is difficult to describe an attack of acute nephritis, for the symptoms are variable.

Even when, as in scarlatinal nephritis, the attack can be noted at the onset, the cases vary widely. Some begin acutely with pyrexia of a marked character fluctuating from 97° to 103° F., and lasting for about a week. The skin is dry, the pulse and the respiration quick. In these cases the urine is diminished, perhaps almost entirely suppressed. This condition yields in the second week, the fever falls, the pulse becomes less rapid, even slower than normal, and the urine increases. In others there are no acute symptoms, and the onset is only known by diminution of urine or by the appearance of albuminuria and hæmaturia. Oedema may be severe, slight, or absent, in either form. The two cases whose onset occurred in our wards were of the latter class.

It is, however, comparatively seldom that the beginning of an attack is seen in general medical practice. The patient usually gives no history except that of slight œdema, or less often of some general malaise. At the time he comes under observation œdema has often disappeared. The condition of the urine is in most cases the chief, and in many the only, symptom of disease.

In this class it must not be expected to find the urine of high specific gravity and of a concentrated character. For instance :

M. 23 adm. in first week	Average of first few days	1,500 cc., sp. gr.	1014–16
M. 29 ,, ,,	,,	1,200 cc., ,,	1012
M. 13 ,, ,,	,,	1,140 cc., ,,	1022–24

Later, when the amount increases, the density naturally becomes lower still.

In a case of nephritis from chill the urea was frequently estimated from the fourth week onward. It was normal in amount. Albuminuria and hæmaturia occur in practically every case. Hyaline, epithelial, and blood casts are found with the microscope.

Only one of my cases was of the acute febrile kind, and in none of those that survived did I find any change in the heart or arteries, or any rise in the blood-pressure. The fundus was examined in several, but in none was any change seen. Retinitis albuminurica has been said to occur in acute cases, but the reports are unconvincing. As a practical rule its existence is a proof that the disease is of long standing.

The course of the cases varies considerably. In scarlatinal nephritis, and especially in the acute form, the prognosis is very favourable. Foord Caiger believes that scarlatina is much less commonly a cause of the nephritis which is discovered in later life than is usually thought.

Of my 20 cases 8 were discharged free from albuminuria. The youngest of these was 8 years, the oldest 29 years old. Four of them were tonsillitic cases.

Eight of the remainder had albuminuria on discharge. Two of these were little girls of 4 years old, showing that even in little children an acute nephritis is apt to lead to permanent disease.

Four patients died, one of them of typhoid fever. The other three cases are the following :

Mary B. Wright, aged 5, was quite well until, on August 3rd, she was seized with vomiting, which lasted several days. On August 4th a purpuric rash appeared. She was admitted on August 12th. She was a well-nourished child, with œdema of the eyelids. The retinæ were natural. There was slight albuminuria at first, but on August 16th much. Casts and blood were found in the urine. On August 26th she passed only $8\frac{1}{2}$ ounces. On August 28th the œdema was great. At the end the signs of pneumonia appeared, though the temperature was never raised. She died on September 9th.

Post Mortem. There was a purpuric rash on the skin. There was a little fluid in the pericardium, and hæmorrhages on

the visceral layer. The heart weighed 4 ounces. The left ventricle was dilated and hypertrophied. The valves were normal. The pericardial fluid was sterile, the aorta and the vessels were natural. The colon contained numerous circular ulcers, some as large as a sixpence, which were on the solitary follicles.

Kidneys. Wt. $4\frac{1}{2} + 4\frac{1}{2}$ ounces: swollen. Capsule stripped easily. Surface smooth and finely stippled with minute hæmorrhages. On section, substance soft, reddish, with mottling of the cortex. *Microsc.* Tubes—extreme catarrh. Glomeruli—exudation and epithelial cells in the intracapsular space. Arteries natural. Interstitial tissue—cellular effusion.

William Calverley, aged 7, was quite well till, on April 12th, his eyes and face were swollen. Two days later the legs and body swelled also. On April 16th he began to vomit.

He had had no illness but measles four years ago; and had had no such attack as this before.

Admitted April 17th. A pale boy, bloated with œdema; slightly feeble-minded. The retinæ were natural. The heart was normal. The pulse 120, the pressure normal. The urine scanty, acid, a cloud of albumen and no blood.

April 28. Only a few ounces of urine, much albumen.

May 3. Urine almost solid with albumen.

May 5. Urine about 10 ounces. Is being sweated freely twice a day by a hot bath. Urine almost solid with albumen. No casts visible.

May 6. Only 5 ounces of urine. Not drowsy.

May 14. Still very little urine. Only 5 ounces to-day. But he shows no symptoms of uræmia, is quite sensible, talks freely, takes well, is very thirsty and has not been sick or had any twitchings.

May 21. Urine 6 ounces. Œdema great.

May 22. No urine in last 24 hours. T. 100·6, no signs of uræmia. Southey's tube into left leg, but it did not drain well.

May 23. Delirious last night.

May 24. No urine passed. Vomited thrice yesterday. No delirium. T. 102° F.

May 25. Constant sickness. Quite conscious. Gasping respiration. T. 103° F., later delirium, death.

Post Mortem. General anasarca. Lungs œdematous. Heart 4 ounces, normal. No hypertrophy. Aorta and cerebral vessels natural. Ascites. Liver and spleen natural.

Kidneys $4\frac{1}{2}+4\frac{1}{2}$ ounces. Smooth, pale; capsule stripped readily. Stellate veins conspicuous. On section, cortex broad and pale. *Microsc.* Convoluted tubes—epithelium flattened and fatty, lumen plugged with granular débris. Collecting tubes —epithelium natural, lumen plugged as above. Glomeruli—no intracapsular exudation. The tufts fill the capsules entirely, and appear crowded with nuclei, as if the cells belonging to them were increased. Arteries natural. Interstitial tissue—cellular effusion in parts.

Florence Poynter, aged 10, had old hip-disease but was otherwise in good health until, on June 25th, her face and one leg swelled, the other leg swelling a few days later. On June 30th she had headache and vomiting, and the urine was dark in colour.

On July 2nd she was admitted very œdematous, with hæmaturia. Casts of blood cells were found in the urine. She had a temperature of 104·6° F. and was unconscious. She died in a few hours.

Post Mortem. Purulent meningitis. Meningococcus intracellularis in pure culture.

Kidneys, 14 ounces together; red; acute exudative and catarrhal inflammation in both glomeruli and tubes.

Meningitis was no doubt a terminal infection.

The two first cases illustrate the ordinary symptoms in severe cases.

The small ulcers in the colon of the first case were probably due to necrosis from hæmorrhages such as were seen in the skin and pericardium. The low pneumonia in the first and the meningitis in the third case are instances of the tendency which these patients have to terminal infections, and their lessened power of resistance.

The chief symptom of the second patient, extreme diminu-

tion of the urine, is the prominent feature in many fatal cases. Its duration was remarkable. In a boy of this age it is often, and was in this case, impossible to collect the whole urine. Only occasionally could it be done. If these days were fair samples, then from April 28 to May 25 the boy was passing something like 5 ounces of urine only per diem.

Later on I will discuss suppression of urine in connexion with a case of chronic nephritis. Here, I will only point to the combination of great œdema and partial suppression of urine, without severe cerebral symptoms, and indeed with very few symptoms of any kind except in the last day or two of life.

Klebs was the first to speak of glomerulo-nephritis as a distinct species, and Klein, by finding the glomeruli constantly affected in a series of scarlatinal cases, added importance to the name. But it is doubtful whether cases can with any truth be separated into those with glomerular inflammation and those without.

Such authorities as Brault, Cornil and Ranvier, and Weichselbaum, appear to consider that scarlatinal cases resemble any other infective form, and that infective nephritis much resembles both the nephritis that can be produced artificially and the nephritis whose cause is not ascertained.

Thursfield and I,[2] working with the kidneys of nephritis in a later stage, were unable to classify cases by their glomerular lesions. 'We would liken the conditions of this form of nephritis to those of an eruptive fever, and would say that the variations above mentioned are no more striking than those observed in the eruptions of variola or scarlatina, which sometimes involve much, sometimes little, of the skin, and even occasionally in scarlatina fail to appear at all. We do not, however, suppose latent scarlatina to be a different disease because there is no rash, nor a discrete variola to be due to a different poison from that of the confluent form.'

The probability is that all acute inflammations of the kidney are diffuse in character, affecting in varying degree the convoluted tubules, the glomeruli, and the interstitial tissue also.

It is difficult in the human subject to be sure that slight changes are morbid and not the natural result of post-mortem decomposition. But it is generally allowed that the absence of staining in the epithelial nuclei, and indistinctness in the structure of the cells are early signs of disease in the convoluted tubes. They are often seen in the kidneys

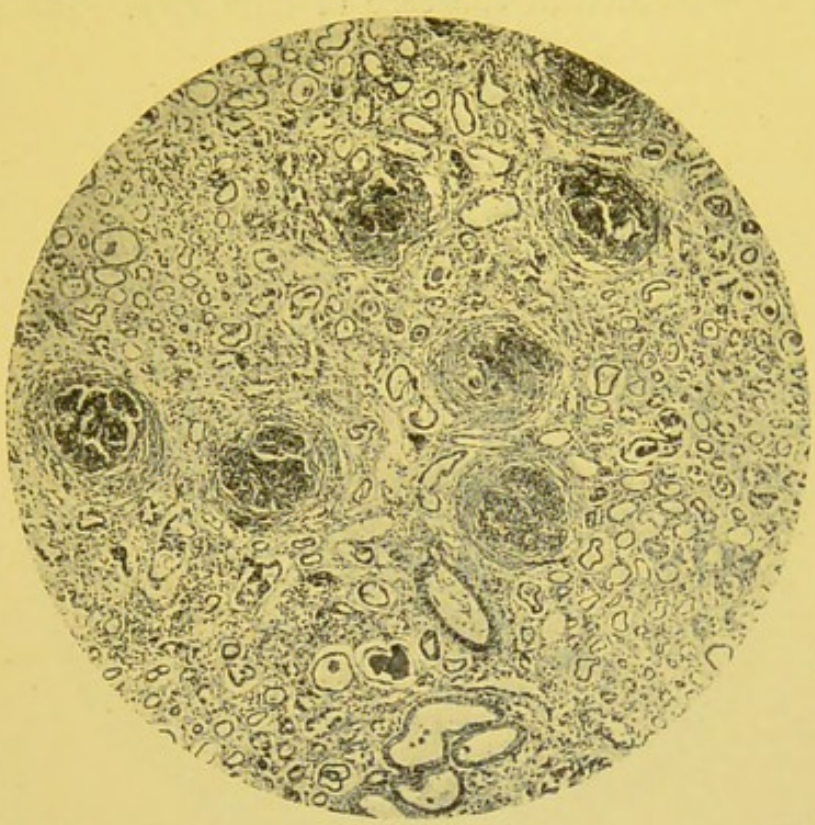

Fig. 1. Winifred Searle, 15. No history could be obtained of any renal symptoms previous to the final attack, which was of short duration. The condition of the kidneys, however, especially the fibrosis, which was very marked, proved that the disease was of considerable standing. This figure gives a general view. × 55.

of children dying from diphtheria who have passed albumen during life. A severer, or perhaps a more prolonged inflammation, produces catarrh and proliferation of the epithelium, which is then thrown off into the lumen of the tube and gradually broken up. The lining of the tube is not perfect, gaps remaining where some of the cells have fallen out. Appropriate stains will show fatty drops in the cells. Various substances may be seen in the lumen of the tube. Sometimes the tube contains nothing but blood-cells ; sometimes there are

remains of epithelium ; and sometimes there is nothing but a structureless hyaline plug. These correspond perhaps to the various casts seen in the urine during life.

The collecting-tubes are often filled with similar contents, but the epithelium is generally unaffected.

The earliest change seen in the glomeruli is the condition of the tuft described in the case of Calverley. The tuft fills

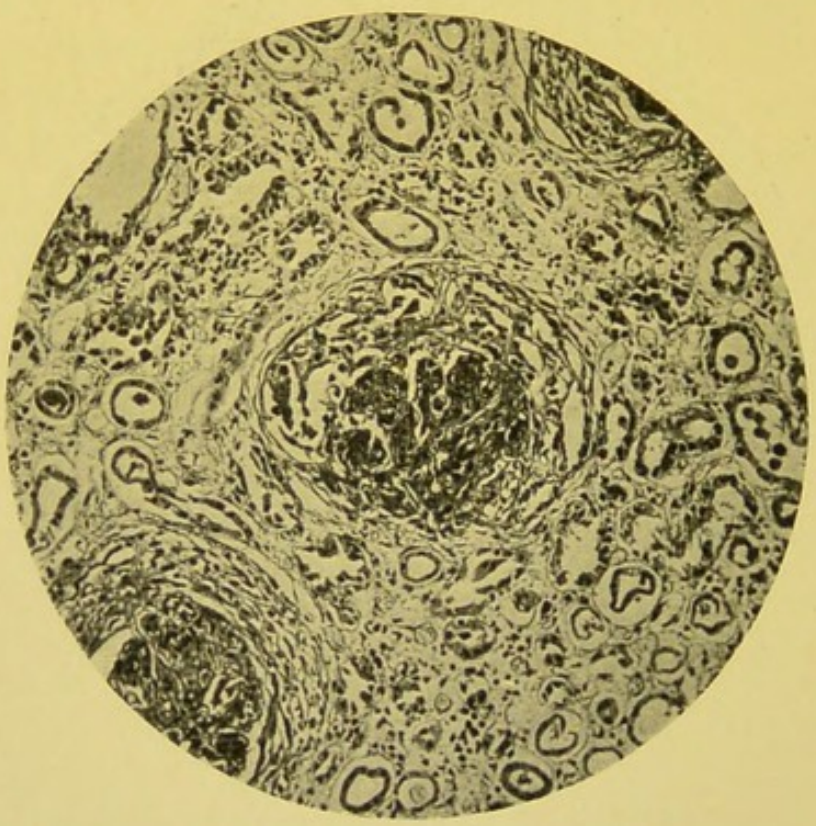

Fig. 2. The same case. A glomerulus showing an early stage of intracapsular inflammation, exudation into the space, with nests of cells. × 120.

up the whole space of the capsule and has apparently more cells in it than natural. Yet the epithelium of the parietal layer of the capsule is not altered. It seems difficult to believe that the visceral layer could proliferate alone.

A further stage is the exudation of a structureless material into the intracapsular space (Fig. 7). This I suppose to be the chief source of albuminuria. Next comes the proliferation of epithelial cells from the lining layers, and their desquamation into this albuminous matter. They are sometimes scattered at random, at others collected into nests, between which

strands of the structureless material pass. In other cases there seems to be a concentric lamination beginning, and again in others this has gone so far that a fine meshwork of cells and intercellular material lies against the capsule which much resembles fibrous tissue.

Thursfield and I were inclined to look upon these conditions as successive stages of the same process and suggested an

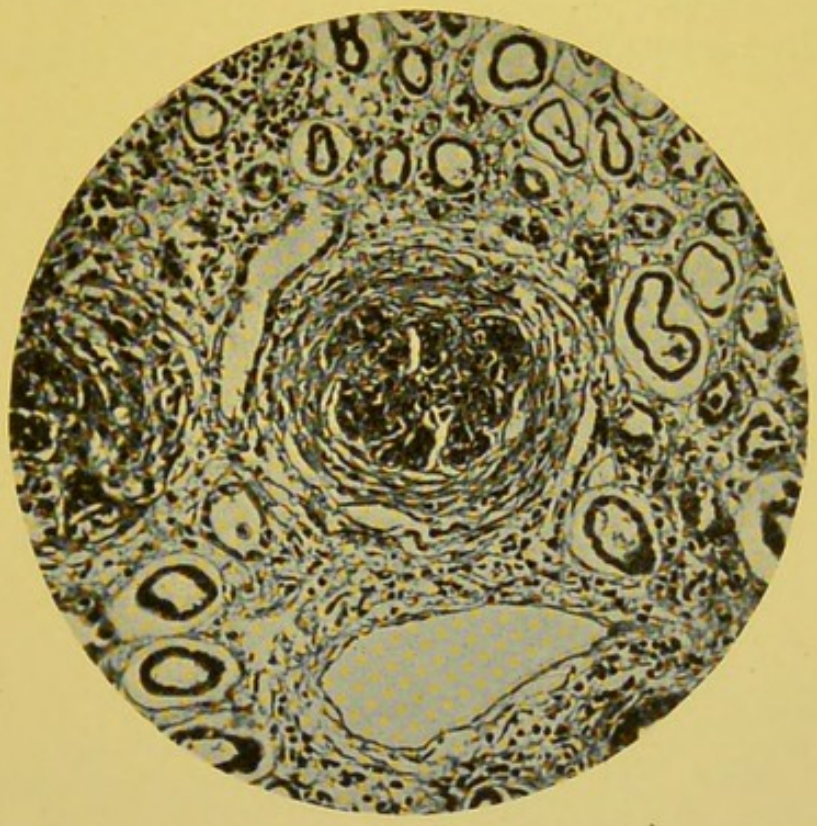

Fig. 3. The same case. The inflammation at a later stage, when the spaces are flattened out, and the exudation with the cells in it are beginning to resemble a concentric formation of fibrous tissue. × 135.

explanation. The tuft is first damaged sufficiently to allow of an escape of the plasma into the space. Next follows epithelial catarrh of the parietal and visceral layers of the capsule. The cells are shed into the plasma. So far the process has tended to the compression of the tuft. Later the tuft expands again, presses the exudation and cells outwards, and thus produces the effect of lamination which is carried to its furthest pitch in the fine meshwork of the last stage. This may very possibly form fibrinous material and become organized.

The interstitial tissue is the seat of a sero-cellular effusion, which widens the spaces between the tubes, and increases the size and weight of the kidney. Small round cells lie in these spaces, which at a later stage help in the formation of fibrous tissue.

References.

1. Geier, *Jahrbuch. f. Kinderheilk.*, xxix. 1.
2. Herringham and Thursfield, *Trans. Path. Soc. Lond.*, 1904, lv. 284.

CHAPTER XIV

SUBACUTE AND CHRONIC DIFFUSE NEPHRITIS

CHRONIC PARENCHYMATOUS NEPHRITIS, LARGE WHITE KIDNEY, CONTRACTED KIDNEY, ETC.

Cases of primary acute nephritis seldom, except in childhood, recover completely. Most of the adult cases are left with a chronic form of the disease. The causes, therefore, of acute, are also causes of chronic diffuse nephritis.

In the course of septic endocarditis, nephritis is common. It does not begin acutely, and the albuminuria and hæmaturia are often attributed to cardiac failure and to pyæmic embolism. Further, it has to be remembered that chronic nephritis lays a patient open to septic endocarditis, in which case the sequence of causation would be reversed.

But every one who has looked into the question will recognize that the cases of chronic nephritis which can give a history of an acute beginning or are connected with heart disease are a small minority. Far the greater number begin insidiously, with no severe symptoms. They are either discovered accidentally, or an acute exacerbation supervenes which is at first thought to be a primary attack, until careful inquiry shows that symptoms have existed already for a long time.

For instance, a girl, aged 17, was admitted for epilepsy, from which she had suffered ever since infancy.

The heart, the pulse, and the artery were perfectly normal, the retinæ were healthy, and there was no œdema. But the urine constantly contained a large amount of albumen. She had no idea that her kidneys were diseased, and could give no history of any renal symptoms. There was no vaginal discharge.

A young lady, aged 23, was attended for some slight illness, and in the course of attendance the urine was examined. It was found to be albuminous. Upon inquiry it was found that she had had a long bathe a few months before and had felt cold after it. This was selected as the cause of nephritis. But when she consulted me I found, first, that no renal symptoms whatever had been noticed after the bathe, and, second, that her mother remembered her sometimes having puffiness of the face and eyes in childhood. I thought it probable that the condition was of long duration. But, at any rate, it did not begin acutely.

The causation of these cases is obscure.

I am sure that they cannot all be ascribed to zymotic diseases or to chills. I have minutely cross-questioned a large number of these patients, and no doubt remains in my mind as to this point. The majority of them, I am certain, cannot be ascribed to either of these causes.

It has been supposed that some form of self-poisoning, either chemical or microbic, may be at the bottom of them. The known facts of acute nephritis due to chemical poisoning render a similar origin possible for the chronic complaint. It is very tempting to suppose either that a patient has been taking repeated small doses of a chemical irritant, alcohol for example, or that some faulty metabolism on his part, such as is commonly assumed to exist in gout, has produced abnormal substances which damage the kidney during excretion, or even that an excessive ingestion of food has led to such overwork of the kidneys that damage has resulted. The difficulty is to obtain satisfactory evidence that such events actually occur. A great number of these patients are under 30 years of age and many of them women. Alcohol and excess of any kind can be definitely excluded in many of these cases.

So, too, in the case of bacterial poisons. It is well known that *B. coli* produces at times acute inflammation of the bladder and of the renal pelvis. One of my cases even suggests that it may sometimes produce acute nephritis. But the majority of these cases are infected from without. How often

B. coli is conveyed to the kidney in any other way than from the bladder is uncertain. Except in the rarest instances no microbes other than those of infectious or septic diseases are known to be conveyed by the blood. But it is supposed that perhaps *B. coli*, or some other organism, may pass directly or indirectly from the intestines to the kidneys and may be the cause of some cases of nephritis. A second theory is that, if not a microbe itself, then some toxin, as in diphtheria, may be absorbed from the intestinal tract. So far, however, no evidence has been produced of such an infection.

The syphilitic origin of chronic nephritis in children, and perhaps in adults, has been argued with considerable force by Guthrie, Sutherland, and Sawyer [2] in England, and by others abroad. The evidence is hard to get, but there seems to me sufficient to render it probable that some cases arise from this cause.

This is perhaps the best place to refer to the occasional heredity of nephritis. Dickinson [1] recorded a remarkable family tree including four generations. Three out of five individuals in the first generation, four out of six in the second, five out of one family of six in the third, and one, a child, in the fourth were affected with albuminuria. The kidneys of one fatal case were examined by Dickinson and are figured. The appearances are those of diffuse nephritis of the contracted kind, which is described in this chapter. (Cp. Family Hæmaturia, p. 72.)

Besides these cases, which have been insidious from the beginning, we see a good many others in acute exacerbations. These are the cases which are usually called acute nephritis. They give, however, either in their history when carefully questioned, or in their symptoms when carefully examined, satisfactory evidence that the condition is of old standing. For the moment they have acute nephritis, but it is not the primary disease but an acute inflammation supervening upon a chronic.

When in their usual condition, these patients may show very few symptoms. Indeed, as I have said, in many the disease is not suspected, and is discovered accidentally. But

if the physician is on the look-out he will generally notice the two signs which mark them, a slight anæmia, and a slight waxiness or puffiness of the lower eyelids. Examination of the urine discovers albuminuria.

In the mildest cases these three symptoms are of the slightest possible degree of severity. The urine is of normal quantity, appearance, and density, and contains only a trace of albumen. But if this is constant, and if occasionally a cast is discovered under the microscope, the diagnosis is undoubted.

To show how little the urine is altered, I will quote the figures for the case of the young lady I mentioned above. In twenty-four hours on an ordinary fish diet she passed

Urea	22·0	grammes
Cl	6·5	,,
P_2O_5	2·8	,,

which is normal.

In such a case the very slight degree of albuminuria implied very slight damage to the glomeruli and probably to quite a small proportion of them. It is likely that five out of six microscopic sections might not show any that were diseased.

Similarly, the passage of a normal quantity of urea and salts showed that there was abundant epithelium left for the purposes of life. It must be remembered that we start with an amount of kidney greatly in excess of our requirements. No surgeon hesitates to remove one kidney if the other is sound. He knows that one is enough. The evidence of a renal lesion, albuminuria and casts, will therefore appear before the excretory power shows any diminution.

There could, however, be no doubt that in this case the kidneys were in part structurally diseased, and after childhood such kidneys cannot be expected to return to a healthy condition.

The risk of such a state is not immediate. Indeed the prognosis depends very much upon the patient's circumstances. If he is sufficiently well off, and sufficiently free to take care of himself, he can prolong his life almost indefinitely. I knew

well a man who had albuminuria at 18, who suffered greatly from gout, so that his hands were covered all over with small chalk stones, and who yet lived the exposed and arduous life of a farmer up to his death, which did not take place till he was nearly 50. I played cricket with him when we were both over 40. But such a patient is never robust, he generally shows a tendency to anæmia and to slight œdema. Above all, he can take less risks than other men and is very liable to chill, or to feel the effects of even slight excess.

If he lays himself open to these, which in the case of a labouring man or woman it is almost impossible to avoid, he gets an acute attack, he shows all the symptoms of acute nephritis, and at the end of it he convalesces, but is left with a permanent increase in his albuminuria and a permanent lowering in his standard of health.

So the disease reaches a second stage of severity. And from this point it may develop in one of two directions. It may tend almost entirely to epithelial degeneration, which in extreme cases produces the large white kidney. Or, along with parenchymatous inflammation, there may be a marked interstitial fibrosis, which gradually produces a contracted kidney. These two forms are not consequent the one to the other. They are, on the contrary, divergent. Each is the terminal form of a special morbid evolution. In acute nephritis, as has already been said, the inflammation is diffuse, and the parenchymatous inflammation is accompanied by a cellular infiltration of the interstitial tissue. Doubtless the same is true of the early stages of the insidious and chronic form. And, just as in phthisis one case proceeds by a continuously spreading broncho-pneumonia with softening, while another tends to fibrosis, so one case of renal disease will differ from another in its course. The reason for this difference may lie in the quality of the original infection or in the tissues of the host. We cannot tell. That the disease is one and the same is proved by the countless intermediate forms which link the two extremes. Yet typical cases of the extreme forms differ so widely both in clinical symptoms and in post-mortem appearance, that they might be two separate diseases. This

is again nothing more than occurs in phthisis. There is no greater difference in these forms of diffuse nephritis than there is between a case of caseating broncho-pneumonia and fibroid phthisis.

Of these two forms of renal disease, the former, the large white kidney, is much the rarer. It is marked by great general dropsy, and by the absence of arterial disease, retinitis,

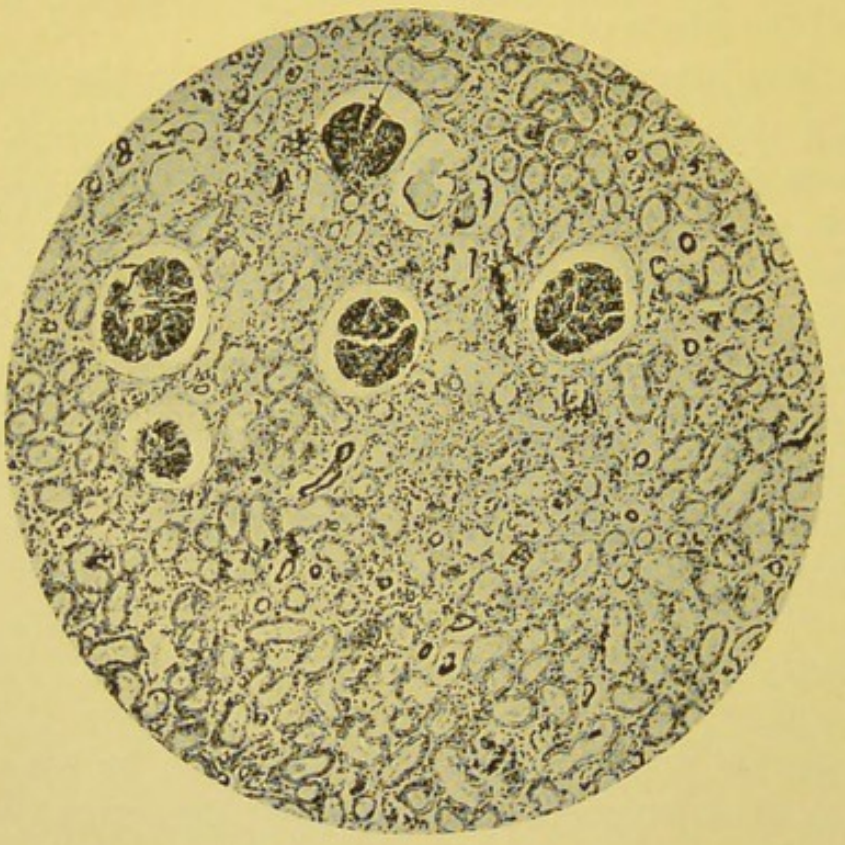

Fig. 4. Amy Morell, 19. Exudation into convoluted tubes. A patch of round-cell infiltration. × 55.

and uræmia. The patients die by gradual asthenia. The following is a typical case :

Amy Morrell, 19, single, was admitted in March 1906 for severe general dropsy.

There was no history of an acute onset, or of scarlatina at any time.

There was no retinitis, and no thickening of the radial. The blood-pressure was a little increased, but the arm was œdematous, and œdema raises the reading of the sphygmo-

manometer above the true level. Before death the reading fell to the normal, 120 mm. of Hg., which probably corresponded to a pressure considerably below the normal. The heart was enlarged. Its apex was $4\frac{1}{2}$ inches from the middle line. There were no murmurs. The bases of the lungs were œdematous. The urine was always scanty, had a specific gravity of 1010, and was loaded with albumen.

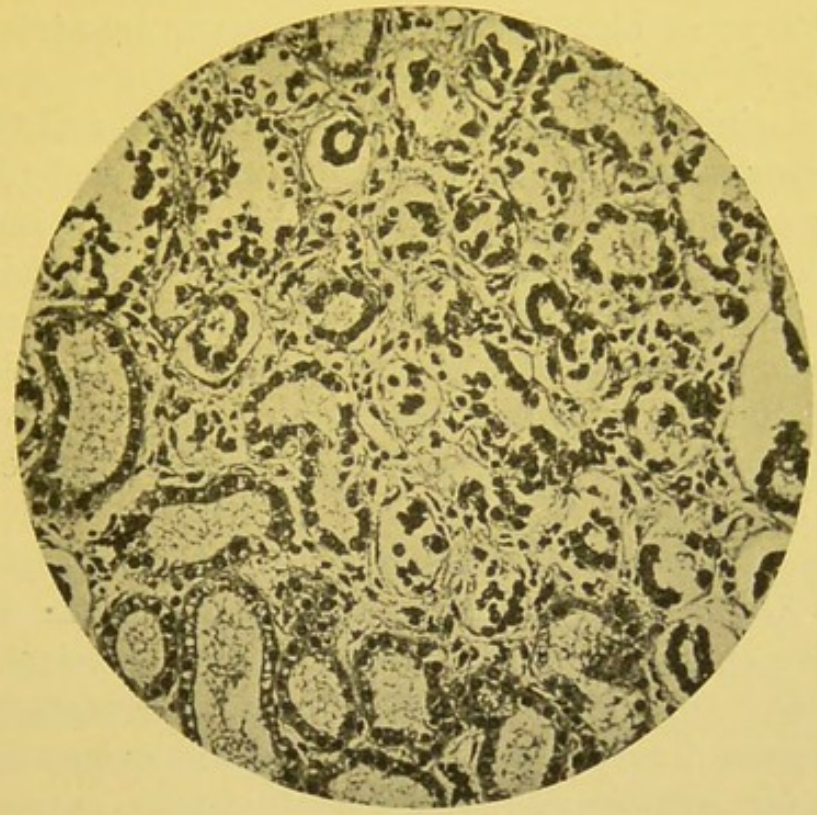

FIG. 5. The same case. × 170.

She improved sufficiently to be sent to the convalescent home at the end of April, but she returned worse in a fortnight, and died on May 22nd. During the last fortnight she had some vomiting and a little headache, but no coma or convulsions. She died of gradual asthenia.

The kidneys were very large, pale, and smooth ; the cortex whitish yellow.

Under the microscope there was everywhere an infiltration of the interstitial tissue with small round cells, but nowhere a definite fibrosis. The arterioles were natural.

In the area examined, the glomeruli were comparatively

little affected, only 10 out of 150 showing inflammatory changes. In other similar cases, however, the glomeruli have been greatly diseased.

The tubes were typical of catarrhal nephritis, and the epithelium was fatty. The lumen was stuffed with débris.

There was fatty degeneration of the muscle of the heart, and of the liver cells.

Of 10 fatal cases of this type, the youngest was 7 and the oldest 33 years old. Four of them were connected with pregnancy.

The remaining 6 included 3 males aged 7, 12, and 32 years, and 3 females aged 16, 17, and 19 years. In 4 of them the fundus was examined. It was natural in all. The heart was slightly hypertrophied in 2 cases, natural or only dilated in the rest. The blood-pressure is noted as natural in 4 of them. The one case in which it was raised is the case just detailed, and the record is explained by the œdema. There were no convulsions in any of the cases, and œdema of severe degree in every one of them.

I have detailed microscopic notes in 4 of the 6 cases.

Percy Atkins, aged 7, had been repeatedly in the hospital for dropsy and albuminuria. On the sixth occasion he had peritonitis. On the seventh the disease terminated fatally with extreme dropsy. A week before death a rigor occurred, and the temperature was high from that time onward. He had no retinitis and no convulsions.

The heart weighed 3 ounces and was not hypertrophied. There were specks of atheroma in the mitral valves and in the aorta. There was peritonitis, both old and recent. The kidneys weighed 6 ounces each; the capsule stripped cleanly, the surface was smooth, the cortex distinctly enlarged and of a yellowish colour.

Microscopically the convoluted tubes were all catarrhal and plugged with débris. The collecting tubes contained similar plugs. The glomeruli did not show inflammatory changes. The connective tissue was not increased. The arterioles were not diseased.

Stephen London, aged 32, had served in the African War:

He gave no history of renal symptoms until the face swelled on February 18th, 1906. He was admitted ten days later with an acute exacerbation. He had slight general anasarca. The retinæ were natural. He vomited several times. On March 10th he had severe pain in the left ham and calf, which was thought to be due to thrombosis. On the 22nd the heart failed and he died without convulsions.

The heart weighed 13 ounces, and there was some hypertrophy of the left ventricle. The aorta and other vessels were natural and there was no thrombosis in the vessels of the left leg. There was some ascites.

The kidneys weighed $9 + 8\frac{1}{2}$ ounces, and were of the large white smooth type.

Microscopically, there was much catarrh in the convoluted tubes with granular and hyaline plugs. In an area of 0·72 sq. cm. there were 111 glomeruli, of which 23 were natural, 85 were inflamed, and 3 were fibrous. There was marked cellular infiltration of the interstitial tissue, and in some places a definite fibrosis.

Amelia Amato, aged 15, who was admitted in July 1908, gave no history of renal symptoms earlier than November 1907, since when she had had continuous dropsy. She had had scarlatina, æt. 6, but no renal symptoms at the time.

She had no retinitis, but extreme œdema. Vomiting began early in August and was obstinate. On August 8th she had otitis media on the left side, and two days later the tympanum perforated. On the 17th she had a membranous sore throat which contained the spirillum and fusiform bacillus described by Vincent. On September 12th a mastoid operation was performed. She gradually sank, and died without convulsions on the 26th.

She had a minute cerebral abscess in the left occipital lobe and a slight amount of meningitis over the left lobe of the cerebellum.

There was pericarditis. The heart weighed 13 ounces and was hypertrophied. There was a little ascites.

The kidneys weighed 15 ounces the pair. The capsule stripped cleanly and the surface was smooth.

Microscopically, the convoluted tubes were all catarrhal, and were plugged either with desquamated cells, or débris, or hyaline material.

Of 78 glomeruli, 37 were natural, 28 were inflamed, 3 were degenerate, and in 10 the tufts were hyaline.

The connective tissue was very œdematous, but there was no real fibrosis and little cell-infiltration.

This is a border-line case, but I have classed it here on account of the state of the kidneys and the clinical symptoms.

Four of the cases were connected with pregnancy. Florence Izzard, aged 20, was confined of her first child in October 1893. She had had no previous renal symptoms, and there had been no dropsy during pregnancy. She got up at the end of two weeks. About a fortnight later dropsy set in and the urine became red. She was admitted early in December with general anasarca. The eyes were not examined. Suppurative otitis media supervened. She had severe vomiting and died in coma.

The heart weighed $10\frac{1}{2}$ ounces, and was dilated but not hypertrophied. There was some fatty degeneration. The kidneys weighed $10\frac{1}{2}$ ounces the pair, and were smooth. They were mottled white and dark red.

Microscopically, the convoluted tubes were catarrhal, and were distended with plugs, some hyaline, some granular, and some composed of blood. The collecting tubes were full of similar plugs. The glomeruli were extremely inflamed. In an area of 0·96 sq. cm. there were 161, of which not one was natural. 145 were inflamed and 16 were in various stages of degeneration. There was general increase of the interstitial tissue, which was densely infiltrated with round cells. A few of the arterioles showed hyaline swelling of the intima.

The appearances were those of an old-standing nephritis with acute exacerbation.

Annie Wilson, aged 21, was confined of her first child in July 1892. In February 1894 she had a miscarriage. In December 1894 she was admitted, eight months pregnant, with extreme anasarca and albuminuria. She had worked in a lead factory, but gave no history or sign of plumbism. The

eyes were reported upon by Mr. Vernon, who thought that the disks were pale and the neighbourhood of the macula slightly œdematous. Labour was induced. The child died. The anasarca continued in spite of repeated tapping. She began to vomit, and died of exhaustion in September 1895. During the last month the temperature was very irregular and there were signs of disease in the lungs.

There was tubercle in the lungs and pleuræ. The heart weighed 7 ounces and was natural. The main vessels were quite healthy, but peripheral vessels, such as the radial, the tibials, and the facial, were the subject of circular calcification of the media. The head could not be opened. The right kidney weighed about 2 drachms, and was represented by a small mass of renal substance corresponding to one pyramid. The rest was fibrous tissue. The left kidney weighed $10\frac{1}{2}$ ounces, and was smooth, pale, and fatty.

Microscopically, the convoluted tubes were in many places wide, and the epithelium flattened. Neither they nor the collecting tubes contained plugs. The epithelium was granular and in many places fatty. The glomeruli showed much inflammation: in 1 sq. cm. there were 5 natural, 82 inflamed, and 6 with hyaline tufts. There was universal cellular infiltration and increase of the connective tissue. There was slight endarteritis of the larger arterioles.

There was fatty degeneration of the liver.

The radial and posterior tibial were beautiful examples of calcification of the media and elastica. There was also some endarteritis.

Kate Stanger, aged 23, noticed when in the last month of pregnancy anasarca of the legs and vulva. No history of renal symptoms previously.

On admission, November 12th, 1895, she was restless, sleeping and feeding badly. The eyes were not examined. The heart was not hypertrophied. The urine was almost solid with albuminuria, and contained much blood.

Labour was induced on November 13th. The symptoms were not improved. The quantity of urine was very scanty, from 2 to 10 ounces only. It contained only 0·4 per cent. of urea.

She became drowsy and had diarrhœa. On November 18th she had a rigor. In the last week of November she improved. The urine increased to between one and two pints, the urea to 0·8 per cent. On December 3rd she vomited several times and had convulsions. On December 5th she again was convulsed. On December 12th she died.

The head could not be opened. The heart weighed $9\frac{1}{2}$ ounces and was natural. The uterus was in a state of subinvolution. The kidneys weighed 18 ounces the pair, and were smooth and mottled.

Microscopically, the convoluted tubes were enormously distended with cells and débris. The collecting tubes were plugged with similar material. The glomeruli were much inflamed. The connective tissue was everywhere increased, and in some areas there was great cellular infiltration. The arterioles were not diseased.

Mary Burgess, aged 33, had already borne four children. She had had no symptom of renal disease until this pregnancy, when in the sixth month the legs and body swelled. The face swelled later. The urine had been 'porter-coloured'.

On admission, August 9th, 1896, in the ninth month, labour was induced. Pleural effusion and œdema of the lungs supervened. A loud cardiac murmur developed. She became cyanotic and died of pulmonary symptoms on September 3rd.

The heart weighed 12 ounces and was dilated. The valves were natural. There was some atheroma of the ascending aorta. There was some peritoneal effusion. The liver was fatty, the uterus was normal, the kidneys weighed 16 ounces the pair and were smooth and pale.

Microscopically, the convoluted tubes were full of epithelial débris. The glomeruli were inflamed. There was considerable patchy increase in the connective tissue. The arterioles were natural.

The relation of pregnancy to nephritis requires a chapter to itself. Here it is only necessary to remark that the four cases above detailed do not differ in kind from the remainder of the series.

In this form of the disease the kidney is large, pale, and

smooth, to the naked eye. With the microscope it can be seen that the tubes and glomeruli show every degree of catarrhal change, and that the epithelium of the former is full of droplets of fat. The spaces between the tubes, which are hardly to be recognized in health, are greatly increased by œdematous swelling. There is in some cases a good deal of infiltration with round cells, and in some others a little organized fibrosis. But fibrosis never exists to the degree in which the contracting kidney exhibits it. The clinical symptoms of this form are characterized by the absence of retinitis and of high blood-pressure, and by the presence of severe dropsy. There is no recognizable sclerosis in the peripheral vessels, and in the kidney arterial changes, if present, are but slight. The heart is most often merely dilated, but occasionally a little hypertrophy has taken place as well. The severe nervous symptoms which are common in the contracting kidneys are rare in this form. Death is usually by asthenia or by dropsy with internal effusions, or by septic inflammation.

The fibrous and contracting form of chronic diffuse nephritis is the commoner. The following is a typical case.

Mary Anne Goodman, 37, was admitted on June 26th, 1907.

She had never had an acute attack, nor indeed did she appear to have had any symptoms until five months ago, when fits began. Two months ago the eyes and feet swelled for a time, and one month ago nausea and morning sickness came on.

When admitted she was dull, and a little indistinct in speech. She complained of violent frontal headache. There was no paralysis, and no œdema. She had very severe albuminuric retinitis with many hæmorrhages. The heart's apex was in the nipple line, the second aortic sound much accentuated. There were no murmurs.

The radial was not particularly thick, but the blood-pressure was very high, and was repeatedly estimated at over 240 mm. Hg., which was the highest that the instrument I then used would register. The urine was scanty from the first; usually

between 30 and 40 ounces per diem, sp. gr. 1005–1010, with from 0·1 to 0·2 per cent. of albumen.

She had a severe fit directly after admission, and was bled to 10 ounces. The fits ceased for the time. On July 15th the fits recommenced. She was again bled, but her general condition did not warrant the removal of more than 7 ounces. Hot-air baths were given during the next few days, but without improvement; she became delirious, had more fits, and died on July 19th.

At the post-mortem examination, the heart weighed 15 ounces, the left ventricle was hypertrophied. There was great arterial degeneration in the aorta, carotids, subclavians, and cerebral vessels, though the radial and posterior tibial, which I examined under the microscope, showed little, if any, disease. The kidneys were contracted.

Convulsions are sometimes replaced by other nervous symptoms.

Thomas Dunford, 27, was admitted January 12th, 1910.

When 3 years old he had scarlatina; when 18 he had some weakness in the loins which may possibly have been the lumbar pain of nephritis. A year ago he had bronchitis.

For some years he had been subject to frontal headache, chiefly in the morning. Nine months ago he had pain behind the eyes, slight giddiness, and since then partial failure of sight. For some time he had been vomiting once a week, and vomited six times on the day of admission.

He had severe frontal headache; marked albuminuric retinitis; hypertrophy of the heart; blood-pressure varying from 190 to 220 mm. Hg.; urine copious, up to 2,700 c.c. per diem, sp. gr. 1013, albumen 0·5 per cent., granular casts.

He improved sufficiently to resume work and was discharged March 12th, 1910, but in April he began to have sleeplessness, and dyspnœa at night. He had a little cough, and brought up some phlegm with a nasty taste. He was sick every morning after breakfast. On June 3rd he vomited fifteen times. He was readmitted on June 4th. He was very pale, and had some bronchitis. The heart's apex was in the sixth space, 2 inches outside the nipple. There was a systolic murmur. The blood-

pressure was 190 mm. Hg. The urine amounted to 1,500 c.c. The blood was examined; it contained red cells 3,000,000. Hgb. 50. Colour Index 0·6. White cells 9,600.

He was exceedingly restless, could not remain in bed, vomited repeatedly, and was very sleepless.

The urine rose in the first week to 3,000 c.c., and was nearly as high in the second week. In the third, however, it fell to about 2,400; in the fourth to about 1,600, and after this it was below 1,000 c.c. The following are some of the daily notes.

June 20. Cramps in the legs at night.

July 5. Slight mental confusion.

July 6. A hot-air bath. No effect. The urine had decreased since June 25. It had now fallen very low, and was often passed in bed, so that the total could not always be estimated. After July 10 estimation was quite impossible.

The headache very bad.

July 8. Extremely restless. Disposition altered. Half-unconscious. Chloralamide, bromide of potassium, paraldehyde, and morphia having been tried without much effect, fifteen grains of veronal were given at night and produced several hours' sleep. He was still very restless, moving aimlessly in bed the whole day long, and incoherent.

July 18. Same condition. Rapidly emaciating.

July 19. Death. No convulsions.

Autopsy. No œdema.

Heart $23\frac{1}{2}$ ounces: marked hypertrophy of left ventricle, some atheroma of mitral valve. Patchy atheroma in aorta, especially in abdominal part, and in the main visceral branches; little in the thoracic part, some in the cerebral arteries. Kidneys $3\frac{3}{4} + 3$ ounces. Typical contracted kidneys.

I have in my notes 26 complete cases which accord more or less closely with this type. They range from the age of 6 to that of 39 years. Six of them are under 20 years, 12 are between 20 and 30, and 8 between 30 and 40 years of age. Ten are females, 16 are males.

The points which are characteristic of the type are:

1. Albuminuric retinitis.
2. Hypertrophy of the heart.

3. High blood-pressure and arterial sclerosis.
4. Absence of severe œdema.
5. Uræmic convulsions or some nervous equivalent.
6. Granular kidneys.

I will take them in order.

In only 3 of the series are the retinæ reported as natural. In 7, the eyes are not noted. In one patient, a woman aged 36, the sight had failed, but the eyes were not examined during the few days which she lived after admission. The remaining 15 had albuminuric retinitis. The youngest case was in a boy of 7 years.

Symptoms connected with the circulation were present in almost all. The heart in all cases but two was hypertrophied, and in one of these it could not be examined. One patient, a boy 12 years old, had a heart weighing only 3 ounces, but he was a very ill-developed child, and it is expressly recorded that in spite of the small size of the organ the left ventricle was hypertrophied. The average weight of the heart in the patients over 20 years of age was 17 ounces.

The one exception was the following :

Edwin Austin, 32, compositor, was admitted for the first time on November 30th, 1895, with an acute access of nephritis. The urine was of low specific gravity, there was slight and transient œdema, and repeated vomiting. The heart was natural and there was no retinitis. He improved and was discharged on February 13th, 1896, but was readmitted on February 28th in convulsions which gave place to mania. The urine was of the same character as before. There was at first considerable œdema of the legs. The mania disappeared, but pericarditis and pleurisy followed and he died.

The heart weighed 10 ounces and was not hypertrophied. There were recent pleurisy and pericarditis ; the peritoneum was opaque and contained six pints of fluid. There was an ulcer, apparently of renal origin, three feet above the ileo-cæcal valve. The kidneys weighed $13\frac{1}{2}$ ounces, and 'had apparently begun to undergo contraction' (pathologist's note), for the surface was granular, though the capsule stripped fairly well, and the cortex was not materially diminished.

There was a very little atheroma, just above the aortic valves. The head could not be opened.

This is an exception which proves the rule. I have included it in this series because of the granular condition of the kidneys. But fibrosis had evidently advanced but little, and the rest of the symptoms proper to this type had not developed.

(For similar border-line cases see Amelia Amato, Stephen London, Mary Burgess, among the group with large smooth kidneys.)

Arterial sclerosis is mentioned in 9 cases; in 8 cases the arteries are said to have been natural and in the remainder the point is not noted. Disease of the arteries is, therefore, less commonly found than disease of the heart. It is natural to infer that the hypertrophy of the heart is the first, and arterial sclerosis the second event to occur. But it is much more difficult to estimate disease of the arteries than hypertrophy of the heart. Unless a pathologist sees marked atheroma, or pipe-stem arteries, he is apt to put down the vessels as natural. Many of these patients, either from the severity of their symptoms, or from other causes, could not be examined so accurately as is desirable during life, and I am not, therefore, inclined to lay great store upon this piece of evidence.

Œdema was present to a slight extent in 9 of the cases—one of them was the case of Edwin Austin just quoted. It was never of the extreme degree characteristic of the large smooth kidney.

Uræmic convulsions were present in 12; restlessness, delirium, or coma in 5 others.

All of them had granular kidneys. In 17 cases the weight of the two kidneys together was less than 10 ounces, in 7 it was above this weight, and in 2 the weight is not recorded.

I have detailed microscopical notes in 18 of these cases, and it is interesting to compare them with that of the former class. The accounts of the convoluted and collecting tubes, and of the glomeruli, are practically the same. And in this as well as in the former set there are variations. In some, the tubes are stuffed with enormous cellular masses which distend them. In others, they contain small hyaline plugs only. I imagine this to mean that in the one case, acute inflammation

was in process at the time of death, in the other, disease was quiescent. In most too of these cases there was extensive glomerular disease, but in a few the glomeruli are little affected.

Charlotte Thomas, aged 21, was admitted on November 21st, 1901. She had had scarlatina, had never been strong, was often sick in the morning, and was generally short of breath. She had been more breathless for the last three weeks. During the last three days her legs had been swollen and her sight dim.

She was anæmic and had orthopnœa. The heart was dilated, the rhythm cantering. There was much œdema of the legs and loins, and retinitis albuminurica.

On November 25th, December 31st, and January 7th, her legs were drained of large amounts, up to eight pints at a time, of dropsical fluid. She was very noisy and half mad at times. The urine was always scanty, contained a great deal of albumen, and about 1·4 per cent. of urea. On January 9th she vomited 2 ounces of blood, became very exhausted, and died on January 11th.

Five small ulcers lay close together near the pylorus. One of them had perforated and had caused death by peritonitis. The heart weighed 24 ounces. It was hypertrophied, dilated, and fatty. There was extensive atheroma of the aorta. The kidneys weighed 4 ounces each and were granular.

Microscopically, in an area of cortex 0·33 sq. cm. there were 36 glomeruli, of which 6 were diseased, and the rest healthy.

Ellen Lucas, aged 21, was admitted on May 30th, 1902. She had had scarlatina, æt. 4, and diphtheria, æt. 17 : for a year the legs had been swollen ; for five months she had had headaches ; and for two months, loss of sight.

She had albuminuric retinitis, arterial sclerosis, and uræmic convulsions, of which she died on September 30th.

The heart weighed 17 ounces : there was recent pericarditis and a purpuric eruption on the skin. The peritoneum was thickened and opaque and there was turbid fluid in the pelvic part of it. Blood taken with antiseptic precautions from the heart before opening, gave a pure culture of streptococci. The kidneys weighed 4 ounces each and were very granular and shrunken.

Microscopically, in an area of 0·42 sq. cm., of 85 glomeruli, 83 were natural.

But the special characteristics of this type are arterial changes and fibrosis. The interlobular arterioles of the kidneys and their branches show hyaline swelling of the subendothelial

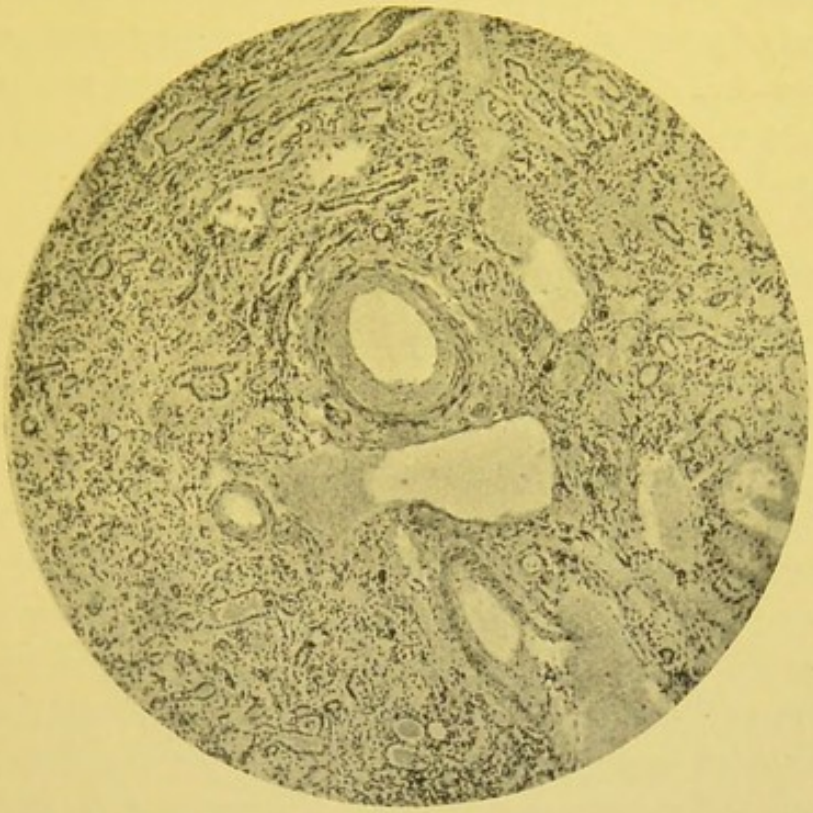

FIG. 6. Charles Stephens, 33. No history of acute nephritis or scarlatina. Teetotaller. For the last five months headaches. Then a fit for which he was admitted semi-comatose. Retinitis albuminurica. Blood-pressure 135 mm. Hg. No dropsy. Improved and got up. A month later convulsions repeated. Death. *P.M.* Kidneys 4+4 oz., granular. Tubes full of catarrhal products or of hyaline plugs. Very few glomeruli traceable, only 28 in 1·3 sq. cm., all in various stages of inflammation and degeneration. The interlobular artery in the centre shows great endarteritis. There is general fibrosis, which in some parts was very cellular. × 55.

layer, and subsequent proliferation of the intima (Fig. 6). Of the 18 cases, 10 show this in a marked degree. The youngest of them is a boy of 12 years old. In a boy of 7 years, the endarteritis was of a rather different type. It was very rich in cells. I have seen two or three instances of this, and have suspected that it might be syphilitic, but I have not sufficient evidence to prove it.

The presence of endarteritis does not seem to influence the course of the complaint, and in especial it is to be noted that hypertrophy of the heart and retinitis occur both when the renal arterioles are healthy and when they are diseased.

The fibrosis is of any degree up to the extreme. It is not confined to, and I think is not even greatest in, the neighbourhood of arteries. It is often patchy, sometimes universal. When patchy, the tubes in the fibrous area are squeezed small, but the cells are often natural. Neighbouring tubes are dilated by traction.

A certain number of cases of chronic diffuse nephritis supervene on septic endocarditis. I have notes of 9 such cases under 40 years of age. The clinical symptoms of renal disease are usually subordinate to those of the general infection. The state of the organs found after death varies considerably.

In a girl of 15, who had been acutely ill for six weeks only, there were a few depressed areas on the kidney, which weighed 62 ounces the pair. Microscopically, the picture was not that of ordinary nephritis. There was no proliferation or desquamation of the epithelium, but the cells were so far altered that about half the nuclei would not take the stain. Two or three cells in a tube stained clearly and sharply, the rest not at all. There were no plugs filling up the lumen. Of the glomeruli, the great majority were normal, but in a few the tuft was a hyaline, structureless body, and in one or two there was a hyaline effusion into the capsular space containing a few cells. Here and there, sometimes in the neighbourhood of hyaline glomeruli, were minute areas of dense, round-celled infiltration, in which the capillaries were choked with blood. Nowhere was any fibrosis to be seen. The arteries were perfectly natural.

In another patient, aged 23, who was admitted with cerebral embolism, the duration of the disease, though known to be short, could not be accurately ascertained. The microscopic appearances were similar to the last. The kidneys weighed 8 ounces the pair.

In two other patients, aged 16 and 22, in whom the symptoms were of longer duration, these same features were present in

increased degree. In one of them, few of the glomerular tufts were natural: they were nearly all hyaline. In both, the interstitial spaces were considerably widened by œdema. The kidneys weighed 20 ounces and 14 ounces the pair, respectively.

The special characters of this group are the absence of what are generally called catarrhal changes, the alterations in

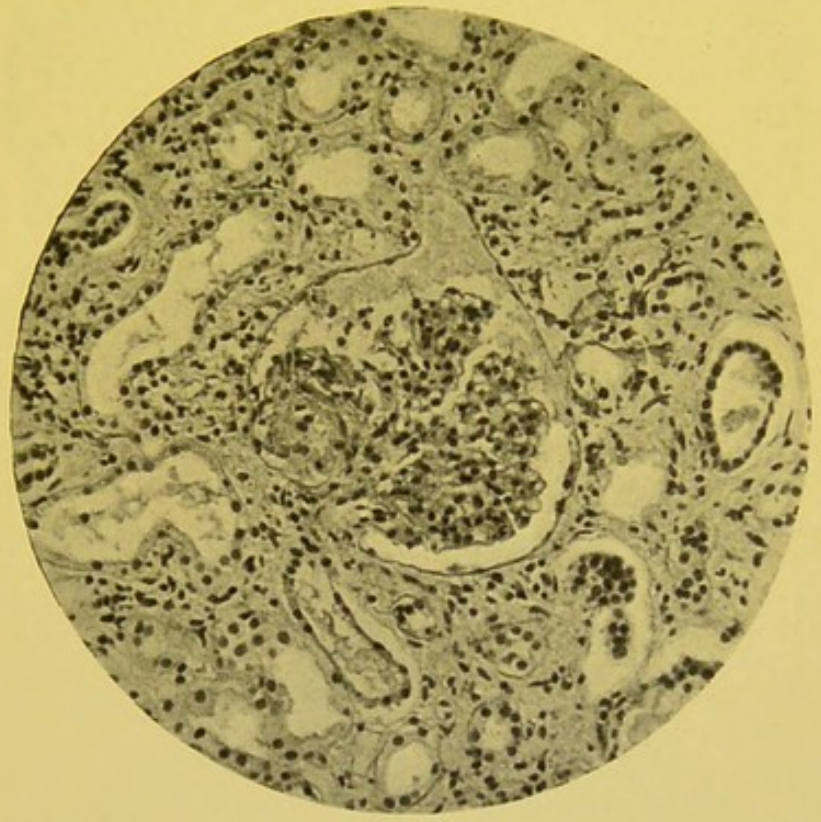

Fig. 7. Rose Lancaster, 16. Rheumatic fever 3 years ago. Cardiac symptoms ever since. Admitted for heart disease September 24th. Nephritis began about November 24th. Death December 4th. *P.M.* Adherent pericardium, old mitral and aortic disease, septic endocarditis. Pleural adhesions. Ascites, splenic infarction. Kidneys 10+10 oz., smooth, mottled. *Microsc.* Exudation into tubes, and desquamation of epithelium. Exudation into glomerular capsule, mouth of tube beginning. Intertubular œdema. ×150.

the tubular epithelium which prevents it taking stain properly, the hyaline change in the glomerular tuft, and the small areas of inflammation dotted here and there. Thursfield and I[3] suggested that this appearance in the glomeruli, which is occasionally seen in other cases, implies a toxic condition. I should think the same is true of the epithelial change also.

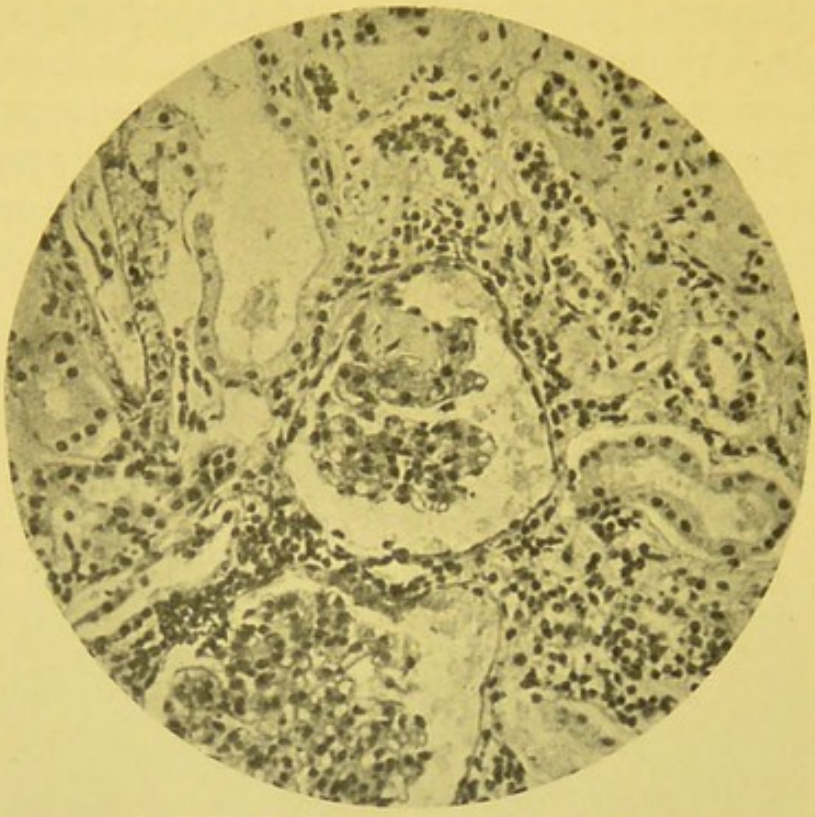

FIG. 8. The same case. Hyaline degeneration beginning in tuft. × 175.

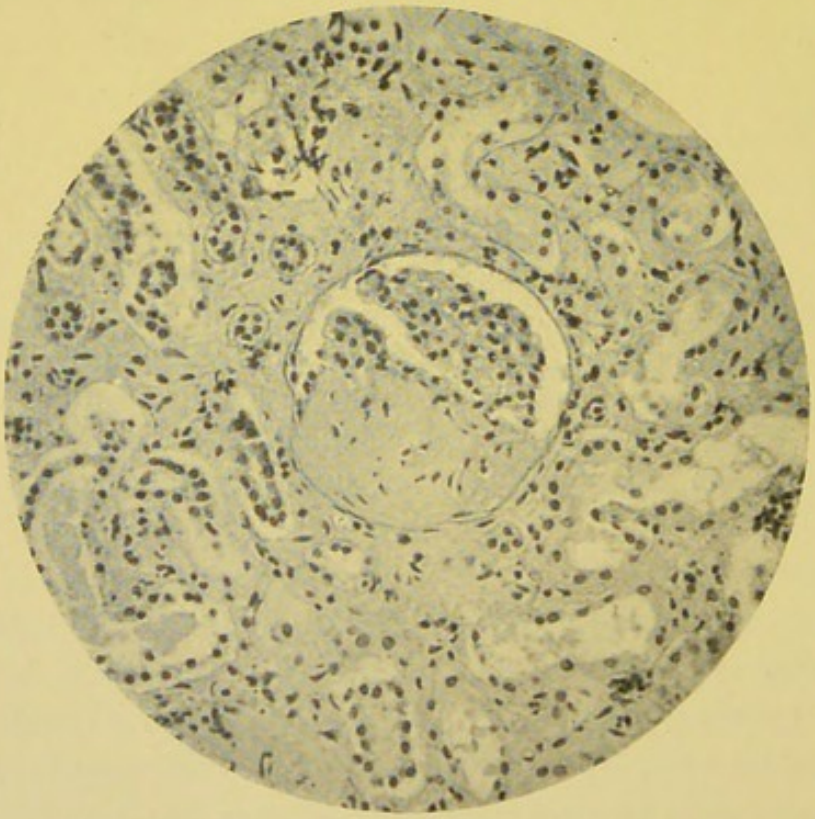

FIG. 9. The same case. Hyaline degeneration more advanced. × 170.

I have included these cases in chronic nephritis, but they are a group apart.

There are others in which, though malignant endocarditis is present, its connexion with the condition of the kidney is less certain.

A man of 26 (Edwin Smith) had had joint pains for nine months, and dyspnœa for six weeks. He died with malignant

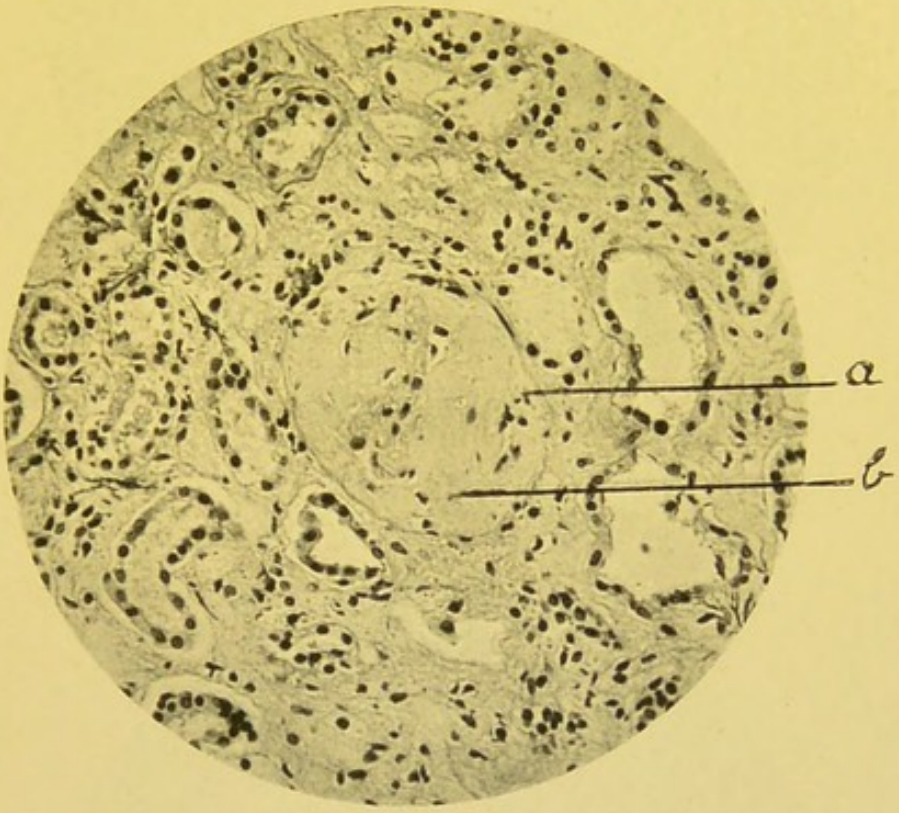

FIG. 10. The same case. Degeneration of the whole of a tuft, with exudation outside it. The curved line from *a* to *b*, which is easily visible with a lens, and the nuclei along it, mark, I think, the visceral layer of the capsule. × 180.

endocarditis, infarcts in the spleen and kidneys, and an aneurysm of the splenic artery. The kidneys weighed 18 ounces together.

Microscopically, the convoluted tubes were the subject of ordinary desquamative inflammation, and were full of granular material, interspersed with the remains of cells. The glomeruli were almost universally diseased, the capsular space filled with a cellular laminated deposit, or the tuft diminished, and in some wholly destroyed. There was a considerable increase

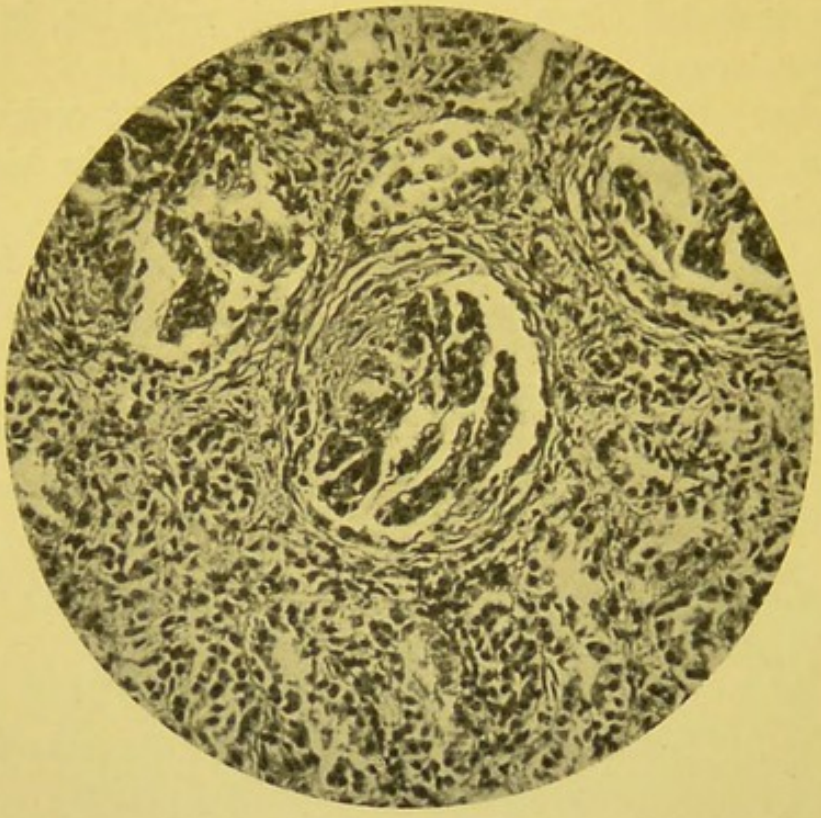

FIG. 11. Edwin Smith, 26. Tubular and glomerular inflammation. × 150.

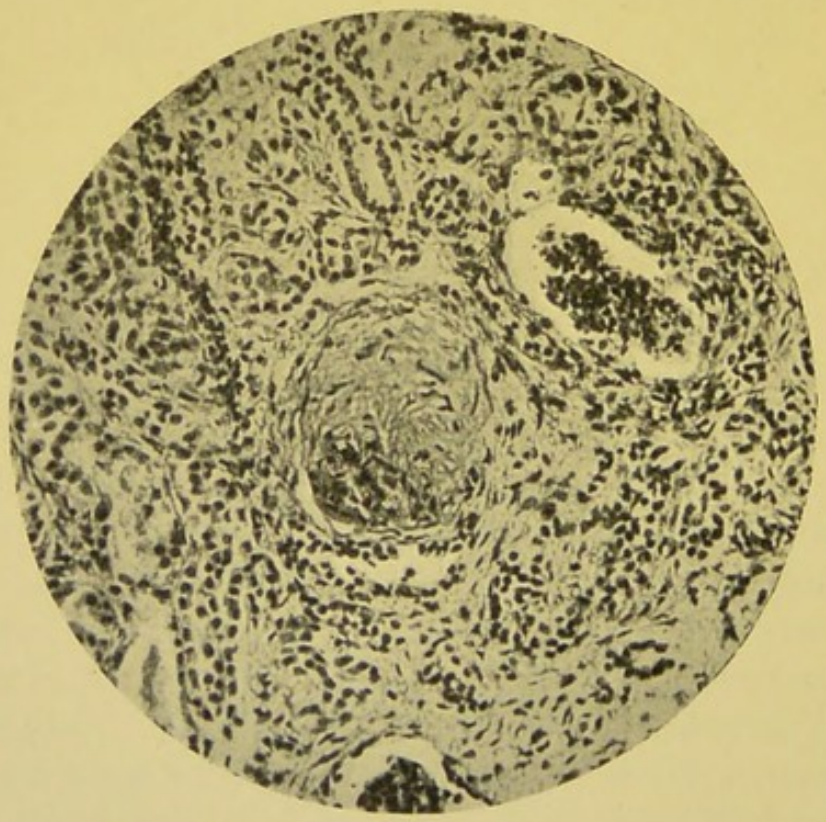

FIG. 12. The same case. Showing degenerative changes in a glomerulus. × 150.

in the interstitial tissue throughout. The arteries were natural.

The changes in this case are undistinguishable from those of chronic diffuse nephritis. I think it probable that the nephritis arose independently of the cardiac lesion, and possible that the septic infection of the heart was one of the terminal infections common in this form of disease.

References.

1. Dickinson, *Trans. Path. Soc. Lond.*, xl. 144.
2. Sawyer, *St. Thomas's Hosp. Reports*, 1906, xxxv. 459, with bibliography.
3. Herringham and Thursfield, *Trans. Path. Soc. Lond.*, lv. 283.

CHAPTER XV

SUBACUTE AND CHRONIC DIFFUSE NEPHRITIS (CONTINUED)

Beside the main points given above certain details are required to complete the clinical picture.

The amount of the urine passed is of great importance. It does not indeed always follow that because a patient is excreting a fair amount uræmia will not appear. I have known more than one case in which convulsions supervened while the amount of urine was almost or quite up to the average. On the other hand I have known many in which the excretion was very low for a long time together and yet no severe symptoms appeared. These, however, are exceptions. As a broad rule the amount of urine is the best guide we have to the condition of the patient.

Occasionally the urine becomes extremely scanty.

Mary Ann Powell, aged 38, of alcoholic habits, was admitted in December 1899. For the last six weeks the urine had been scanty and red. She vomited repeatedly.

On admission the tongue was moist and clean. The heart was not hypertrophied and the pulse was small. There was albuminuric retinitis, in the form of white spots round the macula, in the right eye. The left retina showed nothing abnormal. She died nineteen days after admission. During that time the average excretion of urine was about 240 c.c. per diem. There was almost as much sputum as urine. The vomit was of a watery character and contained urea. It continued even when for several days she was fed only by the rectum. The amount vomited was considerably more than that of the urine. It amounted one day to over a litre. There was also during the last week intractable diarrhœa. No headache, convulsions, or other severe uræmic symptoms occurred.

Complete suppression is an uncommon event under any condition. It is seen sometimes in the course of acute nephritis, especially of the scarlatinal form. Roberts gives a case in a child of 7 years. Only seven ounces of urine were passed in the last seven days of life. It occurs in the course of acute diseases such as cholera, or in acute fevers. Large doses of such irritants as turpentine or cantharides may cause it. Internal injuries accompanied by shock or collapse produce it. It occasionally also follows in some unexplained way the passage of a catheter, or some equally slight operation on the urinary passages. Brouardel [1] records cases of sudden death from trifling causes, such as digital examination of the vagina, which he ascribes to some reflex inhibition of the heart. Something of the same kind appears to occur in the urinary system of these cases of suppression.

When such cases occur as the result of acute nephritis, they lead to great restlessness, vomiting, and marked nervous symptoms, such as coma or convulsions.

In this they contrast remarkably with cases in which the urine is obstructed. These cases of ' obstructive suppression ', as Roberts called them, are usually produced by calculus. The commonest case is that one kidney has already been disorganized and the second is put out of action by the slipping of a calculus into the ureter. No urine can then be passed. Yet the symptoms are slight. The patient may survive for over a week before any nervous symptoms appear. Seldom even then is more observed than twitching of the muscles, and great weakness.

But occasionally a case of true non-obstructive suppression follows the uneventful course of suppression due to obstruction. Such a case was under Sir Dyce Duckworth [2] in 1894.

Mary Anne Barker, aged 39, a housewife, had been ailing since June 10th with general pains, headache, vomiting, and cough. The urine was said to be dark and thick. None had been passed between the 14th and the 21st of June. From the 14th she had vomited several times a day, and had had twitchings when falling asleep.

There was no history of previous nephritis.

On admission, on June 21st, the bladder was empty. That night she passed a drachm of urine.

She was stout, and rather pale, but looked comfortable and was not at all distressed. There were no convulsions.

Nothing abnormal was found in the heart, lungs, or abdomen. Vomiting continued. The vomit contained urea.

After consultation it was thought to be most probably a case of obstruction. Laparotomy was performed on June 23rd, but the right kidney was found to be of normal size, and no trace of a stone or any other cause of obstruction could be discovered. That night she had convulsions and died. Suppression of urine had lasted nine days.

Unluckily, permission for an autopsy could only be obtained after repeated application and much delay. In consequence microscopic examination, which I carried out myself, was quite valueless. All that could be said of the kidneys, which were much decomposed, was that they were of normal size, that there certainly was no obstruction, and that the capsules were very adherent. This is, however, good evidence of chronic nephritis, and that was Sir Dyce Duckworth's conclusion at the time. The heart was not enlarged and weighed only $8\frac{1}{2}$ ounces.

The amount of albumen again is extremely variable. As an acute exacerbation is recovering, the albumen nearly always decreases, and the improvement may be fairly measured by this symptom, though as I have before mentioned we cannot pretend to certainty in ascribing it to any one anatomical lesion. But in chronic and severe cases it fluctuates in a way that is often inexplicable. Although here too a steady rise from week to week of the amount of albumen implies that the patient is going down hill, there are daily variations which cannot be referred to changes in the anatomical condition of the kidneys, or connected with changes in the circulation. One of the most curious that I have seen was the entire disappearance of albumen from the urine during the last day of life in the case of one man aged 43. Much work is required on this and kindred points. We are so accustomed to albuminuria, that we forget to ask ourselves why it is present, and

why it varies. We do not recognize how little we know of the anatomical conditions which produce it (see p. 29).

The significance of casts in the urine has been frequently mentioned above. They are not, however, always present. In some cases the urine is perfectly clear, no deposit settles on standing, and no casts can be seen.

A business agent, aged 52, came to me complaining of migraine. He was a man of 15 stone and had no œdema of the legs. The heart's apex was in the nipple line but there was no other abnormality. The pulse pressure measured by Oliver's spring sphygmometer was 210 grammes, which is high. The sight was good and the retinæ natural. The urine was repeatedly examined. It averaged 1,600 c.c., was perfectly clear and had a sp. gr. of 1018. It always contained a large amount of albumen, running up at times to 0·4 per cent. He told me that albumen had been found in it twenty years before. The urea varied between 1·8 and 2·1 per cent. I repeatedly examined this urine under the microscope without ever finding a cast. The patient, however, died a year or two later.

The amount of urea or of the other constituents of the urine which is passed in the twenty-four hours' cycle is always of importance. But, as with albumen, it is not the daily variations, but the broad and progressive changes from week to week, which are significant. French and Butler found that in a patient with subacute nephritis the proportion of urea nitrogen to total urinary nitrogen was not lower when uræmic symptoms were present than at other times, and though the total urea nitrogen was less during uræmia, this was easily explained by the diminution of the food at such times.

I am inclined to think more of a low excretion of Cl. In a series of patients I found that a daily excretion of less than 1 gramme of Cl. was almost confined to fatal cases. But this again is variable. In some the excretion did not fall to this level until a few days before death, and in others it did not ever fall so low. It is, therefore, an ominous sign when it occurs, but its absence does not warrant a hopeful prognosis.

The symptoms connected with the circulatory system are

manifold. The relation of renal disease with arterial sclerosis forms the subject of a separate chapter. Yet I cannot avoid referring here briefly to the cardiac symptoms of these patients.

A slight enlargement of the heart is frequently, though not always, to be detected during life. The commonest is for the apex beat to reach to the nipple line. Two variations of the rhythm are in my experience significant. The one is the tick-tack rhythm, in which the two sounds occur at about equal intervals in the cycle, and much resemble one another; the other is the cantering rhythm, in which the second sound is reduplicated. Neither is confined to cases of nephritis, but they occur, I think, more often in these patients than in others.

Sometimes in the large white kidney, and often at the last stage of the contracting kidney, the heart dilates. This can sometimes be detected by physical examination, but not always, at least I know I have not always succeeded in doing so, even when I have thought it was present. In the latter class of cases the symptoms are those of cardiac failure with dropsy of the legs chiefly. In the former class any special effect of cardiac weakness is masked by the general anasarca and œdema of internal organs, which is, I have no doubt, partly toxic in origin.

The radial artery is usually thickened in the contracting kidney, and the blood-pressure much raised. It is often over 200 and sometimes as high as 250 mm. Hg.

I have, however, given elsewhere my reasons for thinking that these readings cannot be taken accurately to represent the blood-pressure alone. The rigidity of the arteries probably adds to the difficulty of compressing the pulse. The femoral artery often gives a higher reading than the brachial, and if the arteries are examined after death in a suitable pressure apparatus the same difference will be found.

The blood when drawn by venesection sometimes shows a marked lowering of its freezing point. In one patient, a man of 20, the blood drawn the day before death had a freezing point, compared to distilled water, of $-0{\cdot}75^{\circ}$ C., whereas the normal point is $-0{\cdot}56^{\circ}$ C.

Besides these chronic conditions acute inflammations are common, both in the pericardium and in the endocardium. Pericarditis with a great production of plastic lymph, pericarditis with serous effusion, purulent pericarditis, and small hæmorrhages in the pericardial tissue are not infrequent. Acute endocarditis is not so common. Occasionally septic endocarditis occurs as a terminal infection.

It is worth noting also that in two cases such loud apical murmurs were heard that valvular disease was diagnosed without hesitation. Neither of them had any alteration of the valves.

It is of course the rule for cases who die of cerebral hæmorrhage to have granular kidneys. But the reverse is much less common. Of those who die of nephritis, under 40, few have cerebral hæmorrhage. This has an important bearing on treatment, which I will discuss later.

I have seen a case die from embolism of the middle cerebral artery, in which the clot was apparently from a thrombus in the heart which had formed in the course of gradual dilatation and failure.

In one patient, a boy of 15, a tender swelling occurred on the inner side of the left arm during an acute exacerbation of nephritis, which I ascribed to phlebitis of a deep vein. Occasionally, on the other hand, a pain like that of thrombosis is felt in the legs, without thrombosis being actually present.

Severe hæmorrhages are frequent. Epistaxis was noted in five cases. One case had a large hæmatemesis. In two other cases the gums were swollen and bleeding, and one of these patients vomited blood and also passed it by the rectum. In this case raised hæmorrhagic areas were found in the œsophagus, some of which showed slight ulceration. Hæmorrhagic patches and ulcers were also found in the lower part of the ileum and upper part of the colon. This patient also had purpura on the buttocks. The temperature was subnormal throughout. There was great anæmia (red cells 2,488,000, Hb. 40 per cent., white cells 14,000), and he died of exhaustion. In another case both hæmatemesis and melæna occurred, but after death there were no ulcers or erosions, only pigmented spots, the remains of punctate hæmorrhages.

It is not uncommon to find ulceration in the alimentary canal. In our museum there is a specimen showing six small ulcers near the cardiac end of the stomach, which was taken from a patient who died of granular kidneys with failure of the heart. There were, however, in this case no gastric symptoms at all. But a girl of 18 (see p. 146) died from perforation of one of a similar group of small ulcers near the pylorus. It is more common to find them in the intestine. I remember a girl who died, aged 22. She had had epistaxis a long time ; of late she had been suffering much from vomiting, and from attacks of dyspnœa at night. Two days before admission she had brought up blood, but whether from the lungs or from the stomach was not certain. There was retinitis, hypertrophy of the heart, thickening of the arteries, and œdema of the lungs. The ileum was found to contain numerous narrow ulcers whose long axis was transverse to the bowel, but which were not tuberculous. They were deeply punched out, and there was blood-clot in them, but no surrounding inflammation or hæmorrhage.

These ulcers are sometimes ascribed to thrombosis of a thickened artery, and digestion of the area thus deprived of its blood supply. They sometimes give rise to a bloody diarrhœa, but at other times to no noticeable symptoms.

Vomiting is not so common in the contracting as in the large white kidney. But it occurs in the former also, and is occasionally the symptom which leads through exhaustion directly to death.

Occasionally the amount vomited is even more than the urine, and the vomit contains urea. A case of this kind is quoted above, and another in the chapter on Treatment. Another was the patient Edwin Austin (see p. 144), and a fourth was a young man, aged 26, who was a typical case of the contracting form of nephritis. His kidneys weighed only 4 ounces, his heart was hypertrophied, retinitis was present, and he had convulsions.

In one case a violent and continued diarrhœa was combined with great anæmia, and the patient died of sudden syncope. There was no gross lesion of the intestine.

There is sometimes acute peritonitis either as part of a general septic poisoning, as in a case quoted just below, or occasionally from perforation of the stomach. More often it is of a chronic character, and is confined to adhesions about the spleen and liver. Occasionally there is a general opacity and a serous effusion.

Some of these cases are of a very chronic character. Hale White has drawn attention to the fact that chronic ascites which survives repeated tappings is usually due to a chronic universal peritonitis in patients who have granular kidneys.

In the less severe stages of the disease there is a great tendency to bronchitis. In the later stages pulmonary symptoms are common. Many die of asthenic pneumonia, and in the series of cases from which I have been quoting, bronchitis, œdema of the lungs, low asthenic pneumonia, and pleural effusions occurred several times. They are not infrequently discovered first on the post-mortem table. Sometimes this is because they have supervened only in the last day or two of life. I have known that happen several times. But often the patient is in so bad a condition that the physician hesitates to disturb him for examination. I remember such a patient, whom I saw in consultation, dying actually from the movement necessary for an examination of the bases of the lungs. Still, wherever it is possible, the examination should be made daily, for many a case of dyspnœa is put down as uræmic, which is really due to pleural effusion.

It is not uncommon for affections of the skin to occur in the course of nephritis. Purpura is the commonest. Herpes, urticaria, erythema, and eczematous eruptions both vesicular and purulent are seen. In one patient, a girl of 17, admitted for chronic nephritis, there appeared a vesicular rash beginning as small blebs on the hands and feet, which later coalesced into bullæ like those of pemphigus. It lasted about two weeks and then disappeared.

Towards the end of chronic nephritis, especially when there is much dropsy, erysipelas and other septic infections are very apt to occur. This fits in with an observation of Flexner that

in chronic nephritis the bactericidal power of the serum is below the normal.

A boy, aged 7, died in the hospital in 1895. He had been often admitted for renal dropsy, and with it had repeatedly had erysipelas. On one occasion the scrotum sloughed; on another the erysipelas occupied the right thigh.

In his last illness he complained of tenderness in the lower part of the abdomen, and there was some fever. He was too ill to allow of any exploratory operation. At the autopsy it was found that there were many adhesions in the abdominal cavity, and that there was also a recent purulent peritonitis. The pus was collected in pockets formed by the adhesions. In one of these a communication existed with the bowel, and this had also opened at the navel, forming a fæcal fistula. The kidneys were large and white, weighing 12 ounces. The heart was not hypertrophied.

A girl, aged 11, was said to have been quite well till January 20th, when œdema appeared. Vomiting and diarrhœa followed the next day. She had had no fever recently, there was no case of fever known from which she could have been infected, and no other cause of nephritis could be discovered. The abdomen was very tender, but no free fluid could be recognized. The urine was scanty, and almost solid with albumen. On the 28th there was a pink blush and a tender swelling over the right thigh, and effusion in the right knee-joint. On the 30th the same symptoms in the left leg. Violent delirium occurred at night. On the 31st small sores appeared on the back and neck, which spread so rapidly that on February 1st the sore on the neck extended to the nipple. The surrounding skin was discoloured. On February 2nd she died. Fever and diarrhœa had been present throughout. The autopsy showed chronic nephritis, peritonitis, and slight double pleurisy. The case was evidently septicæmic, but occurred before bacteriological examinations were commonly made.

In another patient, a girl of 15, acute suppurative otitis, necessitating operation on the mastoid, took place, and the case was further complicated by a membranous angina due to a spirillum, of the type described by Vincent (see p. 137).

The symptoms connected with the nervous system are the most serious of all.

The changes in the ocular fundus are of various kinds.

1. The arteries are unusually brilliant, like copper wire. Where they cross a vein they cause it to bend, and perhaps a little dilatation of the vein on the distal side is visible, showing that it is obstructed by the pressure of the artery; where the crossing takes place the vein does not show through the artery as it does normally. Lastly the wall of the artery outside the central column of blood is thicker than usual.

These changes, to which attention was drawn by Marcus Gunn, show arterial sclerosis. They do not prove the existence of nephritis. This is, however, so common an accompaniment of arterial sclerosis that when these changes exist chronic nephritis should be suspected.

2. The commonest appearance in cases of chronic diffuse nephritis under 40, is that of white woolly patches scattered all over the papillary part of the retina, interspersed with hæmorrhage. The white patches are patches of œdema. They lie in the superficial layers and often conceal both the vessels and hæmorrhages. They are irregular in shape and indistinct in outline. The hæmorrhages are usually arranged in long flame-shaped patches radiating from the disk. Sometimes they are more irregular in shape. Sometimes, especially in the periphery, they are punctate.

This form occurs at any stage of diffuse nephritis, but always, so far as I have seen, in those cases in which there is some fibrosis and rise of blood-pressure.

3. Around the yellow spot are sometimes seen a ring of small white spots, sometimes brilliant, sometimes rather yellow than white. They lie in the deepest layer of the retina.

These are generally thought to be more chronic in character than the last kind. Nettleship, however, records one case where they appeared in one month. The man, aged 29, had in July the woolly patches and hæmorrhages but no bright dots. In August the white dots were visible. In October the retina had cleared, but the white dots remained.

4. A few cases show merely papillitis with a little haze of the surrounding retina.

These changes can clear up, especially the œdematous patches, but I have never seen this happen, though I have seen them improve. Nettleship [3] mentions instances.

The prognosis is made much worse by the presence of albuminuric retinitis. Most of such patients die within two years, but Nettleship gives a case in which he saw a child of 8 with albuminuric retinitis, which child lived to be a woman of 25, in good health. He notes that I, who was working under him at Moorfields at the time, repeatedly tested the urine and found it of sp. gr. 1010 with a cloud of albumen, and that the radial artery was hard. Such a case is quite exceptional.[a]

In my cases the liability to albuminuric retinitis is greater in females. Thus taking all forms of chronic nephritis, both fatal cases and those that recovered, in patients under 40 years of age, I find that

Of a total of 40 male cases the eyes were not examined in 12 cases; retinitis occurred in 13 of the remaining 28 cases.

Of a total of 25 female cases the eyes were not examined in 7 cases, retinitis occurred in 13 of the remaining 18 cases.

This, however, is not in accord with Nettleship's statistics. He found that in ophthalmic practice the proportion of male to female cases of albuminuric retinitis was about 2 to 1, which is roughly the proportion of cases of nephritis.

The following case shows an unusual complication.

A man, aged 25, had had hæmaturia off and on since 9 years of age. At the age of 23 he had scarlatina. Hæmaturia had continued ever since and was complicated with some pain and difficulty in micturition. In December 1895 he became nearly blind, and began to suffer with headaches and vomiting. He was admitted on January 8th, 1898, and then had albuminuric retinitis, and a raised blood-pressure. He was diagnosed as chronic nephritis with cystitis. He died in a fortnight, and was found to have in addition pyo-nephrosis of the left kidney and enormous dilatation of the ureter. A calculus of uric

[a] It must be remembered that a retinitis similar to the albuminuric form occurs occasionally without nephritis.

acid about the size and shape of an acorn lay in the bladder. The right kidney weighed 4 ounces and was granular.

Amblyopia and amaurosis sometimes occur without any ocular changes. They are then ascribed to cortical affection, though no gross lesion is found. In this respect they correspond to certain paralyses which will be mentioned later. A similar condition occurs in puerperal women. Stephenson [4] in an exhaustive paper on the subject argues that this is the result of a special puerperal toxæmia, analogous to that of renal disease, but not the same. No treatment directly affects these conditions.

Uræmic headache is often very severe. It is usually frontal. It lasts for many days and is not relieved by sleep. It is sometimes, but not always, accompanied by vomiting. It is naturally referred to the high blood-pressure which commonly accompanies it.

This headache may be for months the only symptom of illness noticed by a patient. An officer, aged 42, quartered in India, complained of a headache which had troubled him for several months. It only occurred during exertion. If he kept quiet he did not feel it. He looked and felt in perfect health otherwise. His doctor found, however, albumen in the urine, which was rather copious, and of sp. gr. 1009. His arteries were thick, his blood-pressure was 210 mm. Hg., and his heart was hypertrophied.

Giddiness is probably a consequence of sclerosis of the cerebral vessels.

Cramp in the muscles is sometimes a troublesome symptom. It usually occurs in the calves when the patient is in bed. Sometimes it is more widespread.

We had a man, aged 38, in the hospital for chronic nephritis. For the last few weeks before his discharge he suffered much from cramp in various muscles brought on by slight movement, For instance, holding a cup of tea would cramp the muscles of the thumb, turning over in bed would cramp his calves, his thighs, and even his abdominal muscles. There was no tenderness to pinching in the muscles themselves, and the joints were quite normal.

In one case a man had severe pain in the leg which was referred to thrombosis. There was, however, nothing in the vein. It was quite natural. Sometimes pain which is obviously nervous, resembling sciatica, is a marked feature.

Drowsiness is usually the first warning that severe symptoms are approaching. The next is some twitching of the face or limbs. Then may follow a severe general convulsion in which consciousness is usually lost. Sometimes a severe convulsion precedes any other symptom. A man may be walking in the street, or doing his business, apparently in his usual health when he is seized. It is possible that some of the unexplained cases of sudden death are due to such an attack. At any rate, Dr. Horder found in our post-mortem records of St. Bartholomew's that out of 72 cases of sudden death after the age of 4 years, 12 died with no other lesion than kidney disease, and 45 had renal disease in addition to the vascular, cardiac, or pulmonary lesion which actually killed them.

A general uræmic convulsion cannot be distinguished from epilepsy by its appearance. In some cases it might be mistaken for the convulsions of cerebral tumour. One day a patient was admitted when I was in the wards. He had just given me a history of intense headache, vomiting, and loss of sight, when he was seized with a violent convulsion. I had thought at first of a cerebral tumour, and had said so to my clerks, but while he was in the fit I laid my finger on the pulse. I found the artery so thick, and the blood-pressure so high, that uræmia at once became the most probable cause. As soon as the fit was over we found typical albuminuric retinitis in the fundus and a considerable amount of albumen in the urine. The latter, however, is not a certain guide. Many an epileptic fit is followed by a transient albuminuria. Indeed, not only albuminuria but hæmaturia may occur. I remember a man, aged 40, who was admitted for a fit. He had become unconscious while walking home, and had fallen down. He recovered consciousness in about an hour and a half. The convulsions had ceased before he was brought to the hospital. There was a history of a similar attack sixteen years before. There was no paralysis on either occasion. The urine at first contained

both albumen and blood, but four days later the blood, and the next day the albumen, disappeared, and the urine remained normal.

In doubtful cases the presence of granular or epithelial casts is good evidence that nephritis exists.

There are, however, many grades and varieties of uræmic convulsion.

Sometimes there may be nothing but isolated twitchings of certain groups of muscles, in the face or in one of the limbs. Sometimes the movements are like those of chorea or of athetosis (Rilliet and Barthez). Rarely the spasms are tetanic in character. Sometimes they are localized to one side, and may in that case affect first one side and on another occasion the other.

Occasionally paralyses occur, hemiplegic or monoplegic in form, for which after death there is no gross lesion to account. It is usually thought that these are due to serous, as distinct from hæmorrhagic effusion. It seems to me as probable that they are toxic in character.

Sometimes dyspnœa, without sufficient pulmonary or cardiac cause, is the chief symptom. It seems to be nervous in origin. It is relieved by the inhalation of oxygen.

Occasionally the breathing becomes of the Cheyne-Stokes type. This, as far as my experience goes, is usually of fatal augury. Quite recently such a case occurred in a man, aged 52. He had been vomiting much and was thin and pale. He had albuminuric retinitis, a hypertrophied heart, thick arteries, and a blood-pressure of 160–170 mm. Hg. He breathed in cycles. There was a period of apnœa lasting thirty seconds, then faint respirations began which gradually increased in depth, reaching a maximum in about ten seconds, and then gradually died away again into apnœa. He began to spit blood, from patches of congestion in the lungs, as we found after death. The day before death he dropped his cup while drinking, and was found to be paralysed on the right side. This was due to an embolus in the middle cerebral artery. An ante-mortem clot was found in the right auricular appendix. But sometimes such cases recover. We had a man, 59 years

of age, in my wards who had retinitis and violent headache. When he was admitted he was incoherent, dazed, and unable to recognize his family. He also had Cheyne-Stokes respiration. To my great astonishment this man improved and was discharged sane, and feeling comparatively well, in a fortnight. His improvement coincided with a rise in blood-pressure. It was about 200 mm. of Hg. during the first week, and about 230 mm. the second week.

Sometimes a terrible restlessness takes the place of convulsions. The patients are anæmic and wasted, they take hardly any food, they sleep very little, they are sometimes half unconscious, but always in great distress, tossing continually, pulling the clothes in every direction, and trying to get out of bed. A typical case has been related in the previous chapter.

Coma usually appears at the end after convulsions. But Fagge describes the gradual onset of a comatose state with a dry brown tongue which might be mistaken for typhoid fever.

Delirium of a mild kind is frequent. Occasionally hallucinations are present. Still more rarely the patients become maniacal.

Edwin Austin (cp. p. 144) was for a time quite insane. He laughed and cried without reason, and called his attendants 'Mother' or 'God', or a day of the week, indiscriminately.

A woman, aged 39, was admitted in what appeared to be an acute attack of insanity. She had had several fits about eight days ago. They were thought to be hysterical. For two days before admission she had been insane. When admitted she had delusions. She would not, or could not, protrude the tongue. She appeared to have some dysphagia, but took food well the next day. The lungs, however, became œdematous, and she died in coma. The brain showed no lesions except some œdema of the membranes. The kidneys were granular.

On reviewing the whole field of chronic diffuse nephritis, I feel sure, both from clinical and pathological observations, that no definite distinction can be made between the two types. The second class does not run a wholly different course from the first. The symptoms which mark the first class can often

be found in earlier stages of the second. Many cases seem to be on the border line between the two.

Moreover, each group contains cases which vary similarly. Cases with little and with intense glomerular change can be found in each, the condition of the tubes is variable and similarly variable in both. The interstitial tissue, whose increase and contraction is the dominant factor in the second class, is not unaffected in the first.

Some authors, especially in this country Guthrie and Sawyer, have argued that the early cases of granular kidney are a type apart. They and Sutherland ascribe many such cases to syphilis.

That syphilis is a cause of nephritis in children seems to me, as I have already said, probable.

But my own experience does not lead me to think that either clinically or microscopically such cases form a class apart. Cases of granular kidney in children are not common, and I will consequently give a few in detail.

1. A girl, aged 6, had had jaundice three years ago, had never been well since, and had had occasional joint pains. For two months she had been worse, with vomiting and pain in the left side. For two weeks she had been in bed. She was very anæmic, the heart's apex was $1\frac{1}{2}$ inches outside the nipple, there was a loud systolic murmur. The urine was of low density, sp. gr. 1010, and contained albumen. The eyes were not examined and she was diagnosed as a case of mitral regurgitation.

She died in three weeks and was then found to have pericardial effusion, with an old patch of lymph near the apex, which may perhaps have caused the murmur, and natural valves. The heart weighed $5\frac{1}{2}$ ounces and the left ventricle was hypertrophied. The kidneys weighed 3 ounces together, the capsule was adherent and the cortex diminished. Microscopically, the convoluted tubes were full of débris, some of the glomeruli showed inflammation and others were natural, the interstitial tissue was everywhere much increased, and the arteries were not diseased. The liver showed nothing but fatty infiltration.

2. A boy, aged 7, had been noticed during the last six months to be passing more urine than usual. Headaches and dimness of vision had come on, and he had begun to suffer with constipation and abdominal pain. He had never had scarlet fever nor any acute nephritis. There was no trace of syphilis. He had had a severe wetting some months ago, but it was not followed by any bad effects. The parents were healthy.

The disease gradually got worse. Albuminuric retinitis was found. Abdominal pain and cramps in the legs were the most marked symptoms. Epistaxis was frequent. The skin became much bronzed, dry, and inelastic. Five months after he was first seen anuria and œdema set in. He became comatose and died.

Only the kidneys were allowed to be examined. They were both small and typically granular. Unfortunately, when I received them their condition did not admit of minute examination of the epithelium or of the glomeruli. There was universal fibrosis, with few cells in it. The arteries were the subject of a great cellular increase in the intima.

3. John Bibby, aged 12, a stunted, ill-developed boy. He had been delicate since birth, had had measles at $3\frac{1}{2}$, had not had scarlatina. No sign or history of syphilis could be obtained.

The eyes were not examined. The heart was not enlarged; the radial was thick. The urine was of sp. gr. 1009 and contained albumen and casts. He died in convulsions.

Though the heart weighed only 3 ounces, the left ventricle was distinctly hypertrophied. The vessels did not look diseased, but the radial, which I examined microscopically, showed distinct endarteritis. The kidneys weighed $1+3$ ounces. The left kidney was a mass of cysts. On microscopical examination of the right kidney the convoluted tubes were all found to be catarrhal and the lumen full of débris. The collecting tubes were also plugged with débris. The glomeruli were scanty. In an area ·72 sq. cm. there were only 26 visible, of which 12 were natural, 13 showed inflammation, and 1 was fibrous. Probably many had disappeared. There was great diffuse fibrosis, and in some places an effusion of

cells as if from recent inflammation. The interlobular and larger vessels showed endarteritis.

4. Alice Leighton, aged 16, could give no history of renal symptoms before eighteen months ago. There was no sign or history of syphilis. She was a well-developed girl.

She had retinitis, hypertrophy of the heart, and twitching of the muscles. She died with convulsions.

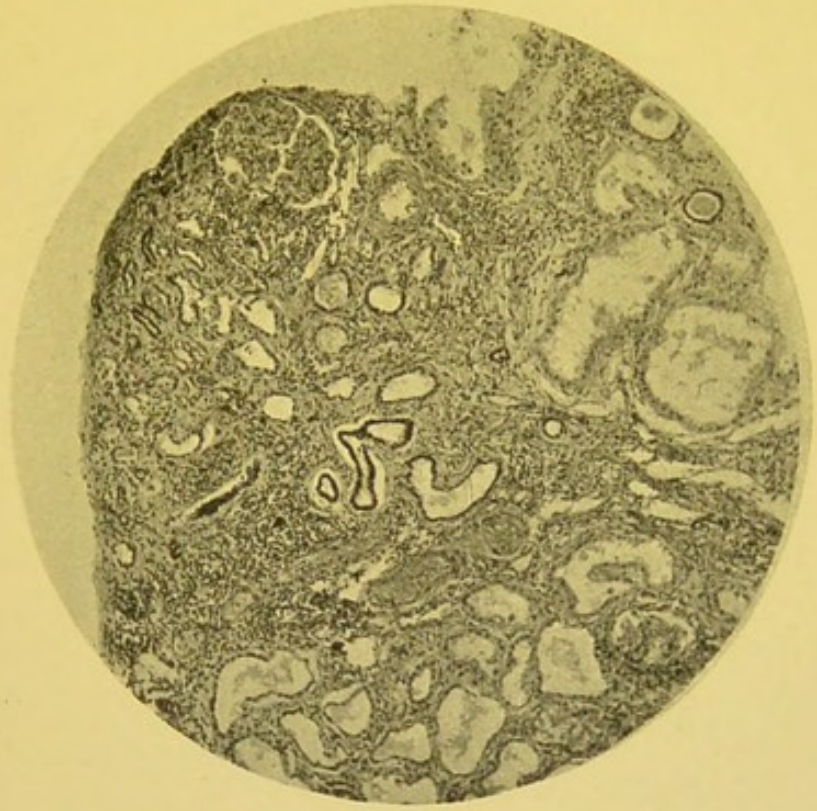

FIG. 13. John Bibby, 12. Showing general fibrosis with the usual changes in the tubes. The middle coat of the artery cut in cross-section is slightly thickened and degenerate. ×55.

The heart weighed 10 ounces, and was hypertrophied. The kidneys weighed $3\frac{1}{2}$ ounces the pair and were granular. On microscopical examination the convoluted tubes were all found to be catarrhal and plugged with débris. The collecting tubes were similar. Out of 117 glomeruli only 24 were natural, the rest were in all stages of inflammation. Many of the tufts were hyaline. There was much increase of the connective tissue, and it was much infiltrated with round cells. There was some endarteritis in the large arteries of the boundary

zone, none of the interlobulars. Arteries of the spleen showed hyaline swelling, those of the skin and meninges were natural.

5. Jos. Sawyer, aged 17, under Dr. Morley Fletcher, was ill-developed and anæmic, with a depressed nasal bridge and eczematous ulcers about the mouth and nose. The teeth were not syphilitic. His mother had had no miscarriages. His brother and sister were healthy.

FIG. 14. Alice Leighton, 16. Various stages of glomerular disease from exudation up to complete degeneration. × 55.

He had scarlatina æt. 7, and had never been well since. He had dropsy then and renal symptoms ever since.

The eyes were not examined. The heart was not enlarged, the radial was thick, and the blood-pressure was increased. The blood was anæmic. Red cells, 1,600,000, Hb. 30 per cent., C. 1·98. White cells, 12,420. He had convulsions and was bled 10 ounces, and injected with saline solution to $2\frac{1}{2}$ pints. The urine was of sp. gr. 1005 and contained albumen. He died in two weeks of convulsions.

The heart weighed 9 ounces and the left ventricle was hypertrophied. There was atheroma of the aorta and other

vessels. There was perisplenitis. The liver was fatty. The kidneys weighed 3 ounces the pair and were granular. On microscopical examination the convoluted tubes were in places much dilated, and in others crushed in the connective tissue. They showed in some places flattened, in others proliferating epithelium, and plugs of débris, or hyaline material. Of 70 glomeruli, 11 were natural, 12 inflamed, 41 fibrous and degener-

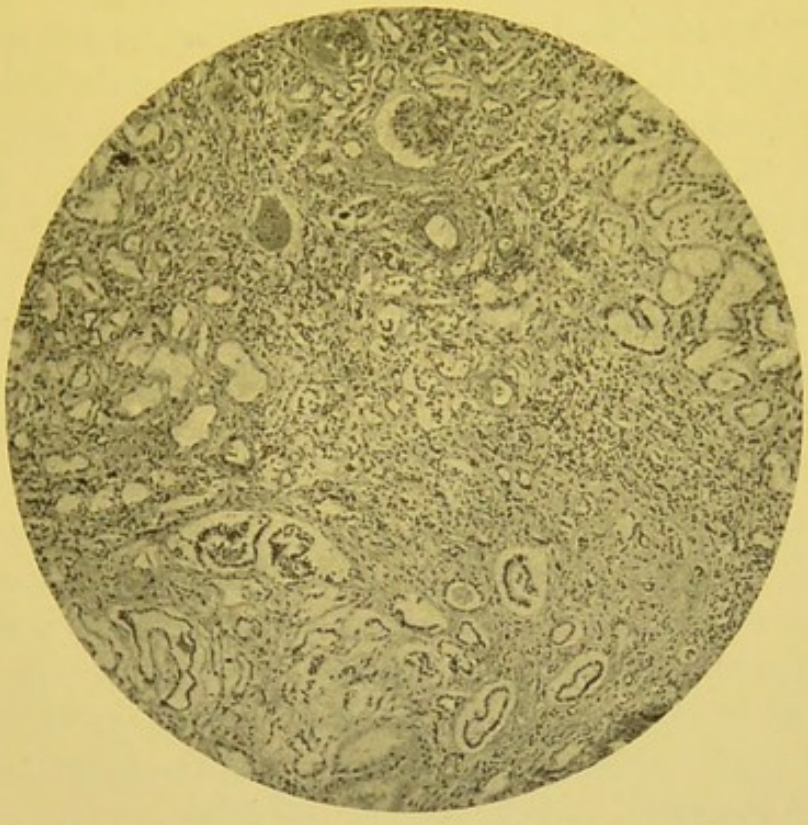

Fig. 15. Joseph Sawyer, 17. Showing general fibrosis dilatation of some tubes, crushing of others, with little if any disease of the arteries.

ate, and in 6 the tuft was hyaline. There was dense fibrosis, with much cellular infiltration. There was no noteworthy change in the arterioles.

One or two of these cases may have been syphilitic, but they do not differ, that I can see, either clinically or pathologically from the ordinary run. In them, just as in the remainder of the class, the parenchyma is affected, as well as the matrix. It seems to me quite impossible to say that any of them were the subject of an inflammation confined to or even starting in the interstitial tissue alone.

Some of these cases of early nephritis are like the third and fifth of the cases above described, extremely stunted and ill developed. Such was a case in the hospital under Dr. Morley Fletcher, and shown by him at the Royal Society of Medicine in 1911. The boy, though 6 years old, was only 2 ft. 7 in. high, and weighed 21 lb. Dr. Sutherland showed a similar case to the Association of Physicians of Great Britain and Ireland. The patient was a girl of 15, who had not grown since the age of 6, had only two teeth of the second dentition, and was of childish intellect. She had persistent rickets, a dilated colon, albuminuric retinitis, polyuria, and arterial sclerosis. There was, however, no albuminuria. In both these cases the Wassermann reaction was negative.[5]

What happens, I imagine, in chronic diffuse nephritis is that from various causes, many of which are still unknown, the kidney tissue is damaged and gradually becomes inflamed. The degree to which the several structures are at first affected differs in various cases, but the difference does not correspond constantly to any difference in the cause, and is not sufficient to form a difference in type. The inflammation progresses, and after a variable time takes one of two forms. In the one the patient develops a certain power of resistance. His system responds to the strain by a hypertrophy of the heart and a rise in blood-pressure. This is accompanied by arterial sclerosis. Later on the arterial disease leads to hæmorrhages in various parts, which, if irritated by the passage of food and digestive juice, may become ulcerated. From the arterial disease, and also from the toxic character of the blood, other changes occur, retinitis, headache, and finally the other manifestations of uræmia.

In the other form, the power of resistance is absent. The parenchymatous disease progresses without producing cardio-vascular changes, and without, or almost without, the local fibrosis which occurs in the former class. The symptoms which result either wholly or partly from the changes in the circulation are in consequence absent.

I have drawn all my illustrations of chronic diffuse nephritis

from patients under forty years of age. My reason is this. After forty years of age, chronic interstitial nephritis and cardio-vascular changes are so common that they may almost be regarded as a natural result of senile degeneration. They are constantly complicated with true diffuse nephritis, but, when they are, it is impossible to tell how much to ascribe to one factor and how much to the other. No true picture of diffuse nephritis can therefore be drawn, unless we restrict the instances to a time of life at which arterial sclerosis from other causes is, if not unknown, at any rate extremely rare. I think we may fairly say that with very few exceptions arterial sclerosis and high blood-pressure in patients under forty, if not due to valvular disease, or syphilis, depend on nephritis, and that the description which I have drawn from such patients is the description of nephritis and its results.

References.

1. Brouardel, *Mort et Mort subite*, Paris, 1895.
2. Duckworth, *Clinical Journ.*, 1894.
3. Nettleship, *Roy. Lond. Ophth. Hosp. Reports*, xv.
4. Stephenson, *The Ophthalmoscope*, March, 1910.
5. See a discussion on infantilism and chronic nephritis, *Proc. Roy. Soc. Med.*, 1911–12, v. *Dis. of Children*, p. 38.

CHAPTER XVI

THE TREATMENT OF DIFFUSE NEPHRITIS

So long as the patient is in the acute stage, whether this be a primary or a secondary attack, he must be treated, like any other patient who is acutely ill, in bed, and put upon a milk diet, including, as he can take them, junket, custard, rice simmered for several hours in milk, cornflour, arrowroot, rusks, bread and milk, or bread and butter. A little tea does no harm and is of all things the drink that sick people like. When milk is disliked, it can often be taken with soda water. He will probably have a good deal of thirst, for which lemonade with acid tartrate of potash in it, a drachm to the pint, is a good drink. The local pain can be a little relieved by hot fomentations or belladonna liniment. A grain or two of calomel and a saline purge to follow should be given at once. Careful observations should be made immediately on the state of the fundus, on the pulse, the arterial wall, and the blood-pressure, and the heart should be accurately examined and mapped out. These points, coupled with careful inquiry into the history, will indicate whether the attack is really a primary nephritis, or an acute exacerbation of a chronic disease. They will also serve as a standard by which to measure any changes that may occur subsequently. At the same time the simple saline diuretics should be given such as

℞ Pot. acet ; Pot. citrat ; Sod. tartrat ; āā gr. xx ter die.

If the urine is very scanty, and especially if there is any tendency to dropsy, it is advisable to diminish the amount of fluid as far as possible. Bartlett recommends that for two or three days not more than 500 c.c., say a pint, of fluid should be given in small doses, and no solid food. Every one knows

from experience the first stage of a cold in the head, when the nasal mucous membrane is intensely congested and swollen with blood, but has not yet begun to secrete. The kidney is probably just in the same condition. Its failure of function may be due to mechanical pressure, but I think it is more probably a real paralysis of the cells from the poison which has set up the inflammation. The kidney is struck dumb. Nearly always the organ rights itself, and the urine begins to increase within two or three days, but if not, further steps ought to be taken.

Something may be done by purging and sweating. The fluid extracted from the blood by either of these methods contains a small amount of solid substances besides water. Chlorides are normally present in sweat, and urea has been found on the skin in nephritis. The watery purgatives are, of course, the best. There is nothing much better than the Mistura sennæ co. or the Pulv. jalapæ co., or for children the Pulv. glycyrrhizæ co. of our Pharmacopœia. Sweating can be produced by a hot-water bath, or by a hot-air bath. The latter is made by turning a large metal funnel over a spirit lamp, and connecting the small upper end with a tube, metal or rubber, which is carried under the bedclothes. The clothes should be on a cradle or some similar support, so that a hot-air space surrounds the patient.

Miss Curtis, until lately the sister of Colston, my male ward, in a little pamphlet called *Nursing Hints*, which is full of good advice, gives the following directions: 'The patient should lie on a blanket, covered by another light blanket, without a night-dress. Put on the bed two cradles, covered by two blankets, then by a mackintosh or a folded linen sheet, and lastly by another blanket. The blankets should be tucked well round the patient's neck and turned over the cradle at the foot end and round the neck of the tin diffuser at the end of the tube or funnel of the apparatus. (We use Allen's hot-air bath apparatus at the hospital.) When all is arranged, light the lamp. Put a cold compress on the patient's forehead. Give him cold tea or water or lemonade to sip at intervals. Brandy to be near at hand. When the temperature inside the

cradle rises the patient must be carefully watched and the pulse taken. The skin may become moist in a short time, or instead of the skin reacting the patient may feel faint, or in cases of uræmia have a fit. In either of the latter cases the lamps must be extinguished. If, however, he feels comfortable and the pulse is good, the bath may continue for 15 or 20 minutes, but not longer. The lamps having been put out, and the apparatus removed, withdraw the cradles and mackintosh or linen sheet, wrap the patient in the blankets, and leave him for three-quarters of an hour—if sweating well, for half an hour longer—then rub him down with a warm bath towel, put on warm garments, and make the bed as usual, but with blankets next to the patient. Take great care to prevent any chill before, during, and after the bath. Any case of nephritis should always be most carefully guarded from any draught or chill or exposure. A hot bottle is nearly always required for the feet of these patients at ordinary times, as they are specially sensitive to cold.'

Electric radiators can also be used, or a dry hot pack with hot blankets and hot-water bottles or bricks.

Another method is by hypodermic injection of nitrate of pilocarpine (gr. $\frac{1}{10}$ to gr. $\frac{1}{3}$). I quote Sister Colston again: 'Before the injection is given, wrap the patient in two blankets, and have a hot bottle in the bed, and $\frac{1}{100}$ gr. of atropine ready for injection in case of need. Brandy close at hand. Patients react very quickly, and may be sweating profusely in 10 or 15 minutes after the injection is given. Or, the skin not responding, the lungs may fill with mucus. It is then that atropine is of service. This is not usual in an ordinary nephritis in an early stage, but occurs in elderly persons more advanced in the disease. Pilocarpine, if acting well, gives great relief. Leave the patient in the blankets for two hours, then rub him down with a warm bath towel, put on warm garments, and give hot milk.'

But if these means are not sufficient, and especially if there is much lumbar pain, nothing is so efficacious as half a dozen leeches, or, if they cannot be got, wet cups, to the loins. I have known complete anuria rapidly relieved by leeches.

A last resource, which sometimes gives relief, is incision of the renal capsule, or nephrotomy. Reginald Harrison [1] drew attention to the relief obtained by this means. Other surgeons have corroborated him, and quite recently Dr. Wilfred Harris and Mr. Clayton Green have related four cases in which this treatment was pursued with success.

If in spite of these remedies uræmia comes on, it should be treated by venesection and sedatives.

As the acute symptoms pass off, as the urine increases, as the lumbar pain diminishes, and the dropsy subsides, the diet may be gradually increased by the addition, first of milk and carbohydrates, then of vegetable purées, and later still of fish, chicken, and meat, until the permanent standard, which I will discuss later, is reached. The amount of urine passed, and the amount of albumen, should be watched while the alteration is made. If the albumen increases it is safer to lower the diet again for a time. But the estimation should of course be of the whole secretion of the twenty-four hours, and it should not be of one day only. A mere change of diet, even if it be from a higher to a lower scale, will sometimes be followed by increased albuminuria for a day or two.

As a general rule no increase takes place. I have repeatedly made estimations of albumen in the subacute stage in order to show students that an improvement of diet does not increase albuminuria. One such example is the following :

Albert Ryan, 19, was admitted on April 5, 1907. He had never had scarlatina, was a teetotaler, and had had no chill recently. He had no recollection of any acute attack of nephritis, and had been in his usual health until three days ago he had noticed swelling of his face and legs.

On admission there was slight œdema of the face and legs, which soon disappeared. The heart's apex was in the fifth space in the nipple line, and the rhythm was cantering, but there were no murmurs. The radial was not thickened and the blood-pressure was normal. The retinæ were natural.

The following are averages from daily estimations :

April 5–11 . .	Milk diet.*	Ur.,	990 c.c.	Much alb.	Casts.
,, 12–18 . .	Fish ,,	,,	2,520 c.c.	Some ,,	,,
,, 19–25 . .	Milk ,,	,,	1,650 c.c.	·35 % ,,	,,
,, 26 to May 2 .	Fish ,,	,,	1,830 c.c.	·15 % ,,	,,
May 3–9 . .	,, ,,	,,	2,070 c.c.	·13 % ,,	No casts.
,, 10–16 . .	,, ,,	,,	1,980 c.c.	·08 % ,,	,,
,, 17–23 . .	Meat ,,				
,, 24–30 . .	,, ,,	,,	2,190 c.c.	·05 % ,,	,,
,, 31 to June 6 .	,, ,,	,,	2,280 c.c.	·05 % ,,	,,

Sometimes, however, there is more than temporary increase of the albumen. If so the diet should be lowered again for a time.

Hæmaturia usually passes off with other acute symptoms, but sometimes persists although the patient improves in other respects. On the supposition that it depended upon passive congestion the prone position has been recommended. I have tried it, but it was most irksome, and it had not the desired effect. In one case in which there was much lumbar pain, and also much blood, leeches relieved both symptoms. Usually the blood is quite slight in amount. I have tried iron, mineral acids, tannic acid, gallic acid, and hamamelis, which contains gallic acid, without effect. Ergot has occasionally succeeded, and once or twice oil of turpentine in ten or fifteen minim doses has stopped the blood when nothing else would. But it also fails at times, and a small amount of hæmaturia may persist for weeks. It is very difficult to decide what to do with such cases. Ought they to be kept in bed so long as there is blood in the urine, or ought they to be allowed to get up? The question would be easier to settle if we knew on what the hæmaturia depends. If it were always a sign of acute inflammation we should not hesitate. But many of these cases do not seem to be acute. The temperature and pulse are normal, there is no pain, and no general disturbance. In such cases I have after long watching tried getting them out of bed. Some actually improve by the change, and either pass less blood or none. Some remain the same. Some pass more

* Our milk diet includes bread, butter, rice-pudding, and tea.

blood. These last I put to bed again, but the other two classes seem to justify the venture, for it is always better for a chronic case to be up than in bed if it does not render the symptoms worse.

Usually there is a certain amount of anæmia resulting from the illness which requires treatment with the lighter preparations of iron, such as citrate of iron and ammonia.

When such a case has reached a chronic stage, or when we have to deal with a case which has been chronic throughout, and presents a slight but constant albuminuria, occasional casts, some anæmia, and perhaps a little tendency to œdema, without any severer symptoms, we have to consider what rules should be laid down for daily life.

We must bear in mind two things : first, that there is some permanent damage which we cannot expect to remove ; second, that experience tells us that, either from original delicacy or as a consequence of the disease, such kidneys are extremely prone to fresh attacks of inflammation, each of which injures fresh areas and leaves the disease a stage more advanced than before.

In the first place, the kidneys are no longer up to the normal standard. The patient may be compared to a town, part of whose drainage is out of order. He cannot dispose of the same amount of excreta as a healthy man. He must live on a lower plane. Above all, he cannot afford the occasional excesses which others can indulge in, for he has no surplus of kidney tissue, as they have, to cope with them. He must spare his kidneys all unnecessary work.

This applies first to the quantity of food taken, which must be as moderate as is consistent with health. This means a considerable reduction on the usual amount, for, without arguing that half rations are best for healthy men, we at any rate know that life and health can be supported on them. The old Italian, Cornaro, who wrote on long life and spare diet, declares repeatedly that on fourteen ounces of food a day he enjoyed much better health than most of his contemporaries, and much better than he used to possess up to forty years of age while he lived freely.

But beside a reduction in the total volume, we should also reduce especially the nitrogenous elements. It is generally allowed that the nitrogenous products, urea, uric acid and the like, and the salts, which, except the chlorides, are chiefly derived from the proteids, throw much more work on the kidney than the carbohydrates or hydrocarbons. Chittenden has proved that the standard usually adopted, which is about 120 grammes of proteid, can be halved with impunity. His experiments lasted long enough to show that hard work can be done and the body maintained in health on such a diet. It is clearly advisable, since fifty or sixty grammes is sufficient, to spare the kidneys by reducing the proteids to that amount.

But while I firmly believe this, I do not believe that there is any ground, on account of the kidneys alone, to restrict these patients to a poultry or fish diet, still less to a diet of milk, eggs, and vegetable proteids.

I am sure, as a matter of experience, that the milk diet does not as a rule agree, and that such patients do better on flesh of some kind. If flesh is to be given, then I do not know any reason for restricting them to the flesh of fish or of birds. It is quite true that some fishes have a flesh that is more easily digested, that some patients can take poultry more easily than butcher's meat, and that mutton is more digestible than beef. In cases where the digestion is weak these points should be borne in mind. But it is for the sake of the stomach rather than of the kidney.

It is quite true also that some people are much better without butcher's meat. I have known many adults of this kind; and I know boys whom their parents were obliged to bring up without meat, though it was highly inconvenient, because they always became unwell when they ate it. But this is a peculiarity; it is not, in our race, the rule.

There is no such difference either in purin bodies[2] or in extractives, or in any other principle known to us, as would warrant us in discriminating against certain forms of flesh.

On the other hand, it is an advantage to allow variety. It adds greatly to appetite, which is the most potent factor in digestion, and in England the meat and fish are much better

in quality, and less liable to deteriorate and contain harmful products, than in countries where the grazing is not so good and the seaboard farther off.

When we come to things which are not foods, or are unnecessary forms of food, we have to be much stricter.

No one, for instance, would order alcohol to these patients unnecessarily. Although no ill effect is produced by a little of it, yet it is so liable to abuse, and the belief that its abuse is bad for the kidneys is so widespread, that it is safer to do without it unless, as is sometimes the case, it is really necessary for digestion.

Tea and coffee contain principles which are definite stimulants to the kidneys, and must therefore be taken sparingly.

Condiments all contain substances which are probably irritants. Even salt is in some cases excreted with difficulty, and must be used with moderation.

In addition to the regulation of diet, rules have to be made for conditions and habits of life.

We know that chill is a cause of nephritis. It must therefore be specially avoided by these patients. Chill is not the same thing as cold. A severe temperature is not specially dangerous, because the body, when it is prepared, can, by the contraction of its surface arterioles, keep up its internal heat without much difficulty. Chill is the action of cold upon a body unprepared to resist it. The commonest chill is caused by exposure to cold when sweating with all the skin arterioles dilated, and the blood on the surface. This is very likely to happen with young people playing lawn tennis or any other fast game. But most dangerous of all is dancing. This ought to be entirely forbidden. On the other hand, it is bad for such patients to take no exercise or to keep in the house. They should act like ordinary prudent people.

Fairly warm clothing is required, sufficient to guard against sudden chill from a cold wind or a shower. Some people like woollen underclothes best. I think that the open, loosely woven cotton stuff, which shirt-makers call 'cellular', is as warm, and more pleasant. The loins generally sweat a great deal, and, whether flannel or cellular cotton is worn, the wet

things quickly get clammy and chilly. They ought to be changed as soon as possible, and the loins rubbed with a rough towel.

The skin is the natural 'relief' of the kidneys. A dry climate which allows free evaporation is better than a damp. The ideal climate is one which is both warm and dry. If possible, it is best to winter out of England. The best winter climates that I know are Southern India and the Grand Canary. Teneriffe is much damper. The Riviera is subject to icy winds. Cairo itself is damp. The desert on either side, at Helouan or at En Shems, is dry, but it is a shifty climate, and I have felt bitterly cold winds there even in March. Higher up, at Luxor or Assouan, there is less risk of that, but in any part of Egypt the sunset chill is dangerous. Algeria is much the same. Even Biskra is cold at times. I have never been there at Christmas, but take my statement from patients. Andalusia usually has good weather from January to March, and there are good hotels in several places.

The above remarks refer to cases in which the symptoms are but slight. If the disease advances, the general health quickly suffers. The appetite fails, the patients complain of a nasty taste in the mouth, the tongue gets furred, nausea, flatulence, and dyspepsia of various kinds occur, food is refused, and weight is rapidly lost.

Often a good deal can be done by attention to the mouth. The removal of old stumps, the treatment of pyorrhœa alveolaris, which is very common, and the regular rinsing of the mouth and teeth with some antiseptic such as Condy's fluid, chlorate of potash, Sanitas, Listerine, and similar things, improve the patients a good deal.

The state of the mouth reacts at once upon appetite and digestion. But treatment of the latter is also required. No general rule can be laid down for this. It varies in nephritis as it varies in other cases. Sometimes there is merely atonic dyspepsia, sometimes there is chronic gastritis, sometimes the secretion of the gastric juice is increased, and occasionally small ulcers are found in the stomach.

Diarrhœa is not uncommon and is occasionally severe.

Sometimes submucous hæmorrhage takes place in the intestine, apparently from thrombosis, and this may lead to a slough and an ulcer. The tendency to spontaneous diarrhœa should make us rather careful about ordering purges to deplete the kidney. When diarrhœa is present the diet must be for the time as unirritating and simple as possible, and the carbonates of bismuth and soda should be prescribed. A little opium can also be given.

There is a tendency to bronchitis, for which precautions against exposure have to be taken.

Dizziness, slight headache, and inability for mental or bodily work are frequent. For them, occasional courses of nux vomica and phosphoric or hydrochloric acid are the best remedies.

All these symptoms are probably due to the gradual toxæmia produced by the disease.

Ascites occasionally occurs, apart from other effusions, in the course of chronic nephritis, and is then often due to a general chronic peritonitis.[3] Paracentesis may have to be performed several times. Such cases are not necessarily fatal, and the ascites may after a time completely disappear.

If death does not occur from one of these or of other intercurrent affections, the termination of the case is either by gradual asthenia, or by a more or less acute attack of severe dropsy, or by the gradual failure of a hypertrophied heart, or by cerebral hæmorrhage, or by uræmia.

In the first case, the patient, who has probably lost a great deal of flesh, has to be kept alive, and if possible improved, by nourishing food and tonics. There is generally extreme anorexia, and often vomiting.

When vomiting is not severe it can often be stopped by lessening carbohydrates and fats, and giving small tasty meals. People differ greatly in taste. In sea-sickness some like dry biscuits best, but the old prescription was salt junk, and as a rule food that is salt or savoury is easier to take. The addition of some such flavouring as Worcester sauce helps the stomach. It is in these cases that alcohol is useful, and here again the patient's taste must be consulted. For some a little champagne is best, for others spirits.

But some cases are very severe. In them the urine is usually scanty, and the vomiting actually removes more fluid than is passed by the kidneys. I had under me a case of this kind recently. He was a thin, pale, wasted-looking man of 32, and had albuminuric retinitis of slight degree, which improved under observation. The blood-pressure did not rise above 180 mm. Hg. and was usually about 140 mm. He passed a small amount of urine, not more than 30 ounces on the average, which contained a high proportion of albumen. He was repeatedly sick, as often as five or six times a day, each vomit amounting to 5 or 6 ounces. The vomit, therefore, was as copious as the urine. It was independent of food, and occurred at all times of the day and night. Nausea was constant. The vomit was a clear, watery fluid, generally greenish, which was alkaline. There was no free HCl, of course, and very little in combination. Urea to about 0·4 per cent. was found by the hypobromite method, and crystals of the nitrate were obtained by evaporation.

We were not very successful in treating this symptom, and the details of the case will serve as an example of the various means that can be employed. Vomiting began on December 2nd, when bismuth, hydrocyanic acid, and liq. morphinæ acetatis were tried successively without any effect. An effervescing draught of tartrate of soda and citric acid relieved him considerably. Then meat was added to the diet. This for a time stopped the vomiting. When it began again strychnine and hydrochloric acid was given. Then tincture of iodine, one minim in a teaspoonful of water, was given every three hours. This relieved him for a few days. When this ceased to have an effect the effervescing soda draught was again prescribed, and though this did not completely stop the symptom it relieved it for a time. The vomiting ultimately ceased, rather of its own accord, I fear, than at our bidding, and the man improved so much that he was able to leave the hospital.

Bartlett recommends a thorough gastric lavage. Ortner prescribes Cerii oxalatis gr. ijs, Sacch. lactis gr.v, in cachets,

thrice daily. I have used this drug several times, never with any effect.

Severe dropsy is usually accompanied by the same train of symptoms. In addition it produces its own dangers, of which pleural and pericardial effusion, and œdema of the lungs, are the worst. Every effort must be made to increase the flow of urine. The saline diuretics are not of much use, and as sodium chloride has in some cases the effect of producing œdema their use is contra-indicated. Deprivation of salt has indeed been recommended, but I must say that I have never found this method of the least use in renal dropsy.

The following will serve as an instance :—

A man 45 years old was admitted with chronic nephritis, albuminuric retinitis, cardiac hypertrophy, ascites, and œdema of the legs and loins.

The urine was above the normal quantity, sp. gr. 1012–1015, urea about 1 per cent., Cl from 0·2 to 0·3 per cent., hyaline and granular casts.

Period A. September 15–22 inclusive. Meat diet, with a total of 208 grains (14 grammes) of table salt in the eight days besides that used in cooking. Total urine 16,050 c.c. = 2,006 c.c. per diem. Total Cl excreted 42·17 grammes = 5·27 grammes per diem. The œdema was stationary.

Period B. September 23–6. Meat diet cooked without salt, bread and butter made without salt, and 1,200 c.c. of milk. No table salt. The œdema was stationary.

Period C. September 27 to October 5. No meat or vegetables. 1,800 c.c. of milk, saltless bread and butter, egg custard. Total urine 10,440 c.c. = 1,491 c.c. per diem. Total Cl excreted in six days 14·25 grammes = 2·39 grammes per diem. The œdema was stationary.

This method is, however, well worth trial, as it has been strongly recommended in France, and Bartlett's experience is more favourable than mine.

The heart is usually dilated, and therefore the digitalis group of drugs in combination with theobromine are needed.

The prescriptions I have used are, ℞ Tr. digitalis ɱx,

diuretin gr. x, ex. aq., thrice daily, or, if the patient can be kept under observation, every three hours at first. Or substitute for the tincture of digitalis the infusion to the amount of 4 drachms. The watery extract contains the alkaloids in a different proportion. Digitonin and digitalein are easily soluble in water, and the rest are not. Brunton says that the infusion is a better diuretic than the tincture, and I have at times found it so. I do not think strophanthus or convallaria is of much use for this purpose. Theocin sodium acetate (gr. iv) can be substituted for diuretin (see p. 14).

Relief can be given by puncturing the skin. Strict antiseptic precautions are necessary, for fear of erysipelas or suppuration. I use capillary trochars (Southey's tubes) with a long fine rubber tube attached to the canula, which is previously filled with an antiseptic solution, and then hung over the bed with the lower end under the level of a similar fluid. The trochar can be run into the canula through the rubber tubing, and extracted again after the skin has been punctured. The minute opening in the rubber closes hermetically.

Pleural effusion is not uncommon, and may be the cause of dyspnœa, which is called uræmic, or is ascribed to heart failure, or to pulmonary œdema. The patients are often so ill that repeated examination of the chest is deliberately avoided, and effusion takes place quickly and unnoticed. Paracentesis relieves the breathing greatly in these cases.

Dyspnœa is sometimes due not to local changes in the heart and lungs, but to some central affection. This is the true uræmic asthma. It is rare, as West remarks. Oxygen inhalation undoubtedly relieves it. But dyspnœa must never be put down as nervous until the heart and lungs have been carefully examined and local causes of dyspnœa excluded.

A very serious and difficult matter is the treatment of high blood-pressure. It is, I think, responsible to a great extent for the severe headache which is a common symptom of chronic nephritis, and it undoubtedly leads both to cerebral

hæmorrhage and to cardiac failure. It is always to be desired that the peripheral resistance, on which probably it originally depends, should be lessened. It is in any case worth attempting. In the first place, the patient should rest in bed, and his diet should be reduced to milk and farinaceous food. Next, the bowels should be thoroughly opened and kept rather lax. Thirdly, such drugs should be used as are known to dilate the peripheral blood-vessels. These are the various members of the nitrite group; sodium nitrite (1–2 grs.), amyl nitrite in capsules, erythrol tetranitrate ($\frac{1}{2}$–3 grs.), liquor trinitrini ($\frac{1}{2}$–2 min.), or the tabellæ trinitrini, one of which contains $\frac{1}{100}$ of a grain. Of these, erythrol tetranitrate, which is decomposed into nitrite in the system, has the reputation of having the most permanent effect.

I am sorry to say that I cannot report success with any of these drugs. I believe the reason to be that, in the later stages at any rate, the resistance is not due to muscular contraction but to permanent fibrosis of the vessel walls. On pp. 221–3 will be found charts showing how little effect these drugs have had.

On the other hand, I think it wholly wrong to use cardiac depressants. In my opinion the rise of pressure is necessary to maintain the circulation, and if we cannot relieve it at the right end, it is positively harmful to act upon it at the wrong one.

In many cases it can be maintained for several years. We must prevent any unnecessary call being made upon the heart, by forbidding great exertion, by quieting life in every way possible, and by preventing indigestion and constipation. A small dose of calomel at regular intervals has often been recommended, and most physicians believe in the intermittent use of iodide of potassium in small doses.

Its most distressing effect is headache. I do not think the headache in nephritis is entirely due to blood-pressure, because it often exists in a less degree where the pressure is low. But the worst headaches are in those cases where the pressure is very high. They are so persistent that we cannot

rely on antipyrin and similar drugs. We should be obliged to use them for longer than is safe. I have not found salicylate of sodium of much use. Bromides are serviceable. But the best drug that I know is Indian hemp.

℞ Tr. cannabis indicæ . . ♏x–xv
Pot. bromid. . . . gr. x
Ex. aq. ter die

is often most valuable. It must be remembered that the drug is variable, and that some specimens produce hallucinations and delirium. I remember several patients in hospital becoming wildly delirious with a special sample of the tincture.

If the pressure continues to rise, either the arteries yield or the heart. The first is commoner in the old, and may occur in the lungs or brain. The second is commoner in younger persons, and leads to dilatation of the heart, decrease of the urine, anasarca, ascites, and other effusions. In these cases it is imperative to give cardiac stimulants. The blood-pressure may be high, may be even very high, but the symptoms are proof positive that it is not high enough. To overcome the resistance we must at all risks increase the force of the heart. Digitalis is the drug that we use first, and similar to it, though less powerful, are squill, strophanthus, and convallaria. There comes, of course, a time when the heart is played out and can no longer respond. But digitalis will often postpone that time and avert symptoms that appeared at first very threatening. I generally add diuretin (gr. x) to it.

Speaking broadly, there is no symptom so important as the amount of urine. When it becomes scanty, except in the initial stage of acute nephritis, we should always do all that is possible to increase it, as the surest and safest way of eliminating poisons and removing effusions.

The last form of death is that by uræmia. It sometimes takes the form of a terrible restlessness accompanied by delirium. In some of these cases morphia acts well. There do not appear to be sufficient grounds for the old prejudice

against it. I have not myself used it often, and I thought in one case it did harm rather than good, but Osler and others speak highly of it. In the worst case of this kind I ever saw, the patient was never still for several days together. He was most of the time half-unconscious. Chloral, bromides, trional, and paraldehyde were all used without any effect, but 15 grains of veronal gave him a good night's rest. There have been, however, a certain number of deaths attributed to veronal, and I know men who will never give it. West recommends oxygen inhalation for these cases of restlessness.

When other severe nervous symptoms appear, whether they be convulsions, coma, or paralysis, they need prompt and decided treatment. The chief aim is to eliminate the poison, and the natural way to do so is through the kidneys by means of diuretics. If the kidneys are not acting well, we can assist them to some extent, as above described, by purging, sweating, or pilocarpine. But in severe convulsions there is no time for these methods. Relief must be given at once. This can only be done by venesection. Half a pint or more of blood should be taken. This generally stops the convulsions altogether for a fortnight or more. The result need not surprise us. We know that when organic poisons are repeatedly injected into the blood an antidote is formed and immunity is produced. Yet at any time an unusually large dose may kill, or after a long interval the animal may be found excessively sensitive, and—for most of this is recent knowledge—there may be other ways of death unknown to us. Imagine that in chronic nephritis small doses of some poison have been repeatedly absorbed, with a gradually growing tolerance, and that for some reason the formation of antidote begins to fall behind, or perhaps in acute nephritis has not time to take place. The result will be a surplus of poison which will produce convulsive symptoms and eventually death. That something is absorbed which is poisonous to renal cells seems to be shown by Pearce's experiment quoted above (p. 104). Another poison, or the same in larger doses, may be poisonous to cerebral

cells. Indeed, research seems to show that cytotoxins affect other cells than those from which they were derived.

The convulsant dose of such a poison may not be large. When convulsions begin it is because there is just enough of it to produce them. The abstraction of 10 ounces, perhaps 4 per cent. of the total blood, will reduce it below the convulsant level again, and may give the body a chance to recover for a time its tolerance. It is not very infrequent for patients to recover from uræmic convulsions sufficiently to be discharged from the hospital.

But more often the patient is relieved for a time only. The relief is, however, very striking; convulsions, which have been frequent before, cease entirely for the time. The same thing may happen with coma. I remember a woman with chronic nephritis who suddenly after a slight convulsion, the first she had had, became comatose. She was a pale, thin person, and the blood-pressure was not very high. I hardly liked to take blood. But after she had been in coma for about six hours I drew off 10 ounces. She recovered consciousness immediately, but died the next day from cardiac failure.

When the urgent symptoms have been relieved, efforts to increase the urine must be renewed, and hot baths either of air or water given. Some cases under these means recover, but the majority after a fortnight's interval are again seized with convulsions. By this time many of the patients are so ill that venesection does not seem justifiable. But I have once or twice performed it a second time. It again seems to remove convulsions, but usually the interval of freedom is shorter than before, and the patient dies either of a fresh attack or of exhaustion.

The later part of this chapter conveys the impression that our methods of dealing with the later stages of nephritis are not very successful. That is true enough. But that is not the least the feeling that I have in my own mind, or that I wish to convey to others, about nephritis in general. These severe cases, though numerous in a hospital, are very

rare compared to the total number. Even in a hospital, where only severe cases are admitted, the proportion of those who die is small. I think, on the contrary, that there is no disease in which more can be done for the good of the patient by careful treatment than can be done in nephritis. All of us must know many cases who lived for years with well-marked symptoms. It seems to me that the truer thing, as well as the more helpful thing, to say to such a patient, is that he can by careful regulation of his diet and of his habits prevent his condition from becoming worse, and that there is great probability that he can prolong his life almost, if not quite, to the usual length allotted to men. I entirely agree with Bartlett that much depends upon encouragement, and upon our power to make the patient contented and cheerful. Perhaps a sceptic, whether patient or physician, may feel inclined to scoff at this sort of treatment as mere common sense, and not medicine. That is all nonsense. No one can believe less in drugs than I. But I am thankful to say that I am sure that physicians know a great deal, a very great deal, about disease, and I am equally sure that nothing better can be done by any man in any walk of life than to apply the knowledge he possesses with common sense.

APPENDIX ON DIET

General statements do not mean much to the average man. I therefore venture to supplement what I have said in the foregoing chapter.

Milk	contains	3·4	per cent.	of protein.	1 pint	= 18	grm.	protein.
Bread	,,	6·5	,,	,,	1 oz.	= 2	,,	,,
Meat or chicken	,,	20	,,	,,	1 oz.	= 6	,,	,,
Fish	,,	18	,,	,,	1 oz.	= 5	,,	,,
Potatoes	,,	1·2	,,	,,	1 oz.	= 0·5	,,	,,
English cheese	,,	30	,,	,,	1 oz.	= 9	,,	,,
Eggs	,,	13	,,	,,	1 egg	= 6·5	,,	,,

A small helping of meat or fish weighs about 3 oz. An ordinary slice of bread as big as one's hand weighs about 2 oz.

Breakfast.

Two cups of tea with 2 oz. of milk and a slice of bread	= 4 grm. protein.
Butter or jam *ad lib.*, fat bacon negligible.	
An egg	= 7 ,, ,,
A small helping of fish or egg kedgeree, or a fish rissole, say	5 ,, ,,
A plate of porridge (2 oz. oatmeal)	= 7 ,, ,,

Selecting from these a man may have a good breakfast with less than 20 grm. of protein.

Lunch.

3 oz. of meat	18 grm.
Vegetables	say 1 ,,

Exceptions are peas and beans which are rich in protein, asparagus which is a renal stimulant, rhubarb and strawberries which in some people cause hæmaturia.

It is impossible to estimate the various farinaceous puddings, pastry, sponge cakes, and so on. They are made with milk and eggs, and therefore contain a certain amount of protein, but for an ordinary helping it would not be far out to allow 5 grm. of protein.

Cooked or raw fruits and biscuits and butter negligible.

Therefore a man may have a good lunch on 25 to 30 grm. of protein.

Dinner. Soups made with meat stock should be avoided, as they are simply solutions of extractives, which though appetizing are renal stimulants.

Purées made with milk and cream (artichoke, cauliflower, rice, potato, parsnip, spinach, carrot, tomato) are also appetizing and not irritant.

A plate of soup would contain about 5 oz. of milk .	say 5 grm. protein.
3 oz. of fish	,, 15 ,, ,,
Or 3 oz. of meat	,, 18 ,, ,,
Pudding as before	,, 5 ,, ,,
Or a savoury made with egg, or sardine, or a little game paste on fried toast	,, 7 ,, ,,

Dinner therefore need not be more than 35 grm. of protein.

I can further give the regular diet of a doctor who two

years ago was suffering severely from symptoms of high blood-pressure. He takes :

For Breakfast : Porridge 4 oz., 2 poached eggs and 2 oz. toast, bread and butter 2 oz., cream 1 oz., tea (with milk and sugar) half a pint.

For luncheon : Chicken 3 oz., potatoes 3 oz., greens 3 oz., bread 1 oz., apple tart and cream 6 oz.

For afternoon tea : Bread and butter and cake 3 oz., tea (with milk and sugar) half a pint.

For supper : 1 pint new milk, bread and butter 4 oz.

This works out at about 90 grm. of protein, and 2,600 calories.

Under this diet he has lost all unpleasant symptoms, and the blood-pressure is now only 150 mm. Hg., which for his age, 63, is not excessive. The urine contains a slight haze of albumen and no sugar. The weight remains constant at 12 st. 6 lb. He looks fresh and hearty, and feels in the best of health. He has kept constantly to this diet for two years, and has given up all alcohol and tobacco.

References.

1. Reginald Harrison, *Lancet*, 1896, i. 18, and *Brit. Med. Journ.*, 1901, ii, Presidential Address.
2. Walker Hall, *Purin Bodies*.
3. Hale White, *Clin. Soc. Trans.*, 1888, xxi. 219.

A good deal of this chapter appeared in the *Brit. Med. Journ.*, 1910, vol. ii, as an Address given at Toronto to the Canadian Medical Association.

CHAPTER XVII

CHRONIC INTERSTITIAL NEPHRITIS

I HAVE always felt this to be the most difficult of all subjects connected with renal inflammation.

The process is usually described as a slow increase of the interstitial tissue, not caused by parenchymatous inflammation, nor part of a diffuse inflammation of all the renal structures, but an independent overgrowth followed by contraction of the tissue so formed, with destruction of the parenchyma enclosed in its meshes, and diminution of the volume of the gland. The process is not spread evenly throughout the kidney. It involves the cortex more and earlier than the medulla, and it involves some parts of the cortex more than others. In consequence, the cortex shrinks relatively more than the medulla, and shrinks unevenly, with a series of depressions on its surface, each of which corresponds to a fibrous area beneath. The process is not confined within the gland, but involves also its fibrous capsule, which becomes thicker both in its enveloping layers and in those processes which run into and attach it to the kidney. Upon the surface are often seen small cysts which are formed by the dilatation of convoluted tubes compressed by fibrous tissue within the kidney. The result has been described as a small granular kidney, red, grey, brownish (Roberts), or red and yellow (Dickinson) in colour.

These appearances, can, however, be simulated by the fibrosis of diffuse nephritis. I cannot too strongly assert my conviction that the contracted kidney produced by this disease cannot be distinguished from the former by the naked eye. The size, the granulation, and the varying colours of the one, even the deep red, are seen also in the other.

Confusion has in consequence resulted. Firstly, pathologists have expected to find macroscopic differences which do not

obtain, and, secondly, they have tended to ascribe all the granular kidneys of later life to chronic interstitial nephritis alone, whereas both their clinical symptoms and their morbid anatomy shows that a large number of them cannot be distinguished from those produced by the diffuse disease as seen in earlier life.

In order to discover whether the two processes could be distinguished from one another, I tried to find the earliest stages of chronic interstitial nephritis by making microscopic sections of a series of kidneys which appeared normal, or very slightly diseased, taken from patients who had not during life shown renal symptoms. I chose kidneys from patients who had died either suddenly or accidentally while in apparent health, or from a disease unconnected with the kidney, and from others whose main symptoms were those of disease of the heart and arteries. It appeared to me highly probable that there was a stage in which the disease would not betray itself clinically or on the post-mortem table, and yet would be recognizable on minute examination with the microscope. Such in fact is the case.

The difficulty and importance of the subject warrant my quoting some cases in detail.

Henry Allen, aged 29. Brought in dead. The cause of death was pulmonary hæmorrhage into phthisical cavities.

The heart weighed 11 ounces and was normal.

The kidneys weighed 16 ounces the pair, but were in all other respects apparently normal.

Microscopically, the tubes and the glomeruli were perfectly natural. There was no fibrosis whatever. The only change visible was that in some of the interlobular arteries endarteritis was present. The aorta was atheromatous.

Frederick Taylor, aged 34, died of pneumonia. The urine during life contained no albumen.

The heart weighed 12½ ounces, but did not appear hypertrophied.

The kidneys weighed 12 ounces the pair, and appeared perfectly natural.

Microscopically, the tubes showed no catarrhal change. Of the glomeruli, a few showed slight thickening of the capsule, and in one or two out of a large number there was evidence of inflammation. There was slight fibrosis, which in cross-section (parallel with the surface) appeared to radiate from the interlobular vessels. There was no endarteritis seen in

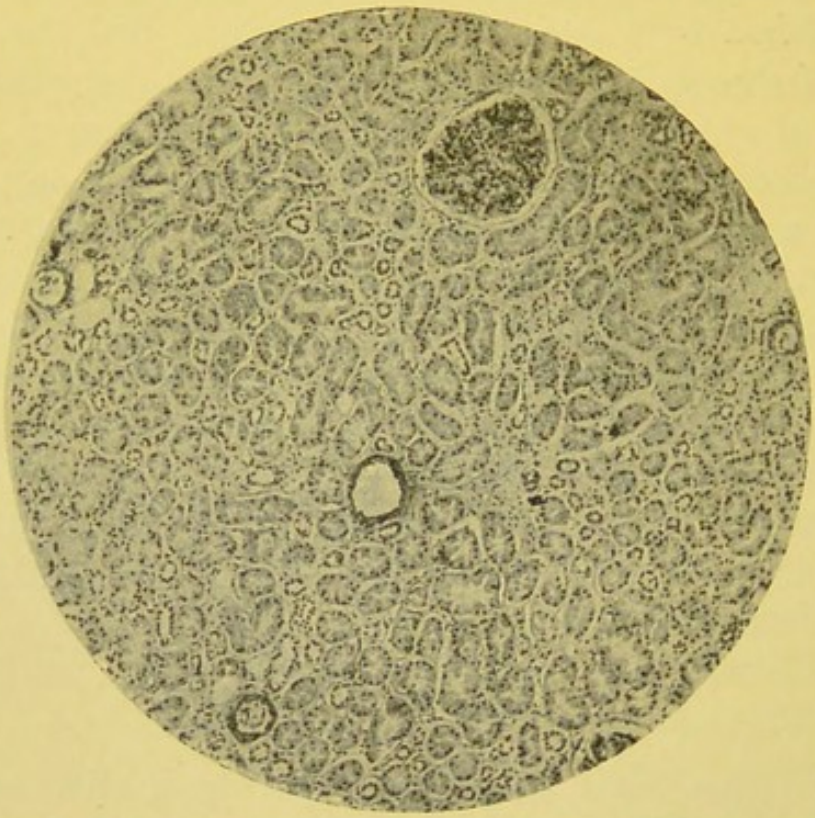

FIG. 16. Frederick Taylor, aged 34. A 'cross' section showing an artery with a patch of fibrous tissue running from it to the right. The kidney is otherwise normal. × 55. A lens must be used.

the interlobulars, but in some of the smaller branches there was hyaline swelling.

The aorta, radial, and cerebrals were natural. There were urates in the joint of the great toe.

Eva Ashley, aged 38, died of cancer of the sigmoid flexure. The heart and vessels were natural. The urine contained no albumen. The kidneys were natural to the naked eye.

Microscopically, the tubes and glomeruli were natural. There were a few small patches of fibrous tissue round the vessels. In some of the interlobular arteries there was

endarteritis, and in a few of the smaller there was hyaline swelling.

George Watkin, aged 42, was brought in dead. The cause of death was not apparent.

The heart weighed 12 ounces. There was no obvious hypertrophy. The aorta and cerebral arteries were natural, the radial and posterior tibial were fibrous (van Geeson's stain), and the muscular coat was less nucleated than usual. The kidneys weighed 10 ounces. Both were apparently healthy organs except that the left contained a calculus in the pelvis. The right one was examined microscopically. The tubes and glomeruli showed no signs of disease. There was marked fibrosis evidently spreading from the large interlobular arteries. Although the arteries in other parts were fibrous, the arterioles of the kidneys did not show signs of disease.

James Garling, aged 43, died of fracture of the skull.

All the viscera appeared natural.

Microscopically, the tubes and the glomeruli were natural. There was a slight general fibrosis, which was greatest around the vessels. The interlobular arteries showed slight endarteritis, and a few of the smaller branches showed hyaline swelling.

Samuel Hood, aged 47, very obese, died of cardiac failure. The urine, on admission, was of sp. gr. 1020 and contained no albumen.

Albuminuria appeared in the last two days of life.

The heart weighed 32 ounces, and was enormously hypertrophied and dilated. The aorta, coronaries, and other branches were atheromatous; the radial and posterior tibial sclerotic. The kidneys weighed 23 ounces, but the capsule was not adherent and the surface was smooth.

Microscopically, the tubes showed no catarrhal change. The glomeruli were natural except for slight albuminous exudation in some. There was considerable general fibrosis. The larger arteries showed endarteritis, and the smaller hyaline swelling.

Charles Richards, aged 52, was crushed to death. The viscera were all apparently normal.

Microscopically, the tubes were natural. Out of 280 glomeruli, 2 were degenerate, the rest were natural. There was general slight fibrosis. The arteries, large and small, showed the changes of endarteritis.

Henry Mortimer, aged 53, died of cirrhosis of liver and ascites with cyanosis. He was enormously fat. The urine during life contained no albumen.

The heart weighed 20 ounces; there was some fatty degeneration of the muscle. The kidneys weighed 8 ounces each, the capsule stripped with some difficulty, but the appearances were otherwise natural. Microscopically, there was no evidence of tubular disease. Of 57 glomeruli, one was degenerate, the rest natural. There was considerable fibrosis in connexion with interlobular arteries, but the arteries themselves did not show endarteritis.

Arthur Webb, aged 53, died of cancer of the œsophagus. He was wasted. During life the urine was of sp. gr. 1020 and there was a cloud of albumen. There was no œdema.

Microscopically, the tubes were not catarrhal. Of 115 glomeruli, 107 were natural, 8 were degenerate. Fibrous tissue spead outwards from the boundary zone along the vessels. The arteries, large and small, showed endarteritis.

These cases show fibrosis beginning independently without inflammation of the tubes or of the glomeruli.

If there are considerable areas of fibrous tissue, the inclosed tubes are often diminished in size. The epithelium in them is smaller, and the nuclei more closely set together. This seems to be simply a result of pressure from contraction of the fibrous tissue. There is not in such tubes any evidence of desquamation, nor are they filled with hyaline, granular, or cellular plugs as in diffuse nephritis.

I have called the glomeruli, in one or two cases, fibrous and degenerated. The condition does not resemble that seen in diffuse nephritis. There is neither the proliferation of the capsular epithelium, nor the laminated exudation described under diffuse nephritis. The glomerulus has lost

its distinct outline. The capsule is no longer recognizable. There is no capsular space. The tuft is an indistinct structure sometimes containing a few nuclei, sometimes without any, which is much smaller than the natural body, and stains like fibrous tissue. This same appearance may sometimes be seen here and there in a section from diffuse nephritis. The characteristic of the arterio-sclerotic kidney is the absence of the true glomerular inflammation.

This degeneration seems to be a starvation necrosis, due to occlusion of the vas afferens either from hyaline thickening of the vessel-wall within, or from strangulation by fibrous tissue without. Either of these events are possible in diffuse nephritis as well as in the kidney of arterial sclerosis.

The above cases show the process in its earliest stage, before the kidneys have become granular. The following cases show the disease more advanced.

Joseph Hammond, aged 41 (Figs. 17, 18), was in good health until he was seized with apoplexy due to cerebral hæmorrhage, of which he died the same day.

The heart weighed 17 ounces. It was hypertrophied and dilated.

The cerebral vessels were atheromatous.

The kidneys weighed 15 ounces the pair, the capsule was slightly adherent in places, the surface here and there slightly depressed, and the substance tough.

Michael McCarthy, aged 49, died of convulsions an hour after admission.

There were two old hæmorrhagic foci in the brain.

The heart weighed 12½ ounces. The left ventricle was not hypertrophied. The pericardium was slightly adherent. The aorta, cerebrals, and carotids were very atheromatous.

The kidneys weighed 12½ ounces the pair. The capsule was adherent, and there were several small cysts in the cortex.

Microscopically, the tubes were natural. Of 386 glomeruli, only 3 were diseased. These were fibrous and degenerate.

There was a general, moderate fibrosis, rather greater round the vessels than elsewhere. The arteries showed the usual changes.

The nature of this case was doubtful. The man had been drinking, and had taken too much. He began to be strange in his manner and was brought to the hospital. Slight facial paralysis of the left side was noticed. He had first

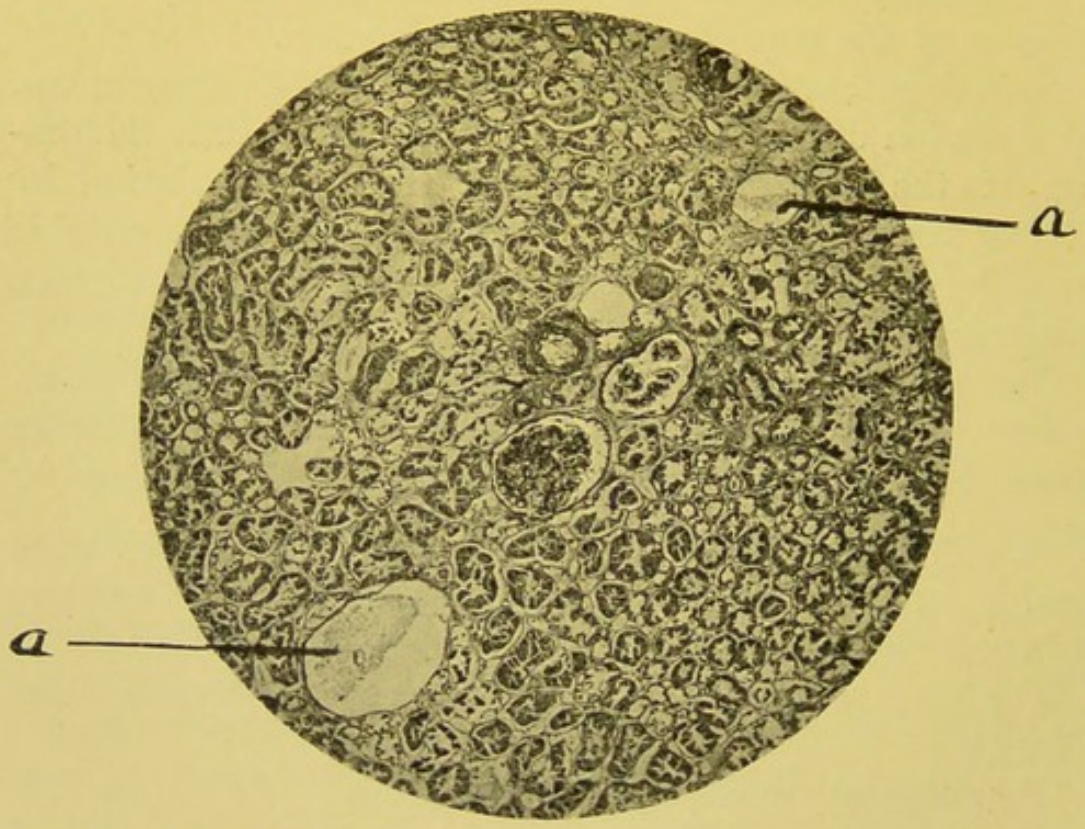

FIG. 17. Joseph Hammond. The changes in the tubular epithelium appear to be due rather to post-mortem fragmentation than to inflammation. The glomeruli in 1 sq. cm. of cortex were counted as follows: 187 natural, 10 with granular exsudation in capsule (*a*), 2 with inflammation, 27 fibrous and degenerate. The arteries were extremely diseased, and the connective tissue increased around them or in lines leading from them. ×55.

one fit, then a second, and then a succession of several. He was bled, but the symptoms were not relieved, and he died very rapidly. It was probably a case of convulsions due to the action of a large dose of alcohol upon a damaged brain.

Robert Swainston, aged 50, died of pneumonia and empyema on the day of admission. He passed no urine. He was a big fat man.

The heart weighed 21 ounces. There was general hypertrophy. There was some atheroma of the aorta and large vessels. The aorta, carotid, and iliac, when tested for elasticity, showed distinct evidence of sclerosis.

The kidneys weighed 18 ounces. The capsule was slightly adherent and there were a few cortical cysts. Microscopically,

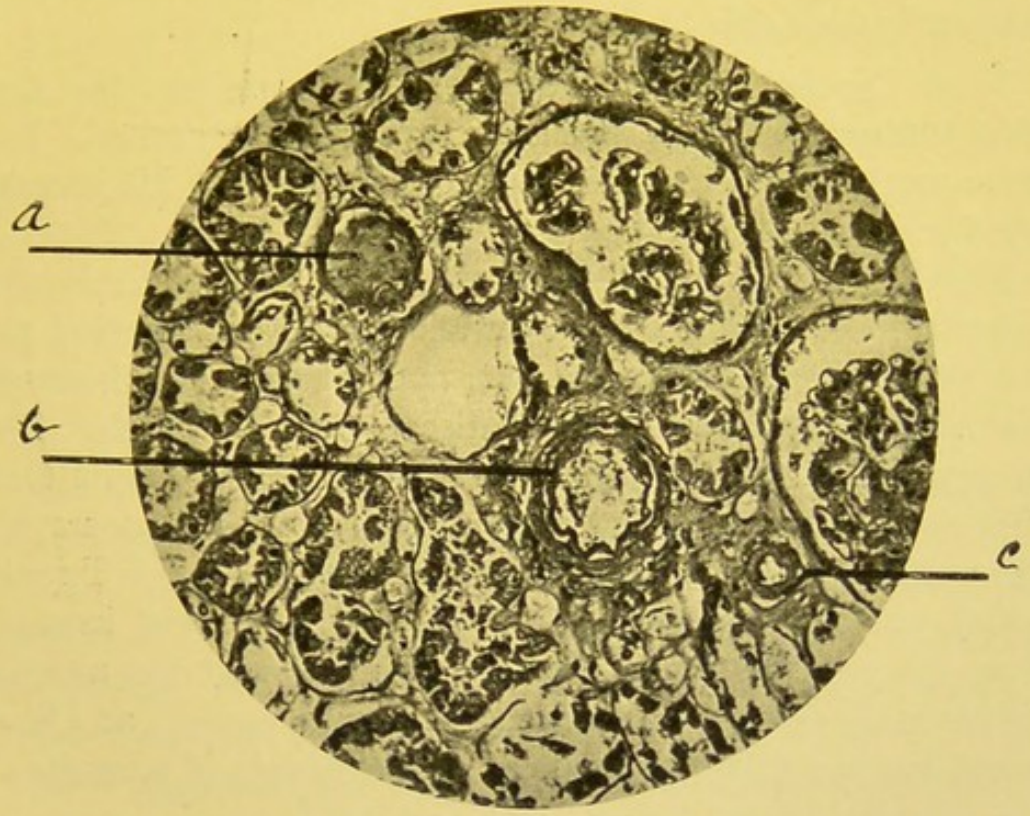

FIG. 18. The same case. Showing at (*a*) a fibrous glomerulus, at (*b*) an interlobular artery with endarteritis, at (*c*) a capillary with thickenings on its walls. Fibrosis round the artery. × 150.

the tubes were natural. Of 147 glomeruli, 141 were natural, the remainder degenerate. There was some fibrosis running in wedge-wise from the capsule, and more in connexion with the interlobular arteries. There was hyaline swelling in many of the smaller vessels, but no proliferative endarteritis was seen.

Walter Howe, aged 54, died of cerebellar hæmorrhage on the day of admission.

He was a well-developed, muscular man.

The heart weighed 26 ounces, and the left ventricle was

greatly hypertrophied. The aorta and the cerebral arteries were very atheromatous. The kidneys weighed 9 ounces the pair, and were granular. Microscopically, the tubes showed no sign of disease. Of 102 glomeruli, 80 were natural, 22 were fibrous. None showed evidence of inflammation. The fibrous tissue was greatly increased, and the fibrosis evidently spread from the arteries. These were extremely diseased.

John Chorley, aged 59, died of cardiac failure the day after admission. There was general dropsy and ascites. The urine was of sp. gr. 1005 with a trace of albumen. He became rapidly cyanosed and died.

The heart weighed 24 ounces. The left ventricle was hypertrophied, and the right auricle was so dilated that the muscular fibres were spaced out, and intervals left between them. There was no marked disease of the vessels. The kidneys weighed 15 ounces and were slightly granular. Microscopically, the tubes were natural. Of 192 glomeruli, 188 were natural and 4 degenerate. There was much fibrosis, which spread outwards along the arteries, and inwards from the capsule, but there was no disease of the arteries visible in the sections examined. The aorta, carotid, and iliac, tested for elasticity, showed distinct evidence of sclerosis.

Henry Dognall, aged 61, died of cardiac failure very soon after admission.

The heart weighed 20 ounces and was much hypertrophied. The aorta and cerebral arteries were much diseased. The kidneys weighed 10 ounces ; they were moderately granular. Microscopically, the tubes showed no evidence of disease. Of 107 glomeruli, only 4 were degenerate. There was much fibrosis, chiefly confined to the neighbourhood of the interlobular arteries. These and the larger arteries showed marked endarteritis.

Patrick Keohan, aged 61, was brought in dead. The cause of death was not apparent.

The heart weighed 21 ounces, and the left ventricle was much hypertrophied.

The kidneys weighed 12 ounces. The capsule was slightly adherent, and there were several small cysts in the cortex.

Microscopically, the tubes and the glomeruli were normal. There was some fibrosis round the interlobular vessels, and also some running in wedge-wise from the capsule. The interlobular vessels showed endarteritis, and one or two of the smaller branches hyaline swelling.

William Niblett, aged 62, died of stricture of the pylorus, the result of poisoning by hydrochloric acid.

The heart weighed 11 ounces and was not hypertrophied. The aorta was but slightly and the cerebrals not at all diseased. The kidneys weighed 11 ounces and were granular. Microscopically, the tubes showed no evidence of disease. Of 203 glomeruli, 24 were fibrous and degenerate. The interstitial tissue was generally increased, but was remarkably free from cells. The arteries showed endarteritis.

Sarah Voellkopf, aged 71, died of pontine hæmorrhage. During life, the urine contained no albumen.

The heart weighed 13 ounces; the left ventricle was somewhat hypertrophied. There was much atheroma throughout the arterial system. The kidneys weighed 10 ounces and were granular.

Microscopically, the tubes showed no evidence of inflammation. Of 382 glomeruli, 13 were fibrous. There was marked fibrosis

(*a*) running in from the capsule;
(*b*) in masses at the base surrounding the large arteries;
(*c*) along the interlobular vessels and spreading therefrom.

The arteries were much diseased.

These are sufficient to show that the same process can be traced into the stage when it produces visible alteration in the kidney, yet remains a pure interstitial disease without inflammation of the tubes or of the glomeruli.

These were not in life cases of Bright's disease. Some of them were at their usual employment, in apparent health, when they met with a fatal accident. Others died suddenly.

Others were in the hospital at the time, under treatment for other conditions. In these alone have I been able to get an account of the urine. In all but two cases (Webb and Chorley) the urine was not albuminous. The appearance of albumen in the last two days of another (Hood) is probably due merely to venous congestion.

It is evident, therefore, that interstitial fibrosis can exist, even in considerable severity, without producing albuminuria or dropsy.

In the histological records two things are to be remarked : the one, that the fibrosis begins and spreads from the places where connective tissue naturally enters the kidney, along the interlobular vessels, and along the vessels of the capsular anastomosis ; the other, that in all but two of these cases the arterioles of the kidney showed evidence of endarteritis, and that in these two exceptions there was arterial sclerosis elsewhere.

It has been customary among pathologists to describe as varieties of the granular kidney, the secondary contracted kidney, the kidney of primary interstitial nephritis, and the arterio-sclerotic kidney. I find no evidence that the last two can be maintained as separate varieties. So far as I have been able to discover, chronic interstitial nephritis without parenchymatous inflammation is always accompanied by local or general arterial degeneration.

Where parenchymatous disease exists as well I see no reason to look upon the disease as other than the chronic diffuse nephritis described in a former chapter. Diffuse nephritis occurs at all ages, and if there is any truth in the view that it may be caused by errors of metabolism we might reasonably expect it to be even more common in the later than in the earlier half of life. The majority of granular kidneys seem to me to result from this form. To it I should refer cases that in life present the clinical features of renal disease, albuminuria with casts, and hæmaturia whether with or without dropsy. They are often accompanied by arterial sclerosis, firstly, because that is a disease which is very common in later life, and secondly, because as we

have seen on a former page, diffuse nephritis has a special influence in producing it. Moreover, we may reasonably suppose that when arterial disease exists the deficient blood-supply renders the parenchyma more than usually liable to inflammation, and thus that arterial sclerosis is in its turn a predisposing cause of diffuse nephritis.

But in such cases as those above related there is evidence of a condition which before any parenchymatous inflammation has taken place produces lesions which are coincident with, and I believe dependent upon, arterial sclerosis alone. This, the pure interstitial form of nephritis, I regard as a disease of the circulatory system rather than of the kidney.

The changes in the arteries do not appear to differ in the two conditions. Both in the kidney of diffuse nephritis, and in that of arterial sclerosis, there is proliferation of the subendothelial tissue of the larger arteries, and hyaline swelling at the same site in the smaller. In the latter form of kidney, however, fibrosis is in early cases confined to, and in later cases evidently spreads from the neighbourhood of arteries. There is, in other words, peri-arteritis as well as endo-arteritis. There is also a marked tendency to degeneration of the muscular coat. In a former publication[1] I gave the results of an attempt to measure this degeneration numerically by counting the muscular nuclei over given lengths of the media in arteries of different sizes, and comparing them with similar counts made in normal kidneys. In the diseased series every case showed a diminution of the number of nuclei, from which I inferred a loss of the muscular cells, and in many instances appropriate stains showed a distinct increase of the fibrous tissue in the muscular layer.

The urine in these cases is usually copious, pale, and of low specific gravity. These qualities are partly due to the rise of blood-pressure, which causes increased secretion of water. In consequence the patients often get up at night to pass water.

It would be desirable to estimate exactly the amount of solids passed by these patients under a fixed diet.

Unfortunately the conditions render this impossible. While the patients are in their usual health they do not come under treatment. When the heart fails the urine becomes scanty, the specific gravity rises, and the whole condition no longer represents the ordinary state of health.

Of the above cases there were only seven in which any record could be made of the urine. Of these one (Chorley) had a trace of albumen, a second (Webb), who was the subject of a cancerous cachexia, showed a cloud. In a third (Hood) the congestion due to heart failure caused albumen to appear in the last two days of life. Before that the urine was scanty, but not albuminous.

It does not seem that arterial sclerosis alone produces retinitis. None of the cases above described were examined for that condition, for they were not suspected of having renal disease, and the circumstances of their illness rendered an ophthalmoscopic examination either impossible or difficult. But I have had many cases of arterial sclerosis without albuminuria, resembling these, under me, in which I have examined the fundus, and I cannot recall any in which retinitis was found. The arteries often have the characters described on p. 163. This is not, however, always the case. Unlikely as it may seem, it is an undoubted fact that arterial sclerosis is sometimes limited to certain areas, and spares others. I have seen several cases in which the retinal arteries were natural though the other parts of the body were severely affected.

In one case (Mortimer) there was ascites with cirrhosis of the liver. In another (Chorley) there was dropsy from heart failure. There is no evidence that this condition of the kidney produces œdema except through failure of the heart.

Vomiting is also absent.

Convulsions occurred in one case (McCarthy). It hardly seems possible that the kidneys can have been the cause of them. It seems more probable that they were connected with the old lesions observed in the brain, and the large dose of alcohol.

The symptoms, when the condition is sufficiently advanced to produce any, are high blood-pressure, thickening of the arteries, and hypertrophy with subsequent dilatation and failure of the heart.

REFERENCE.

1. Herringham, *Trans. Path. Soc. Lond.*, lii. 83.

CHAPTER XVIII

CARDIO-VASCULAR CHANGES

MANY times in the previous pages the connexion has been noted between various forms of renal disease and diseases of the heart and blood-vessels. This relation has been recognized by all writers.

Yet it is extremely difficult to trace the links between the two. The reason of this is that the relation between the two diseases varies. In some cases disease of the kidneys causes disease of the heart and arteries, in others the reverse happens, and in yet another class it is quite possible that each may be producing the other.

It is generally agreed that there is a form of renal disease which is caused by arterial sclerosis. The arterio-sclerotic kidney is a recognized form of chronic interstitial nephritis. My own opinion as above stated goes further than this. Though I cannot say that pure interstitial nephritis never develops except as a coincident, and probably a consequence, of disease of the arteries, I can say that after a considerable experience in microscopical examination of kidneys, I have never seen a case in which it did. I think that all cases of pure interstitial nephritis, cases, that is, which show no sign of parenchymatous inflammation, are cases of arterio-sclerotic kidney.

On the other hand, the changes in the heart and arteries, which are found in company with the fibrous form of chronic diffuse nephritis in the young, appear to me to be the direct consequence of the renal disease. My reasons for thinking so are these. Hypertrophy of the heart with arterial sclerosis is common and severe in these cases, while it is very uncommon in young persons who have no renal disease. There is direct experimental evidence that the renal cells

contain some substance which raises blood-pressure, and also that high blood-pressure can produce both hypertrophy of the heart and arterial sclerosis. But it does not necessarily follow that these conditions are only produced in this way. There may be in renal disease some poison which causes arterial degeneration directly.

It has indeed been suggested that some cases of renal disease in the young are due to arterial sclerosis. That, if it were true, would weaken this line of evidence. But I do not believe it is true. I have never seen any case of pure interstitial nephritis among the many young granular kidneys I have examined. All that I have seen have shown marked and unmistakable signs of parenchymatous disease.

I therefore hold it as proved that diffuse nephritis can produce hypertrophy of the heart and arterial sclerosis.

But in the later years of life, while we have no reason to suppose that the liability to diffuse nephritis becomes less, we know that arterial sclerosis becomes much more common. It seems, therefore, likely that in a patient over forty years old both causes may be at work together. Arterial sclerosis due to other causes may be increasing the fibrous tissue in the kidney, while diffuse nephritis may be at the same time increasing the arterial sclerosis and cardiac hypertrophy. In such cases we could not hope to assign to each cause its exact proportion in the result.

If, therefore, it is allowed that nephritis is a cause of cardio-vascular change, it will be necessary to take examples from the nephritis of the young if we wish to see the effect of nephritis uncomplicated by the many other causes which operate in later life.

Of these I have in my series 41 cases dying between 20 and 40 years of age from uræmia, cerebral hæmorrhage, or cardiac failure. I exclude cases under 20 because hypertrophy is more difficult to estimate at that age.

In 32 of these cases, the heart weighed over 12 ounces and was, therefore, obviously hypertrophied. In one the weight was not noted.

In one case, a woman, the heart weighed 11 ounces, but was described as hypertrophied.

In the following cases the heart was not described as hypertrophied, but I doubt if the first two can be classed among the cases which failed to hypertrophy. Ten ounces is rather above the normal weight of a woman's heart.

F. Age 23. Heart 11 oz. Mitral stenosis. A single large horse-shoe kidney, extremely diseased, pressed upon by a pregnant uterus. Uræmia.

F. Age 39. Heart 10 oz. Kidneys 11 oz., 'contracting.' Cardiac failure with hydrothorax, and ulceration of the colon.

F. Age 30. Heart 9 oz. Kidneys 14 oz., 'large white.' Cardiac failure with anasarca.

F. Age 27. Heart 8 oz. Kidneys 9 oz., 'early interstitial.' Cardiac failure with œdema of the lungs.

F. Age 20. Heart 6 oz. Kidneys 14 oz., 'large white.' Cardiac failure with anasarca and effusions.

F. Age 33. Heart 5 oz. Kidneys 17 oz., 'large white.' Cardiac failure with anasarca; also cirrhosis of liver and ascites.

M. Age 24. Heart 7 oz., very pale, myocardium softened. Kidneys 14 oz., 'contracting.' Cardiac failure.

In the majority of cases the following changes are observed.

The left ventricle hypertrophies and the heart accordingly increases in weight. It may dilate towards the end and the patient die by heart failure, but when death is by uræmia there is often little if any dilatation. In consequence the apex is little displaced, and I have several times seen on the post-mortem table marked concentric hypertrophy which had not shown the signs of enlargement during life. A somewhat increased impulse, and an accentuation of the second sound over the aortic base may be the only evidence of it. On microscopic examination of the wall of the heart or of the papillary muscle I have sometimes seen fibrosis of the tissue and endarteritis of the larger vessels.

The aorta may be natural or much diseased. A man of 26 died of uræmia. His heart weighed 20 ounces, the coronaries

were very atheromatous. He had large atheromatous patches in the aorta. But both it and the common carotid, and the external iliac artery, were as elastic as the normal.

I have tested the elasticity of these three vessels in the cases of five men who died of chronic nephritis between the ages of 30 and 40. As the subject has not been much investigated I will give particulars.

Case 1. George Bayman, 32. Very high blood-pressure. Radial thickened. Albuminuric retinitis. Urine very albuminous with numerous casts. He vomited, had severe headache, became unconscious, and died in convulsions.

Post-mortem.—Heart 16 ounces. Hypertrophy especially of left ventricle. Valves natural. Kidneys 14 ounces, 'contracting.' Aorta 51 mm. wide,[a] natural to naked eye, and to microscopical examination. Carotid and external iliac natural to naked eye and to microscopical examination. Cerebral vessels stiff and gaping. Radial thickened.

Case 2. Edward Leggatt, 32. Hæmaturia and dyspnœa. The blood-pressure fairly high, the radial thick. No retinitis. Much œdema. Urine scanty. Convulsions came on, followed by coma, in which he died.

Post-mortem.—Heart $14\frac{1}{2}$ ounces. Hypertrophy and some dilatation of left ventricle. Kidneys 17 ounces, pale and smooth. Aorta 52 mm. wide, slight atheroma. No microscopical examination. Carotid and external iliac natural to the eye. No microscopical examination.

Case 3. Charles Stephens, 33. Severe headaches. Albuminuric retinitis. Blood-pressure 185 mm. Hg. Urine nearly solid with albumen. Convulsions came on, he became drowsy, and died quietly.

Post-mortem.—Heart 15 ounces. Simple hypertrophy of left ventricle. Kidneys 8 ounces, chronic diffuse nephritis. Aorta 54 mm. wide. No atheroma. Microscopically, considerable endarteritis. Carotid, slight fatty streaks. Microscopically, a good deal of endarteritis. External

[a] The average width of the aorta at this age, when cut open and laid flat, is 50 mm.

iliac natural to the eye. Microscopically, patchy endarteritis. The middle and external coats were natural in all three. The cerebral vessels and radials were natural to the eye.

Case 4. Charles Bell, 38. Very high blood-pressure, slight œdema. Much albuminuria. He suddenly became maniacal, then comatose, and died.

Post-mortem.—Heart 16 ounces. Pure hypertrophy. Kidneys 13 ounces, granular. Vessels thickened. Aorta 50 mm. wide, natural to the eye and to microscopical examination. Carotid, slight specks of atheroma. Microscopically, slight increase of intima. External iliac natural to the eye and to microscopical examination. The smaller arteries throughout the body were thick and gaping.

Case 5. John Hurley, 39. Dyspnœa (one lung collapsed from old pleurisy). No œdema. Blood-pressure from 170 to 200 mm. Hg. Albuminuric retinitis. Died of pleural effusion on the other side.

Post-mortem.—Heart 22 ounces. Hypertrophy and dilatation of both sides. Kidneys 8 ounces, granular. Aorta 55 mm. wide, considerable atheroma. Microscopically, much endarteritis. Carotid, some streaks of atheroma. Microscopically, some endarteritis. External iliac natural to the eye. Microscopically, patchy endarteritis.

The elasticity of the aorta was tested by the method described by Wills and myself.[1] That of the carotid and external iliac by registering the displacement of fluid caused by the gradual expansion of the vessel under a gradually increasing internal pressure.[a]

[a] A solid plug was tied into one end of the artery, the other was tied on to a metal tube which communicated with a pressure apparatus. The artery was placed in a glass cylinder containing oil, sealed above, and below closed by an air-tight valve. A clockwork apparatus raised a vessel of mercury which increased the pressure inside the artery. The expansion of the artery displaced oil, which forced the lower valve downwards. The movement of the valve was communicated to a lever writing on a travelling paper which was pulled by the clockwork. The apparatus was

Aorta.

Load in grammes		50	100	150	200
Extension.	Average of all cases in mm.	88	141	174	>183
,,	Nephritis. Case 1 . . .	90	146	180	199
,,	,, ,, 2 . . .	95	151	187	>200
,,	,, ,, 3 . . .	82	135	170	193
,,	,, ,, 4 . . .	89	138	170	191
,,	,, ,, 5 . . .	77	124	156	179
,,	Average in nephritis	86	138	172	>192

Carotid.

Internal pressure in mm. Hg.		50	100	150	200	250
Dilatation.	Average of all cases . .	52	96	115	123	132
,,	Nephritis. Case 1 . . .	69	124	141	149	154
,,	,, ,, 2 . . .	52	104	121	130	135
,,	,, ,, 3 . . .	55	107	135	150	158
,,	,, ,, 4 . . .	50	107	124	132	138
,,	,, ,, 5 . . .	51	97	117	128	136
,,	Average in nephritis	55	107	123	137	144

External Iliac.

Internal pressure in mm. Hg.		50	100	150	200	250
Dilatation.	Average of all cases . .	69	106	119	129	136
,,	Case 1	98	—	—	—	—
,,	,, 2	115	173	—	—	—
,,	,, 3	102	143	160	168	—
,,	,, 4	—	—	—	—	—
,,	,, 5	47	64	70	74	78

The above tables show that at the lower loads the elasticity of the aorta is very slightly below the average for that age (calculated from 20 other cases), but is above the average with the highest load used. That of the carotid is considerably above the average for that age, which was calculated from 21 cases of all kinds. That of the external iliac is always difficult to estimate because often minute branches are given off which, unless they can be

modified by Dr. Wills from a design of Roy, and made by him. The tracings were paraboloid curves.

These two arteries were chosen because lengths of 4 cm. between the inner ends of the plugs could be obtained free from visible branches.

found and tied, prevent the experiment. Often also the minute branches become permeable at a higher weight when they did not open at the lower. This instantly ruins the experiment. This explains why the external iliac record is unsatisfactory. The first three, so far as they go, are more expansile than the average for that age, which was in this case calculated from 12 cases of all kinds, but the last shows great stiffening.

The chief interest, however, lies in the comparison between these large vessels and the small peripheral arteries, such as the radial and cerebrals. I have never tested the elasticity of these, because I have never been able to devise a method suitable for them. But their structural alteration is very visible. It seems much greater in proportion than that in the aorta at their age. The aorta indeed is little altered, whereas the peripheral arteries are noted as affected three times out of the five, and were almost certainly diseased in the fifth case, though the notes do not mention it.[a]

Of a still smaller size are the interlobular arteries of the kidney, their immediate offshoots, and lastly the vasa afferentia of the glomeruli. In these the lesions visible under the microscope are :

1. Local hyaline swelling of the subendothelial layer in the larger, and of the whole wall in the small arteries.

2. Increase of the subendothelial layer of cells, together with a multiplication of the elastic lamina which lies outside this layer, so that instead of one, it forms a series of concentric rings.

3. Decrease of the muscular layer, and some increase of fibrous tissue in it, as shown by Van Geeson's method of staining.

4. Increase of the connective tissue layer outside the media, which ends indefinitely in continuation with the connective tissue of the kidney.

Similar changes are seen in the vessels of the spleen, and occasionally in those of the heart. But I have not been able

[a] The notes are simply taken from the register, and were not made with any special reference to this subject.

to find them in the arterioles of the skin, or of the muscles, or of the liver. This restriction, if it is confirmed by others, appears to me to have an important bearing on the nature of the process.

These are no other than the lesions originally described by Gull and Sutton, under the appropriate name of arterio-capillary fibrosis. There was at first some idea that the process included a muscular hypertrophy. But it appears now generally allowed that it is, at any rate in its later stages, a degeneration in which an increase of elastic and fibrous tissue, and a hyaline change are the chief features.

In what way does the disease of the kidney produce these conditions ? Probably in more than one.

The hyaline thickening of the intima, and perhaps the hyperplastic endarteritis, seen in the renal arterioles, may be local effects of the poison which is acting at the same time on the kidney itself. The former, for instance, occurs both in the kidney and in the spleen during an attack of scarlatina (Klein).

Thoma thought that in diffuse arterio-sclerosis the primary alteration lay in the media. In this coat, whether the vessel be of the elastic type of the large, or of the muscular type of the smaller arteries, lies the chief seat of function. Senile degeneration shows itself in a loss of elasticity, and in consequent dilatation. The increase of the intima was in effect, according to Thoma, an effort to compensate for this dilatation.

In the former of these views he had been preceded by Roy.

Later writers differ widely. Some, as Adami and Klotz, maintain Thoma's opinion. Others, such as Jorés and Aschoff, think that the intima is the most important coat, that its elastic tissue is gradually increased with the growth of the body up to about 30 years of age, then becomes stationary, and lastly, from about 45 years onwards, begins to lose its power, to yield to the pressure of the blood, and to become permanently stretched. To fortify it, a fresh growth begins; this time it is not elastic, but the lower grade connective tissue which is formed. They lay little

stress on the functions of the media or on the alterations which this structure undergoes.

The exact method by which nephritis produces precocious degeneration is not known. It must be, however, remembered that its results can hardly be compared with those of senile decay. The blood-pressure is often higher, and the cardiac hypertrophy greater, than is usual in the arterial sclerosis of old age.

Seeing that increase of blood-pressure, either mechanical as when the abdominal aorta is compressed or the rabbit hung up head downwards, or toxic as when adrenalin is injected, is followed by disease of the arteries, it has been maintained that the first link in the chain is a rise of blood-pressure. The kidney of chronic nephritis is less permeable than the natural (Thoma, Dickinson), and this was at one time put forward as the cause of the rise. But it has been generally felt that it was not in itself sufficient to produce the effect. Tigerstedt was the first to show that extract of kidney contained a substance that, when injected into the circulation, increased pressure. Some have suggested that in chronic nephritis destruction of renal tissue takes place, and that the products are conveyed into the circulation and raise pressure. Others again prefer to suppose that the effect is due to some secondary change in metabolism.

Increase of blood-pressure implies either an increase in the force of the heart, or an increased peripheral resistance, or both. Probably both are present, for if the heart is stimulated the peripheral arteries contract to resist the too rapid passage of the blood, and the heart is known to hypertrophy in answer to increased resistance. But the exact order of events remains in doubt. It has been suggested that nephritis produces some poison which is a direct stimulant of the heart, and that it is the heart which plays the first card. But the commoner theory is that the peripheral vessels first, either by muscular contraction or by degeneration and rigidity, present a greater resistance, and that the heart hypertrophies in order to keep up the circulation. The pressure tends thus to be permanently raised.

It is remarkable, however, how greatly it varies if observations are made at frequent intervals.[2] This, if the resistance were due to active contraction of the peripheral arteries, might be explained by supposing that for some reason or other a period of relaxation had taken place. But it seems to me that whatever may happen in the early stages, the resistance is at a later date due to some more permanent condition. The effect in these patients of drugs which relax the arteries is not such as I should expect if muscular spasm were the resisting force (see charts, p. 221). Microscopic examination also appears to show changes of a permanent character. Probably, therefore, the difference of pressure depends upon the greater or lesser force of the heart. I do not suppose that the power of the myocardium varies so rapidly. But its contraction is under nervous control, and it is not difficult to imagine many causes which may weaken the stimulus derived from this system.

I make little doubt that a high blood-pressure is necessary for the life of these patients. As I read the case the first change in the cardio-vascular system is the increase of peripheral resistance. If the circulation is to be maintained the pressure must of necessity be raised. The only thing that can raise it is an increase of force on the part of the heart, and if the resistance is permanently increased, the other compensating factors must be permanent also.

The increased pressure brings two dangers with it. On the one hand the vessels may burst, on the other the vessels may hold, but the heart may eventually be unable to cope with the resistance they offer, and may fail.

The former event is exemplified in cerebral hæmorrhage. Statistics of this will be found on p. 109. It is rare before 50 years of age; it is often coincident with emphysema, and it is not as a rule accompanied by very great cardiac hypertrophy. It implies that of the two opposing parties the arteries are the weaker.

The latter causes death by cardiac failure. Although the fifties here also furnish the largest number of any single decade, cardiac failure begins earlier, and is spread fairly

over the years from thirty onwards. The average weight of the heart is greater than in those dying by hæmorrhage, and so also is the average weight of the kidneys. Both these facts are interesting. The latter implies that the factors which increase the weight of the kidney, namely œdema and the various forms of diffuse inflammation, are more common here than in the hæmorrhagic cases. The former throws light upon the process which takes place in the vascular system. Evidently in these patients the heart can respond to the stimulus of increased resistance to a remarkable degree. Death by cardiac failure does not mean that the original power of response is less than usual. It means that the peripheral resistance is so great that even a greatly hypertrophied heart is insufficient and in the end has to yield. These are the cases in which between the tough young arteries and the vigorously growing heart the blood-pressure rises to heights not often seen in later life.

It is a part of the benefit thus obtained that the pressure in the renal artery is raised. Thus the blood-flow through the kidney is increased, and drainage of the blood improved.

It is, however, to be remarked that in disease the quantity of urine excreted—the quantity, that is, of urinary water—does not vary so directly as we should expect with the pressure of the blood.

This is well shown in the following charts:

The reason must surely lie in some local vasomotor change. The vasomotor nerves going to the renal arteries must obey some stimulus other than that which governs the general blood-pressure, and must increase or lessen the flow through the kidneys independently of the general current.

It might perhaps be suggested that local inflammation of the renal tissue might account for the variation. But in the first place the apparent discrepancy alters from day to day in so inconstant a manner that no fresh access of inflammation can explain it, and, in the second place, we should expect, if that explanation were true, that the albumen should vary with the inflammation. A fresh attack would probably result in an increase of the albumen. But no such variation

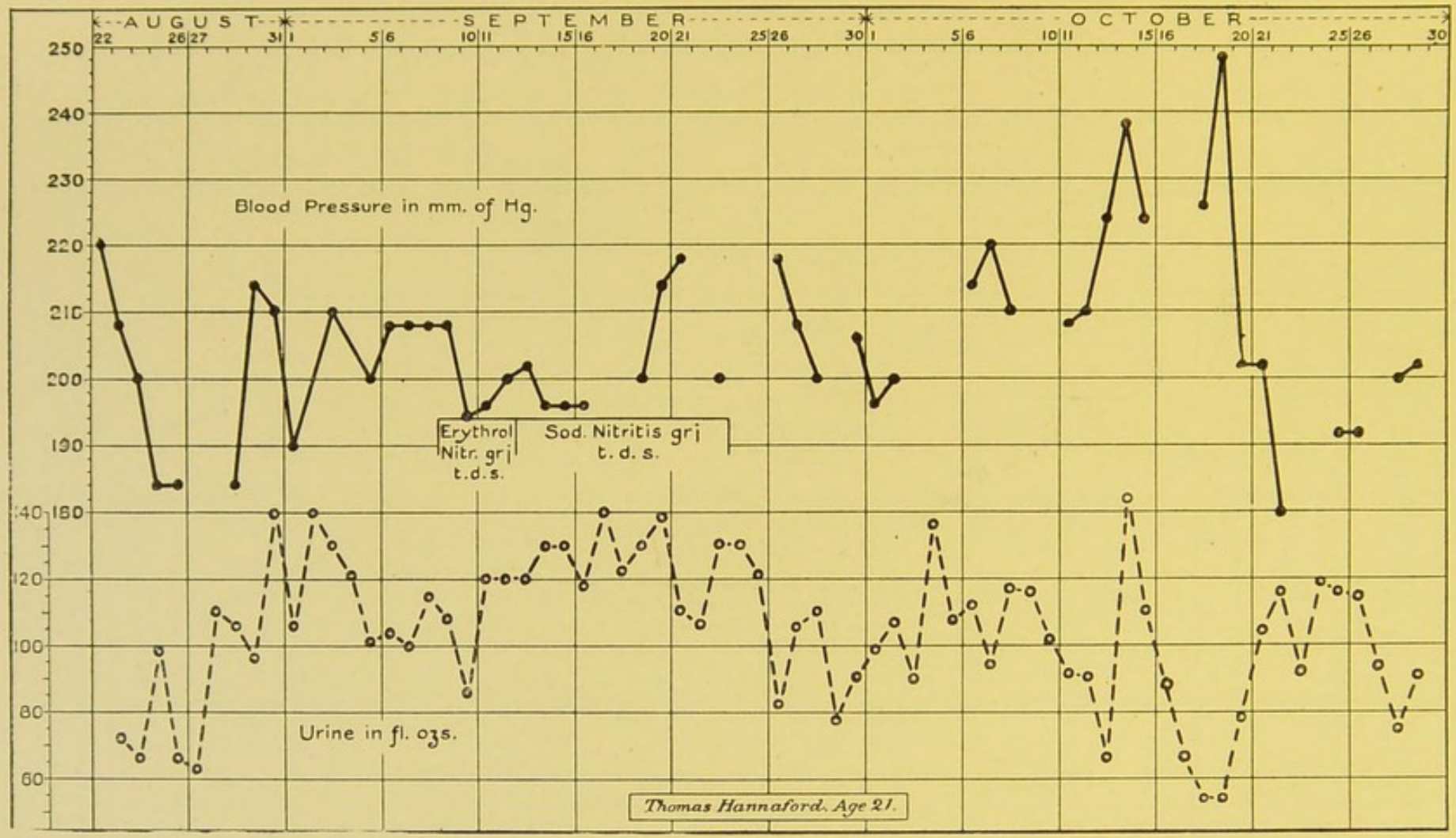

CHART E. The pressure is lower (August 25, 26, 29; September 1; October 22, 25, 26) without drugs than at any time during their administration. It rises (September 21) during their use. It varies so widely that it would be difficult to be sure of the effect of a drug

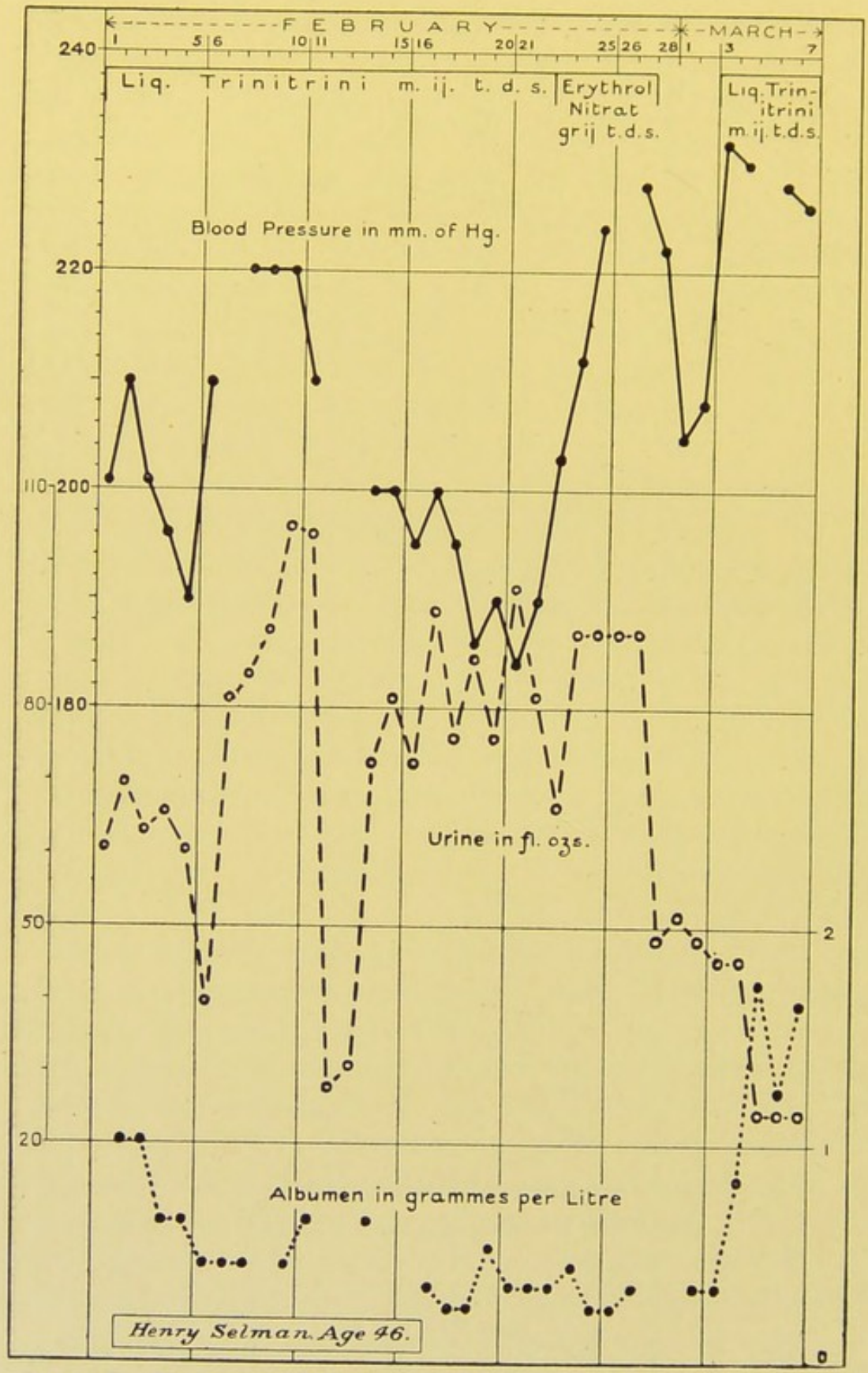

CHART F. The pressure falls, rises, and falls again during the first period under Liq. trinitrini, rises under Erythrol nitrate, and hardly falls at all under the renewed use of Liq. trinitrini.

takes place constantly in the albumen. The decrease of urine is not always accompanied by increase in the proportion of albumen.

But although the amount of urine does not vary from day to day with the blood-pressure in each individual case, it is

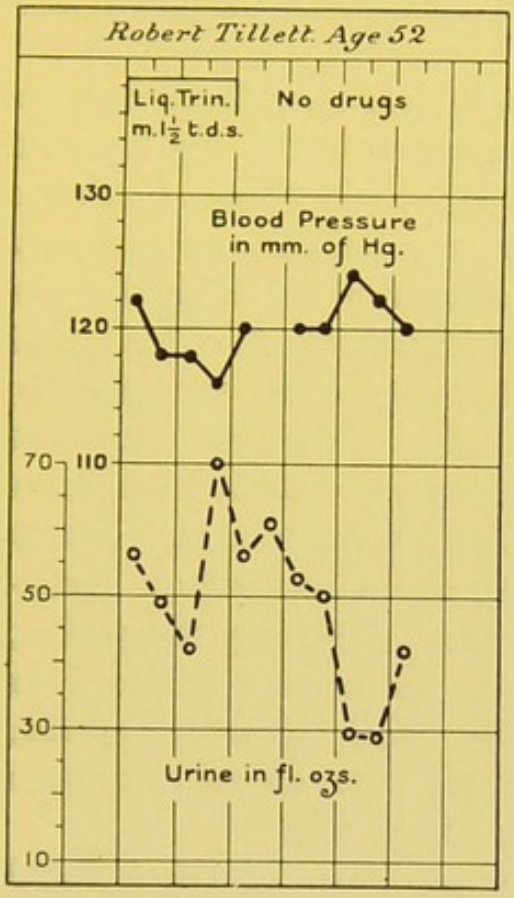

CHART G. The urine diminishes though the pressure remains steady.

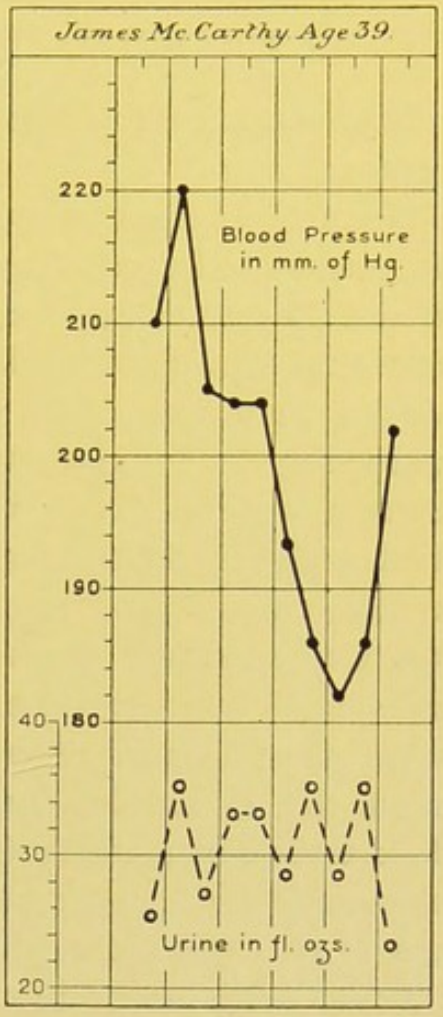

CHART H. The urine remains steady though the pressure falls.

true that, broadly speaking, the two vary together. Cases with low blood-pressure as a whole excrete less urine than those in which the pressure is high, and as I have insisted in the chapter on treatment, we must, if we desire to increase the urine and aid elimination of the poison, use drugs which raise the pressure of the blood.

REFERENCES.

1. Herringham and Wills, *Medico-Chirurg. Trans.*, lxxxvii. 489.
2. Batty Shaw, *Brit. Med. Journ.*, 1910, ii. 1761.

CHAPTER XIX

POLYCYSTIC DISEASE OF THE KIDNEYS

Occasionally the kidneys are found to be converted into a mass of cysts.

When the disease occurs in a typical form both kidneys are greatly enlarged, the commonest weight being between 20 and 30 ounces each, and the cysts, which are of all sizes from that of a pin's head to that of a walnut, are so closely packed that very little renal structure is visible by the unaided eye. Some descriptions indeed run 'no true renal tissue was visible'. The cysts have thin transparent walls, lined with a flattened layer of cells, and project from the surface, as well as occupy the interior, so that the kidneys look like a bunch of grapes. They contain a fluid which varies both in colour, consistence, and constitution. Sometimes it is limpid, sometimes viscid. It may be yellow, green, red, or purple, according to the amount of blood, or blood derivatives, which it contains. Fatty globules, granular cells, cholesterin, and crystals of triple phosphate have been seen in it. Occasionally urea has been found.

These cases occur in two groups, those of infancy and childhood, and those of adult life. It is commonly said that the two are separated by a very wide interval. But this is not quite true. A large proportion of the early cases occur in still-born or newly-born infants, but sporadic cases are found up to ten years of age. We had a case at St. Bartholomew's in a lad 19 years old. Ritchie's collection,[1] which is the largest known to me, includes

Between	20	and	30	years	of age,	3	cases
,,	30	,,	40	,,	,,	11	,,
,,	40	,,	50	,,	,,	33	,,
,,	50	,,	60	,,	,,	17	,,
Over	60			,,	,,	10	,,

There are, therefore, cases in every decade, but they are rare from 10 to 30 years.

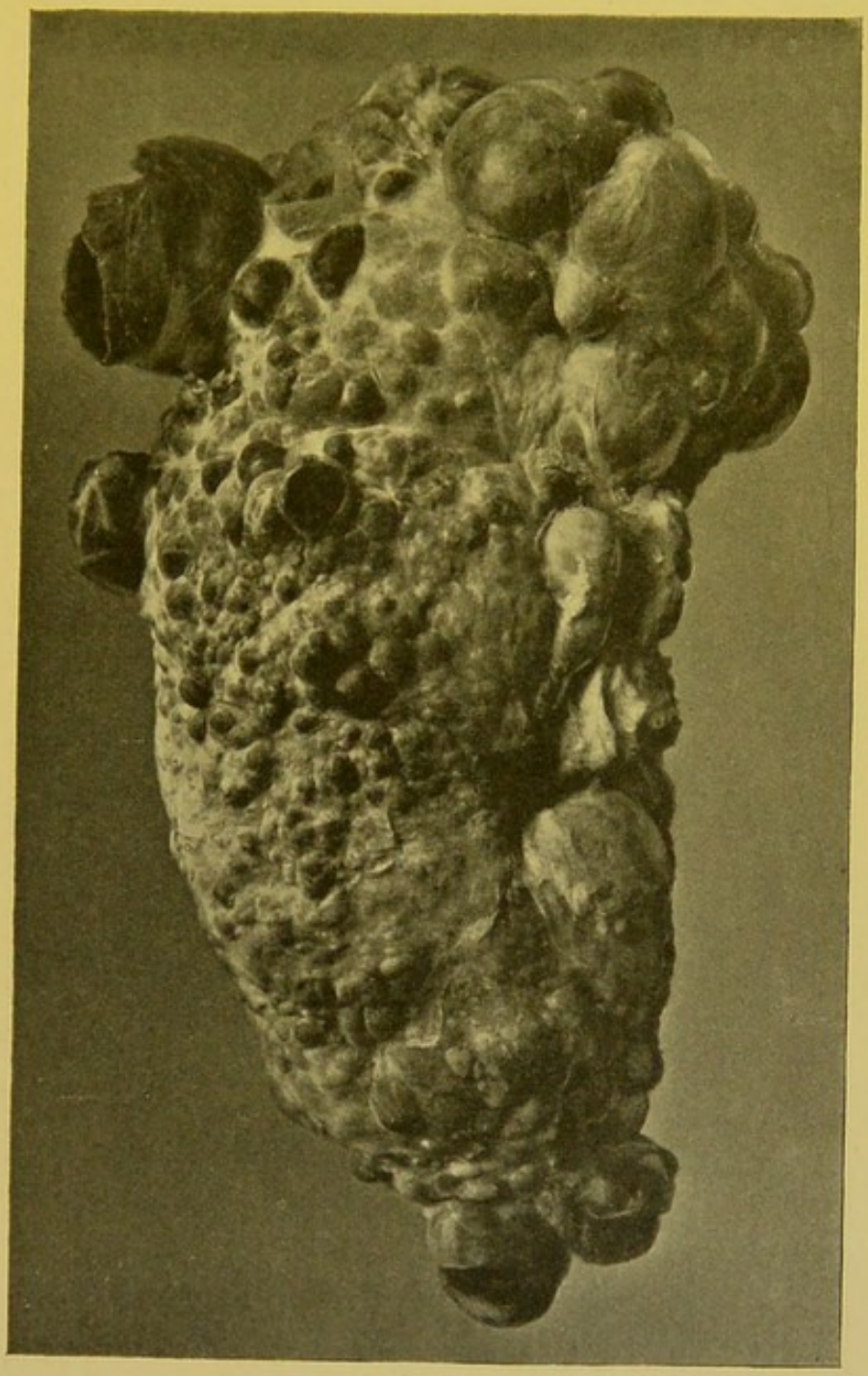

FIG. 19. A polycystic kidney. From the Museum of St. Bartholomew's Hospital.

Boinet and Raybaud [2] quote a paper in which Luzzato has collected 90 cases in early life, but I have not had access to it.

Such cases, whether adult or infantile, are usually bilateral. But sometimes one side is much more severely affected than

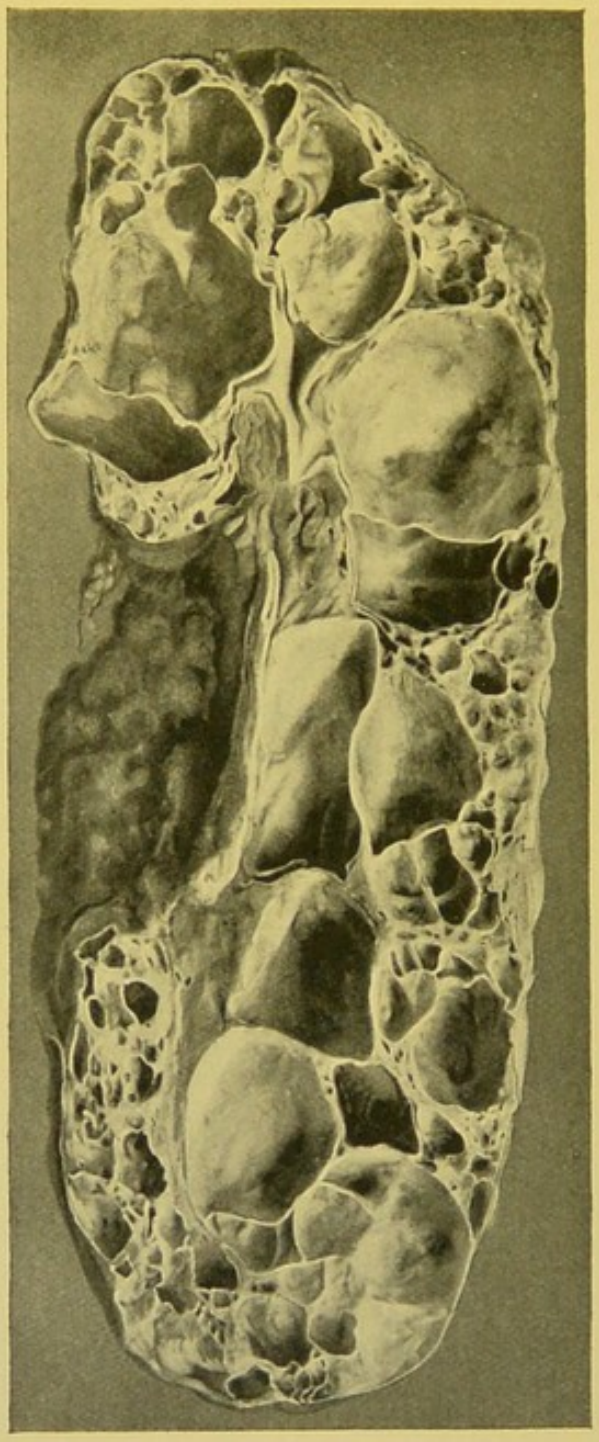

Fig. 20. Section of a polycystic kidney. From the Museum of St. Bartholomew's Hospital.

the other. Hare [3] reported a case in which one kidney weighed 16 lb., the other was only moderately enlarged. We have a specimen in the Museum of St. Bartholomew's

of a left kidney which is very large and full of cysts, especially at the lower end, where they are of the usual appearance, like a mass of grapes. The right kidney was not enlarged or cystic, but was granular, with an adherent capsule and a diminished cortex. The patient, a woman aged 51, died with cellulitis of the arm. Boinet and Raybaud state that in those children who die before or shortly after birth the affection is bilateral in nine cases out of ten, whereas in three-quarters of those who live from three months to five years it is unilateral.

Adult cases, when examined microscopically always, I believe, show changes like those of chronic diffuse nephritis. Tubes, glomeruli, interstitial tissue, and vessels are all altered. Such has been the case in four instances which I have examined myself, and I do not believe that in such cases it is possible to say in what structures the cysts originate. Blackburn [4] describes, for instance, as part of the process the hyaline or, as he calls it, colloid degeneration of the tuft which is seen in many cases of ordinary nephritis.

But infantile cases differ from them. They exhibit many conditions incompatible with life, such as incomplete development, or complete atresia, of the papillæ; but it is remarkable that, as recorded both by Shattock [7] and by Still,[8] the glomeruli and arteries may show no evidence of disease.

The disease is rare. Since the year 1867 I can only find eleven cases of it among our post-mortem records.

These were all adult cases. Seven were in men, one of 19 years old, four between 40 and 50, two between 50 and 60 years. Of the four women one was 40 years old, the others between 50 and 60 years.

The symptoms were in most cases of gradual onset, and rather indefinite. The following are instances:

Frederick Harris, aged 44, had been a soldier, until at the age of 23 he had rheumatic fever, and was invalided for valvular disease of the heart. He was at work as a compositor, and in his usual health until about February 20th, 1903, when he caught a cold and a cough. Pain in the

region of the heart, with shortness of breath, soon appeared. He lost appetite and began to vomit.

On admission he was anæmic and very short of breath. His eyes were prominent, his face cyanotic, and his eyelids and legs œdematous. There were signs of œdema of the lungs. The heart was greatly dilated and there were signs of both mitral and aortic disease. The urine had a specific gravity of 1010 ; there was a large cloud of albumen. He was discharged on April 4th much relieved. The cardiac murmurs remained, but the urine now contained only a trace of albumen, and the œdema had disappeared. Within a fortnight, however, he was re-admitted with the same symptoms, to be again discharged much improved on June 4th. He kept fairly well until July, when he had an attack of faintness, and his legs again began to swell. He was re-admitted, again with cardiac symptoms. The urine was acid, sp. gr. 1015, and contained a cloud of albumen. In the middle of September dyspnœa increased, the pulse became very irregular and feeble, delirium came on, the respiration was of the Cheyne-Stokes type, and he died of cardiac failure on October 22nd.

Not long before his death Dr. W. H. Hurtley made for me an analysis of the urinary constituents, which is contained in the following table :

Date.	*N. intake calculated from diet.*	*Urinary Output.*				
		Total N.	*Cl.*	P_2O_5.	*Na as NaCl.*	*K as KCl.*
Oct. 9–10	circ. 12 g.	10·4673	1·6203	1·4625	0	8·9052
,, 10–11	,, 13 g.	6·1686	0·897	0·9853	0·6629	2·9825
,, 11–12	,, 13 g.	3·802	0·936	1·4850	0·4302	4·0158

The Na and K were weighed as NaCl and KCl, but were evidently excreted in other combinations.

On no occasion were the kidneys felt. The man was muscular, and the abdomen always somewhat distended.

At the post mortem the heart was dilated and hypertrophied : there was chronic and recent endocarditis with mitral stenosis and atheroma of the aortic valve. There

was pericarditis, pleurisy with effusion, congestion of the liver and ascites. The kidneys weighed 32 and 30 ounces respectively and were typical examples of polycystic disease.

Louisa Wood, 52, was brought to the hospital with a history that she had been ill and weak for several months. No symptom connected with the kidneys was reported. When admitted she had râles at the bases of the lungs, gradually became comatose, and died the same day. The urine contained a very slight haze of albumen.

The heart weighed 13 ounces, there were old pericardial adhesions ; the left ventricle was slightly dilated, the mitral valve thickened. There was slight atheroma in the arch of the aorta. The liver weighed 50 ounces, was deformed by tight lacing, and also contained numerous cysts. It is figured in Dr. Rolleston's *Diseases of the Liver* (Fig. 55, p. 447). The kidneys weighed 30 ounces each and completely filled each loin ; they were typical examples of cystic disease.

There are, however, many variations from the type. The kidneys, even in undoubted cases, are not always much enlarged. The kidneys of a male patient, aged 19, the youngest in our series of adults at St. Bartholomew's, weighed only 7 and 9 ounces respectively. A man aged 35 died in the wards with general weakness, polyuria, and uræmia. He had, however, no ophthalmoscopic changes and there was little if any rise of blood-pressure. The kidneys weighed only 6 ounces the pair, and were completely converted into cysts showing no renal substance to the naked eye.

There has long been a dispute as to the nature of these curious kidneys. Some, as Pye Smith [5] and Hoche and Briguet [6] have held that the adult cases are merely aberrant forms of chronic nephritis, with unusually large and numerous retention cysts. It is undoubtedly true that nephritis is almost always, if not always, present, and the patients exhibit the retinal and cardio-vascular changes of nephritis, and often die of uræmia, cerebral hæmorrhage, or cardiac failure.

But I confess I cannot understand how any one can look at one of these kidneys from an adult and believe that they

are of the same nature as an ordinary granular kidney. No one has explained what produces the aberration, if it is an aberrant form, and I do not know of any attempts to show transitional forms. Those specimens in our Museum, which are smaller than the usual, are not at all like ordinary granular kidneys.

It seems to me very hard to separate the specimens found in adults from those found in newly-born children. They appear to be the same disease. I do not think that any one has seriously argued that these congenital cases are produced by ordinary nephritis. The observation made both by Shattock [7] and by Still,[8] that neither the glomeruli nor the arteries were diseased, is of great importance. It would be sufficient, even if it stood alone, to prevent me from believing that nephritis was the cause of the condition in these cases. Virchow's [9] descriptions in four cases read like fibrosis round the vessels and glomeruli, but without inflammation of the glomeruli, or endarteritis.

Almost all writers, however, agree in this, and seek the explanation of the congenital cystic kidney either in neoplasm, which has had a few advocates, or in some form of maldevelopment.

Virchow ascribed it to atresia of the papillæ and consequent retention. Koster [10] refers to Kupfer's work on the development of the kidney and ascribes the condition to some fault of growth in the blastema destined to form the tubules. Shattock put forward the theory that it was due to a retention of part of the original Wolffian body in the metanephros which in man forms the permanent kidney.

It is a remarkable fact that in a certain proportion of these cases, both congenital and adult, cysts are found in the liver also, and in a few the pancreas has been found to have cysts in it. Virchow noted how frequent it was to find other abnormalities in the congenital form. It has also been noted that these cases are apt to occur more than once in the same family.

Still has stated that coincident cystic disease of the liver is much more frequent in female cases than in male. It was

found in two of our cases at St. Bartholomew's, both of which were females, and in Ritchie's collection there are 21 such cases, of which 14 were females. Blackburn,[4] in a very full and exhaustive paper, has added three cases all in females. On the other hand there is no great disproportion between the sexes in cystic disease of the kidney alone. In Ritchie's series there were 45 males to 37 females, at St. Bartholomew's 7 males to 4 females, and Blackburn had 4 men to 7 women.

The combination of cystic kidney with cystic liver, striking though it is, is, however, not easily explained on any theory of mal-development. The two organs are so totally different in origin that no explanation fits the two.

It has been supposed by those who uphold the unity of the early and the adult forms that the latter are cases in which the disease, whatever it may be, is not sufficiently widespread to prevent the kidneys fulfilling their functions during juvenile and early adult life. It is, however, difficult to understand why in that case these kidneys are not found more commonly in persons dying at those ages of other causes. It is also difficult to believe that a woman can live till 74 years of age with this condition (Ritchie). Accordingly the hypothesis has been put forward that these patients have the tendency to cystic disease in an undeveloped form, and that it is started into action by some unknown exciting cause in later life. This also is unsatisfactory.

Ritchie is of opinion that the adult disease is acquired, not congenital, and is due to some irritation propagated through the nervous system. He compares it to cystic disease of the mamma.

Blackburn thinks that it is due to an irritative lesion, that there is so striking a resemblance between the adult and the congenital cases that it seems impossible to doubt that both are instances of the same process, and that no causal relationship can be established with any other disease.

The constant association in adult cases of lesions indistinguishable from those of chronic nephritis forces us to believe

either with Blackburn that there is some peculiar but unknown toxic agency at work, or, with Still, that congenital

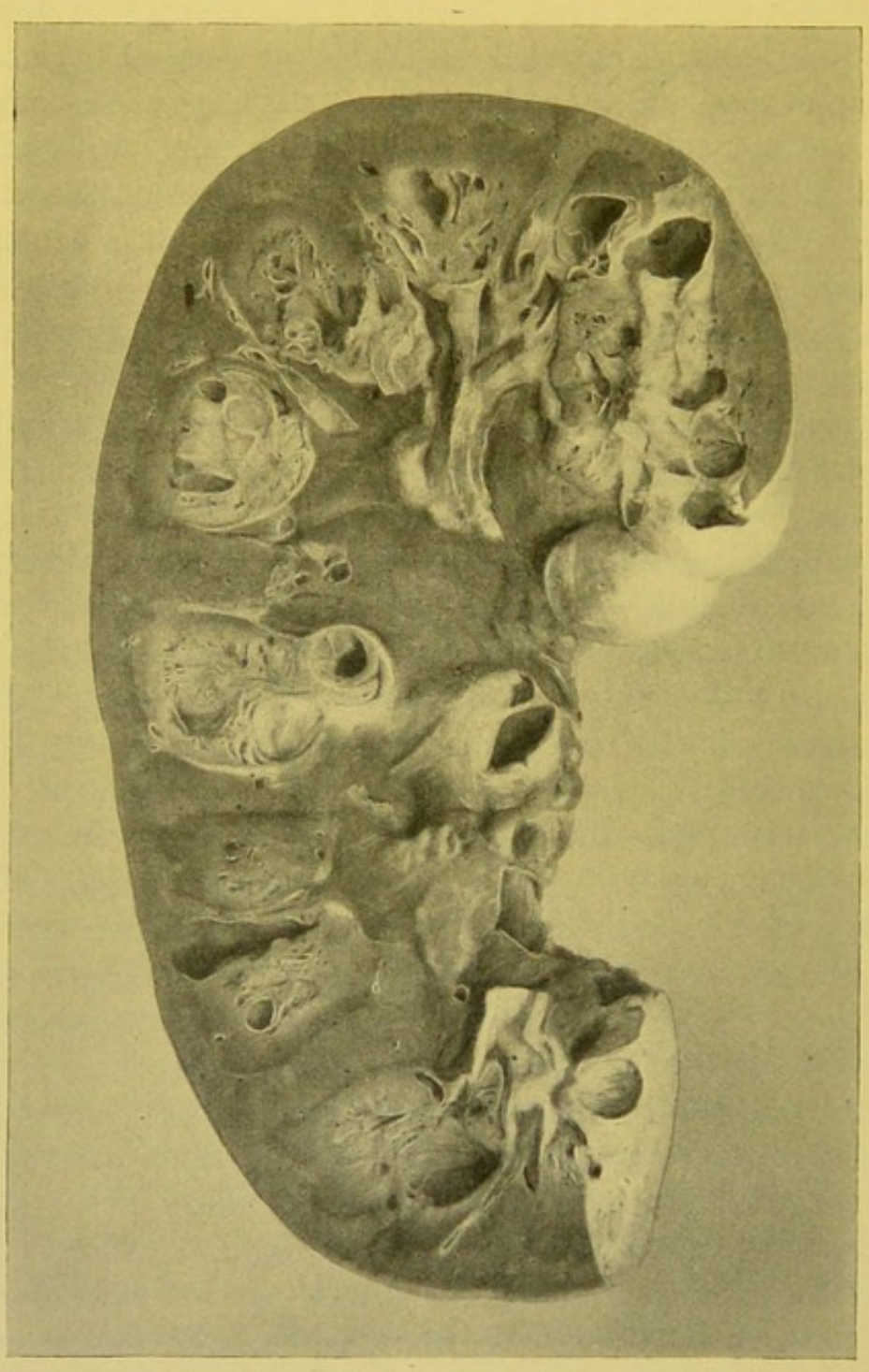

Fig. 21. A kidney with cystic disease of the pyramids. From the Museum of St. Bartholomew's Hospital.

mal-development renders these kidneys specially liable to ordinary nephritis.

In our Museum at St. Bartholomew's we have a curious

variation. A man, aged 62, died of carcinoma of the pancreas. His right kidney was enlarged, the cortex very narrow, the surface slightly granular with a few cortical cysts. The *pyramids* were almost completely hollowed out into compound cysts, in some of which the connective tissue framework of the pyramidal substance persisted, entangling numerous small black calculi of calcium carbonate. The calculi are as big as a pin's head. The cysts were lined with a proliferating cubical epithelium. The left kidney was unaffected.

In adult life cases of cystic disease sometimes remain undiscovered. In other instances tumours can be found in the renal region, on which irregularities are occasionally palpable. If there is such a tumour in each loin, and the patient has the symptoms of chronic nephritis, cystic disease is the most likely explanation.

The diagnosis has to be made from double calculus with pyonephrosis, or double tuberculous disease, which is not difficult, as pyuria and fever are almost certain to be present in these cases. Malignant growths are hardly ever bilateral.

The treatment resolves itself into that of chronic nephritis. A cystic kidney should never be operated upon, unless by its bulk it is endangering life.

References.

1. Ritchie, *Laboratory Reports Roy. Coll. Phys. Edinburgh*, iv. 194.
2. Boinet and Raybaud, *Rev. de Méd.*, 1903, xxiii. 1.
3. Hare, *Trans. Path. Soc. Lond.*, ii. 131.
4. Blackburn, ibid., 1904, lv. 203.
5. Pye Smith, *Trans. Path. Soc. Lond.*, xlvi. 81.
6. Hoche and Briguet, *Lésions des Reins*, Paris, 1904.
7. Shattock, *Trans. Path. Soc. Lond.*, xxxvii. 287.
8. Still, ibid., xlix. 155.
9. Virchow, *Gesammelte Abhandlungen*, 837.
10. Koster, transl. in *Dublin Quarterly Journ. of Med.*, 1868, xlvi. 256.

CHAPTER XX

RENAL DISEASE IN PREGNANCY DEPENDENT UPON TOXÆMIA

By Herbert Williamson, M.D., F.R.C.P.

I. The Toxæmia of Pregnancy

It has long been recognized that pregnant women are particularly prone to a group of diseases which of recent years have been regarded as toxic in origin. Bouchard in 1887 first drew attention to the possibilities of auto-intoxication. He maintained that in health the body contained toxic substances, some of which were ingested with the food, others were formed during the processes of digestion and of tissue metabolism, that these substances were normally excreted by the alimentary canal, the kidneys, the sweat glands, and the lungs, but, if for any reason the toxins were produced in excessive quantities, or were not rapidly eliminated, a condition of toxæmia or auto-intoxication resulted. Bouchard's work laid the foundations upon which the theory of a toxæmia of pregnancy rests, and although the toxins have not yet been isolated, although their chemical composition, their mode of action, and the sites of their formation are still unknown, the evidence accumulated from anatomical and bio-chemical research points to the conclusion that many of the diseases to which pregnant women are liable depend upon the presence of a toxin circulating in their blood. Pregnancy is essentially a physiological condition, but the boundary line between the physiological and the pathological is ill defined. Vomiting in the early months is looked upon as a normal phenomenon, yet probably in its milder degrees, and undoubtedly in its severer grades, is a manifestation of toxæmia.

The metabolic processes of the body are profoundly modified by pregnancy, fat and nitrogen are retained in considerable quantity, the amount of nitrogen excreted in the form of urea is diminished, that excreted in the form of ammonia salts is increased, the urine is relatively poor in chlorides, sulphates and phosphates, whilst acetone and glucose are occasionally found during pregnancies which run a normal clinical course. Whether the great frequency of the manifestations of toxæmia in women during pregnancy is to be attributed to these metabolic changes rendering them more susceptible to the action of toxins, whether the changes of metabolism are themselves responsible for the production of toxins, or whether the source of the toxin is to be sought in the ovum, are questions not yet definitely settled.

The clinical manifestations of toxæmia vary greatly in their nature and severity. Many of the minor ailments common in pregnancy, pruritus, salivation, vomiting and neuralgia are probably toxic in origin. Neuritis, puerperal insanity, affections of the optic disc and retina, are graver manifestations, but as none of these conditions are essentially associated with kidney lesions they will not be considered further here.

Clinically, we can distinguish four groups of cases of pregnancy toxæmia with well-marked renal lesions :—

(1) The kidney of pregnancy.
(2) Eclampsia.
(3) Toxic vomiting.
(4) Icterus gravis gravidarum.

These groups are not clearly marked off from one another, they possess a number of symptoms in common and resemble one another closely in the anatomical lesions discoverable after death. The renal lesions have been studied most closely in the kidneys of women dead of eclampsia, but they are similar in all four groups. It is not improbable that under different conditions different toxins may be produced (some affecting chiefly the kidney, others the liver), which lead

to slightly different morbid anatomical changes; but this is a matter of minor importance and one upon which we lack sufficient definite information to justify us in drawing conclusions.

It must be borne in mind that lesions similar to those to be described may be produced in the tissues of the body by chemical poisons. Thus lesions similar to, though not identical with, those found in the liver in icterus gravis gravidarum may be produced by poisoning with phosphorus or chloroform, and kidney lesions closely resembling those of eclampsia by cantharides or phosphorus. Further, histological changes indistinguishable from those of eclampsia have been found in the kidneys of men, and of women who have never been pregnant but have died from auto-intoxications which can have had no association with pregnancy. In spite of such cases, it is probable that there exists a definite toxæmia of pregnancy, and as we shall endeavour to show later, that the toxins are produced through the activity of the epiblastic covering of the chorionic villus.

At the outset it is necessary to distinguish clearly two groups of cases: (*a*) cases of true toxæmia in which there is no evidence of a previous nephritis, where the urine before pregnancy contained no albumen or tube casts, and where no cardio-vascular changes existed; (*b*) cases where the kidney was damaged previously to the advent of pregnancy, where the urine was of low specific gravity, contained a trace of albumen, and where arterio-sclerosis and cardiac hypertrophy could be demonstrated. In the latter group pregnancy causes a marked increase in the severity of the symptoms, and uræmic convulsions may closely simulate eclampsia. The two groups of cases possess little in common, and failure to distinguish between them has long confused the pathology and led to serious errors in prognosis. It is clearly established, however, that a woman the subject of chronic nephritis may during pregnancy develop a toxæmia; under these conditions the kidney will present two distinct classes of lesions, (*a*) those due to the chronic nephritis, evidently slowly progressive and of long-

standing, (*b*) those due to the toxin, acute, sudden, and widespread. Finally it must be borne in mind that a pregnant woman may be the subject of acute Bright's disease, or that there may be an exacerbation of an old-standing chronic inflammation. The diagnosis between such accidents and pregnancy toxæmia is difficult in the extreme.

II. The Toxic Theory

The theory of a toxæmia of pregnancy dates back to the days of Mauriceau, who attributed the vomiting of pregnancy to the excretion by the stomach of humours resulting from the suppression of the menses. It was not, however, until 1886 that the theory was placed upon a scientific basis; in that year attention was drawn to the association of severe vomiting with paralyses in pregnant women, and it was suggested that both conditions might be due to the presence of a poison in the blood. In 1892 Lindemann, in conducting an autopsy on the body of a pregnant woman who died with the symptoms of severe vomiting and of multiple neuritis, found marked necrotic changes in the cells of the liver and kidneys associated with degenerative lesions in the nerve trunks. Since that time destructive changes have been found also in the heart, the brain, and the supra-renal capsules. The wide distribution of the lesions suggests the presence of a poison circulating in the blood, and this view is confirmed by more recent investigations upon the organs of infants born of eclamptic mothers. The systematic examination of the tissues of such children has proved that the lesions are not confined to the mother, but that changes of a similar character are found in the organs of the fœtus; this observation materially strengthens the theory of a toxæmia.

The characters of the lesions are no less important than their distribution. The tissue-changes are not those of inflammation, but of a rapid necrosis, similar, as has just been pointed out, to lesions produced by chemical poisons, such as chloroform or cantharides.

Finally, it has been demonstrated that the blood of

eclamptics is highly toxic to animals; the demonstration of this fact completes the chain of evidence.

Granted the existence of a toxæmia, it becomes necessary to inquire into the source and nature of the toxins.

The theories advanced have been many, but we shall content ourselves with a brief mention of the three which have obtained the widest acceptance.

(1) The theory of a bacterial origin.

(2) The theory of an intestinal auto-intoxication.

(3) The ovular theory.

The Bacterial Theory.—Deloré and Rodet first suggested that eclampsia was the result of bacterial infection, and succeeded in isolating and cultivating organisms from the urine, the blood, and the placenta. Müller and Albert endeavoured to prove the existence of a bacterial infection of the uterine wall and attributed to this the symptoms of toxæmia. Stroganoff regarded eclampsia as a specific infectious fever and emphasized its resemblance to the exanthemata, pointing out that it was characterized by a raised temperature, that its incidence exhibited marked seasonal variations, that one attack appeared to confer immunity, and that its frequency was relatively greater in lying-in hospitals and under conditions of over-crowding.

The suggestion of a bacterial origin appears to offer a probable explanation, but it has not stood the test of experimental research. In the majority of eclamptics the blood, the urine, and the placenta contain no organisms which can be cultivated by any method known to us, and in those cases where a bacterial infection has been proved it is probable that the organisms were not the cause of the symptoms, but merely evidence of a terminal infection.

The Theory of an Intestinal Auto-intoxication.—We have already stated that normal pregnancy is attended by alterations in the body metabolism, and it has been suggested that poisonous substances may be formed in the intestine during the process of digestion. The theory receives support from both anatomical and clinical observations. In many cases the most marked anatomical lesions are

found in the liver, and are situated at the periphery of the lobules. The blood from the intestinal tract is carried through the portal system directly to the liver, and a toxin conveyed by this route might be expected to exert its maximum effect upon the peripheral zone of the liver lobules. Clinically, it has long been recognized that the symptoms of toxæmia are increased by constipation and are often relieved by free purgation. Dirmoser has shown that not only are indoxyl, skatoxyl, aromatic sulphates and phenols found in the urine, but that the intestinal contents of toxæmic patients are more toxic than those of normal individuals. These facts, however, form very slender evidence upon which to build up a theory; it is well known that under all circumstances the contents of the lower bowel are toxic and that their undue retention leads to the absorption of poisons; it is only reasonable to suppose that if to the toxins of eclampsia are superadded those of the intestine the severity of the symptoms is likely to be increased.

The Ovular Theory.—The fact that this group of diseases is essentially associated with pregnancy points to the conclusion that the source of the toxin is to be sought in the ovum. The frequency with which the kidney of pregnancy is associated with hydatidiform mole, a condition characterized by absence of the fœtus and presence of an overgrowth of the epiblastic elements of the chorion (the syncytium and Langhan's cells), suggests that the toxin is probably formed in these tissues and not in the fœtus. This view is supported by two other facts: (1) Eclampsia occasionally develops at a considerable interval after the death of the fœtus; (2) within the last six years seven cases of eclampsia developing in association with a hydatidiform mole have been recorded.

Other evidence of a less direct character has been brought forward to support the placental theory; it can only be summarized briefly here:

(1) It is clearly established from the examination of the viscera of women who have died during pregnancy that

portions of the villi are constantly entering the maternal blood-stream and are carried round to all parts of the body.

(2) The anatomical relations of the placenta are such as to bring the epiblastic covering of the chorionic villi into the closest possible association with the maternal blood. The surface area of the placenta is large and many of the villi float freely in the maternal blood sinuses.

(3) The placenta is known to possess many powerful ferments, and in the placentæ of eclamptic patients chemical changes have been found suggesting increased ferment-activity.

(4) The injection into animals of extracts of placenta from both normal and eclamptic parturient women have produced conditions similar to eclampsia.

It would be out of place here to give a full account of the experimental work performed in attempts to ascertain the nature and mode of action of the toxins. For details the reader is referred to the articles on 'Recent Work on the Ætiology of Eclampsia' by Dr. Eardley Holland in the *Journal of Obstetrics and Gynæcology of the British Empire* for 1909; we can only refer briefly to some of the more important theories advanced.

Veit as the result of his experiments formed the conclusion that the presence of placental cells in the maternal circulation led to the formation of specific anti-bodies which he termed 'syncytio-lysins', that the placental cells were toxic and under normal conditions were destroyed by the syncytio-lysins; if, however, the amount of placental cells passing into the maternal circulation was greater than could be neutralized by the syncytio-lysins, pregnancy toxæmia developed.

Ascoli arrived at somewhat similar conclusions, but believed that eclampsia was due not to a deficiency but to an over-production of syncytio-lysins.

Weichardt believes that by the action of syncytio-lysins upon placental cells, syncytio-toxins are produced. Under normal conditions an anti-body is formed in the maternal blood capable of destroying the syncytio-toxins, but if this anti-body is not formed toxæmia results.

More recent work has led to the abandonment of the specific placental theory, but has confirmed the view that the toxæmia of pregnancy is an auto-intoxication attended by a profound disturbance of protein metabolism, and has proved that the various toxic substances which have been isolated from time to time and regarded as the cause of eclampsia are products of the disintegration of protein. 'The eclamptic placenta has no special toxicity, but the intracellular ferments are increased in activity. In the light of present knowledge, the most probable theory of the cause of eclampsia is an intoxication of the body by the passage into the maternal circulation of ferments and autolytic products from the placenta, the principal effects of which are to increase the coagulability of the blood and to render more active autolytic ferments already present in other parts of the body.' (Holland.)

III. The Effects Produced by the Toxins upon the Body Tissues.

(*a*) The Renal Lesions.

When the profound changes in the urine of eclamptics were first recognized the condition was regarded as essentially a disease of the kidney, and no distinction was drawn between eclampsia and uræmia occurring in pregnant women the subjects of nephritis. Histological examination, however, showed that the renal lesions were essentially degenerative, not inflammatory, and were strictly comparable to those found in kidneys after the excretion of toxic substances such as phosphorus or cantharides; it was found, further, that the kidneys were not the only organs affected, but that the liver, the heart, the brain, and the placenta showed changes equally striking and characteristic. Upon this anatomical basis the toxic theory of eclampsia was founded; it received strong support when fatal cases were recorded in which no pathological substances could be detected in the urine and post-mortem examination revealed only very slight changes in the kidney-cells. The severity of the renal lesions cannot be taken as an index of the gravity of the disease; in 24

fatal cases investigated by Bar the lesions are described as severe in 4, of moderate severity in 9, slight in 8, and very slight in 3. As Bar points out, the gravity of a lesion from the point of view of function depends not only upon its severity but also upon its extent and upon the rapidity with which it develops: thus a lesion exhibiting no marked epithelial destruction, but developing rapidly and attacking simultaneously all the secreting elements, is of graver immediate import than one limited in extent and of slow evolution.

In the pregnancy toxæmias the lesions are essentially epithelial—that is, they affect the most highly developed element of the gland—they are of wide distribution and are produced with great rapidity, for even when advanced sclerosis bears witness to a morbid condition of long-standing, the acute degeneration of the epithelium shows that a new process of rapid evolution has been super-imposed upon the old condition.

The kidneys are usually enlarged; in only one of Bar's series of cases was their weight below the normal (230–250 grammes); they averaged 310 grammes, and the maximum weight observed was 345; the two were usually of almost equal weight, but in a few instances one was considerably larger than the other.

The naked eye appearances are striking; the cortex is thickened and of a pale colour, forming a marked contrast with the deeply congested central area; effusions of blood are not uncommonly found between the cortex and medulla or immediately beneath the capsule.

On histological examination all parts of the kidney substance are found to be affected, but the gravest lesions are in the convoluted tubules. The lumina are filled with amorphous casts formed of hyaline material, disintegrated protoplasm, and coagulated albumen; the cells lining the tubule are for the most part destroyed and converted into granular masses devoid of all traces of nuclei or of cell outlines. Areas which have escaped total destruction are scattered through the section, in these the outlines of the

cells are still distinguishable and the nuclei are to some extent preserved.

The cells of the loop of Henle are affected less than those of the convoluted tubules; the cell outlines are clearly distinguishable, the nuclei stain well but many of the cells are detached from their basement membrane and lie free in the lumen of the tube. The glomeruli show comparatively slight changes, they are large and completely fill their capsules, the epithelial cells are usually well preserved.

The histological picture is essentially that of a necrosis, as though a virulent toxin in the process of its excretion had killed the cells of the convoluted tubules, affected to a less extent those of the loop of Henle, and spared altogether the glomerular epithelium. The lesions are not confined to the epithelial elements, the veins are engorged with blood containing an unusually large number of white corpuscles, many are thrombosed, and both veins and arteries contain small emboli in which may be recognized epithelial cells, fat, and necrosed muscle cells. The interstitial connective tissue is œdematous but only occasionally shows small-celled infiltration; it is not uncommon to find small fatty masses in the inter-tubular connective tissues.

The presence of these fatty masses in the kidneys of eclamptics has attracted a considerable amount of attention. Virchow and many subsequent workers assigned to them an important rôle in the genesis of the tissue changes; they are found in the inter-tubular connective tissues, in the lumina of the tubules, and in the vessels. They may be free or may be incorporated in the necrotic cellular emboli.

Such are the changes found *post-mortem* when the renal lesions are of the severest grade, but in many fatal cases the kidneys are not so markedly affected, and we are able to trace the earlier stages of the necrotic process. In these the convoluted tubules are lined with well-defined epithelial cells, but the cell protoplasm stains badly and contains fatty granules and masses of colloid material. The nuclei stain well but are displaced towards the attached border of

the cell whilst the free surface is broken and irregular. The lumina of the canals are wide, and contain a fine granular reticulum of coagulated albumen in which hyalin masses and epithelial débris are sometimes embedded. The cells of the loop of Henle show changes similar but less marked, though in some instances evidence of pathological change is entirely wanting. The glomeruli are but little affected and usually completely fill the capsule; it is not rare, however, to find Malpighian corpuscles in which the glomerulus has shrunk away from the capsule and the intervening space is occupied by coagulated albumen. The endothelial lining is not altered. Many of the vessels are thrombosed, the congested veins contain an unusually large number of white corpuscles, and emboli of hyaline and fatty material and of epithelial débris are found in the arteries. There is œdema of the inter-tubular connective tissues but beyond this no pathological changes are noted in them.

Where the renal lesions are still less marked, the cells of the convoluted tubules stain in a normal fashion, but are flattened and contain in their cell protoplasm many fatty and albuminous granules; the ciliated investment of the free surface (about which so many controversies have raged) can usually be demonstrated if the kidneys are placed in Fleming's solution immediately after death, but it is invariably absent from kidneys which show more advanced lesions. The Malpighian corpuscles are voluminous but otherwise little altered and often contain colloid masses; the space separating Bowman's capsule from the glomerulus contains coagulated albumen. The inter-tubular connective tissue is œdematous, the vessels are engorged and contain cellular, hyaline and fatty masses, constituting in some cases true emboli.

In cases of icterus gravis gravidarum, of pernicious vomiting, and of eclampsia complicated by jaundice, biliary pigments may be demonstrated in the blood of the capillaries, in the lining cells of the convoluted tubules and in the intra-canalicular albuminous masses.

We now possess records of the histological changes found in the kidney of pregnancy. This condition *per se* is never fatal, and it is only when a patient dies of some accidental complication, or of trauma, that we are able to study the lesions. In such cases as have been recorded the lesions were identical with those described above, except that in the case published by Blacker (*Proc. Roy. Soc. Med.*, vol. ii, p. 202) it is stated that the epithelial cells of the glomeruli showed well-marked changes. The renal lesions in cases of toxic vomiting and of icterus gravis gravidarum are indistinguishable from those of eclampsia in both their nature and distribution.

(*b*) The Hepatic Lesions.

Eclampsia.—The changes found in the liver are no less marked than those in the kidney and are often more striking to the naked eye. In advanced cases the liver is of a pale yellow colour and small hæmorrhages are visible beneath the capsule. On section the organ shows evidence of fatty change, and areas of necrosis, sometimes pale and anæmic, sometimes hæmorrhagic, are scattered through its substance. On microscopical examination we find necrosis of the liver cells with thrombosis of the capillaries and intra-lobular veins. The lesions are most marked in the peripheral zone of the lobule where the liver cells are degenerate, the degree of degeneration ranging from cloudy swelling to necrosis. The capillaries surrounding the lobule are thrombosed and their endothelial cells are granular, degenerate, and take the stain badly. These appearances suggest that the changes commence in the tissues about the periphery and involve the cells of the lobules secondarily. Thrombosis spreads to the inter-lobular veins, and when these are occluded the areas of necrosis become more extensive. It is probable that the thrombosis is due to the direct action of the toxin or toxins which cause the cellular necrosis.

In the *Kidney of Pregnancy* the lesions are similar, though less marked, and have the same area of distribution.

It is a striking fact that in both eclampsia and the kidney

of pregnancy the histological changes are in many cases confined to the periphery of the lobules.

In *Pernicious Vomiting* the liver changes differ from those described above in kind and in distribution. The lesions are purely degenerative and are not associated with extensive thrombosis or with hæmorrhage. The only change revealed by the microscope is a necrosis of cells commencing at the central part of the lobule and spreading towards the periphery, a lesion similar to that found in acute yellow atrophy.

In *Icterus Gravis Gravidarum* the liver changes reach their maximum. The organ is of a bright yellow or green colour, flabby, and soft. The capsule is wrinkled and subcapsular hæmorrhages are seen in many places. On section the general colour is bright yellow but isolated deep red patches are scattered here and there. Microscopical examination reveals in some places advanced fatty degeneration and in others necrosis of liver cells with hæmorrhages between the necrosed cells. The researches of Opie (*Journal of Medical Research*, 1904) have shown that the process of necrosis commences at the centre of the lobule and spreads towards the periphery.

(*c*) The Cardiac Lesions.

In 60 to 70 per cent. of the cases, areas of necrosis and hæmorrhages are found in the heart muscle. Granular and fatty degeneration of the muscle fibres is always present.

(*d*) The Cerebral Lesions.

Lesions are to be detected in the brain in about 90 per cent. of the fatal cases and are situated both in the cortex and in the deep nuclei. The capillaries are thrombosed, there are many small hæmorrhages, and degeneration and necrosis of both nerve-cells and fibres are found in scattered areas throughout the organ. In some cases extensive subdural hæmorrhages have been noted.

(*e*) The Placenta.

Brindeau and Nattau-Larrier have made a careful study of the placental lesions in eclampsia and the kidney of preg-

nancy. The lesions are of two kinds : (1) Hæmorrhages ; (2) Changes in the syncytium.

(1) *Hæmorrhages* are almost invariably found in the placentæ of eclamptic patients, and are apparently due to rupture of placental vessels. The rupture is preceded by a marked dilatation of the vessels of the villi, so that the vessel occupies almost the whole of the villus displacing the central connective tissue core which forms only a thin layer beneath the chorionic epithelium. If the hæmorrhage is slight in amount a small localized ' nodule ' is formed—the so-called ' hæmorrhagic infarct '—if severe the blood is diffused over a considerable area of the placenta. In some cases the blood collects between the placenta and uterine wall constituting a retro-placental hæmatoma.

(2) *Changes in the Syncytium* are found in the form of localized hypertrophy leading to the formation of small buds composed of granular syncytium containing many nuclei ; over the greater part of the villus the syncytium shows evidence of degeneration.

None of the placental changes described above are peculiar to eclampsia, all of them are found under other conditions but the eclamptic placenta is peculiar in that it combines a number of lesions, viz. hæmorrhages, plasmodial budding, arteritis, œdema, and necrosis.

IV. The Kidney of Pregnancy.

The term ' kidney of pregnancy ' is applied to a condition of toxæmia occurring usually during the second half of gestation and characterized by headache, œdema, the presence of albumen and tube-casts in the urine, and usually by a diminution in the quantity of urine passed.

The condition is common in primiparæ and relatively uncommon in multiparæ. The frequency of its incidence is difficult to estimate for the milder grades are usually detected only when a systematic examination of the urine is made during pregnancy. From observations at St. Bartholomew's Hospital, where the urine of all primiparæ delivered either

in hospital or on the external midwifery district is examined at least once during the later months of gestation, small quantities of albumen and the presence of a few tube-casts are detected in about 5 per cent. of the cases. The condition is commoner in cases of hydramnios, twins, and hydatidiform mole than in normal pregnancies, and in hydatidiform mole develops early, usually between the second and fourth months.

In addition to the presence of a toxin or of toxins in the blood, mechanical factors probably play an important rôle in its production. Compression of the ureters at the brim of the pelvis by the enlarged uterus is of common occurrence, and as the result of such pressure the ureters and renal pelves are dilated; further, the increase in intra-abdominal pressure and the presence of a large tumour in the abdomen may directly compress the kidney; in both these ways the functional activity of the kidney may be impaired. This view receives support from the fact that the condition is most often found in primiparæ in whom the abdominal walls are comparatively firm and unyielding, and with hydramnios and twin pregnancies where the volume of the uterus is unusually great. The reasons for regarding the condition as a manifestation of toxæmia, and for believing the toxin to be of placental origin are discussed elsewhere. That the clinical symptoms of the kidney of pregnancy are present in the majority of cases of hydatidiform mole is a fact of great significance. The essential lesion in the ovum is a marked proliferation of the syncytium and Langhan's cells, the uterus is filled with proliferated chorionic villi and no trace of a fœtus is present. These facts point to the conclusion that the toxin is of placental not of fœtal origin. The term 'pre-eclamptic toxæmia' is sometimes used as an alternative to 'kidney of pregnancy', but it is misleading for the majority of cases do not develop eclampsia; there can be no doubt, however, of the close relation between the two, and it is possible that whether eclampsia supervenes depends upon the dose of the toxin. The disease is not fatal *per se* and post-mortem observations

are few; where autopsies have been made the renal lesions were identical with those described in eclampsia.

Clinical Manifestations.—The severity of the symptoms varies greatly. They may be so slight that the condition is discovered only by examination of the urine, or so severe as to indicate a profound auto-intoxication.

Œdema is usually the first symptom, the patient notices that her legs are swollen towards evening and that the face is puffy in the morning. Œdema of the back, of the vulva, and of the abdominal wall are not uncommon and may be noticed some days before albumen can be detected in the urine.

Headache is common and is often persistent and severe. It is usually frontal but may be occipital, it is rarely unilateral.

Eye Symptoms.—Dimness of vision and flashes of light before the eyes are often complained of, more rarely the sight is entirely lost. There may be no changes discoverable in the discs on ophthalmoscopic examination, but it is not uncommon to find intense œdema with partial detachment of the retinæ (particularly in the lower halves), and yellow areas of degeneration around the maculæ. Hæmorrhages are rarely if ever seen. The rapid and almost complete recovery of vision after the termination of the pregnancy is a striking phenomenon.

Gastro-intestinal Symptoms.—Vomiting is not uncommon, constipation is the rule but in some cases there is obstinate diarrhœa. Acute epigastric pain is sometimes present.

Nervous System.—Giddiness, drowsiness, and apathy are common.

The Urine.—In slight cases there is little diminution in the amount of urine passed, in severe cases it may be markedly decreased. The total nitrogen output is usually decreased but as a rule there is little if any increase in the ammonia coefficient. Albumen is present in amounts varying from a mere trace up to 3 or 4 per cent.; hyaline, granular and cellular tube-casts are usually seen. In very severe cases the urine may contain blood.

Diagnosis.—The diagnosis between toxæmia and Bright's disease complicating pregnancy is difficult, in some cases impossible until after delivery. When it is known that before conception the urine contained no albumen or casts, when there are no cardio-vascular changes, and when no history of a previously existing nephritis can be obtained, it is probable that we have to deal with a case of pregnancy-toxæmia. If, on the other hand, the urine before conception was of low specific gravity and contained a little albumen, if the heart is hypertrophied and the arteries thickened, and if there is a history of scarlet fever followed by œdema some time previously, it is probable that the patient is suffering from an exacerbation of a chronic nephritis. In some cases undoubtedly the two conditions are co-existent as in a case described by Bar. 'The patient was brought into hospital with a history of long threatened uræmia and died soon after admission. At autopsy the kidneys were contracted, and the epithelial tubules were stuffed into the midst of a dense fibrous tissue which constituted the greater part of the kidney. In the convoluted tubules the cells were degenerate, the nuclei were not apparent, the protoplasm stained badly, and in places was reduced to a state of necrotic débris which blocked the tubes. There was in fact a double lesion, an old one which had given rise to the sclerosis, a recent one which had led to the epithelial degeneration'.

Again, it must not be forgotten that during pregnancy a woman may develop acute nephritis. The causes which produce this condition in the non-gravid state may also be expected to produce it during gestation.

Between these different conditions the diagnosis is difficult, sometimes impossible. The examination of the urine affords comparatively little help and we have to rely to a great extent upon the history. The diagnosis is, however, of importance from the scientific rather than from the practical point of view, for the treatment to be adopted is similar under all these conditions.

The Prognosis depends upon the severity of the toxæmia.

In most cases recognized early and treated judiciously eclampsia does not develop. Under these circumstances the prognosis is good, and though symptoms may persist in some cases until after delivery the kidneys are not permanently damaged. After the uterus has been emptied the œdema quickly disappears, and the amount of urine excreted first rises considerably above the normal but in the course of a few days falls to the normal. Tube-casts are found for only a short time but a trace of albumen may often be detected for several weeks. If under treatment there is no amelioration of the symptoms the pregnancy must be terminated or eclampsia is likely to supervene. There are, however, cases of sudden onset and rapid development, characterized by a marked diminution in the excretion of urine, intense headache, vomiting, slight jaundice, and severe epigastric pain ; the prognosis in such cases is grave in the extreme, the patient usually passing into a condition of eclampsia or of coma. The disease does not usually recur in subsequent pregnancies, but is more likely to do so if the second pregnancy follows very quickly.

The prognosis to the child is bad, in a considerable percentage of cases it is still-born, and in some instances dies in convulsions shortly after birth.

Treatment.—As soon as the condition is recognized treatment should be commenced. The poisons may be eliminated in one of three ways : (*a*) by the kidneys, (*b*) by the bowels, (*c*) by the skin ; and attempts are made to increase its excretion by each of these routes.

The patient is confined to bed and carefully dieted ; if the symptoms are severe a strictly milk diet should be given, but in milder cases eggs, bread and butter, cocoa, chocolate, custard, and fish may be allowed. The effect of such a diet must, however, be carefully watched, and if the amount of albumen does not diminish a milk diet should be substituted. Meat, meat extracts, and vegetables should always be forbidden. Large quantities of fluid such as barley water, or lemonade made with cream of tartar, or distilled water should be taken and, perhaps most important of all, a

free evacuation of the bowels should be secured daily. The sweat-glands may be made to act freely by hot baths or hot packs, but pilocarpin should not be injected on account of its tendency to increase pulmonary œdema and bronchial secretion.

Under this treatment there is usually a rapid improvement, the œdema subsides, the urine contains less albumen, and the headache is relieved.

The total amount of urine passed should be measured, the albumen estimated by Esbach's albuminometer, and the amount of urea by such an apparatus as Doremus's ureometer, daily. It must be remembered, however, that the urea estimate is of little value unless the patient be kept upon a fixed diet.

It has been our experience with hospital patients that so long as they have been treated in this way their condition has improved, the œdema has disappeared, and the albumen been reduced to a small amount ; when, however, they have been discharged and allowed to return to their own homes the symptoms have rapidly recurred, but have again improved after the patients have been readmitted to hospital and placed upon the same treatment. In such cases the treatment must be persisted in throughout the remainder of the pregnancy.

If in spite of the treatment outlined above there is no improvement in the symptoms, the pregnancy must be terminated.

V. Eclampsia.

Eclampsia may be defined as a disease peculiar to pregnant, parturient or puerperal women characterized by epileptiform convulsions followed by more or less prolonged coma, and caused by toxins of unknown origin circulating in the blood.

Occasionally pregnant women die with the symptoms of a profound toxæmia but without convulsions ; this condition is sometimes spoken of as ' eclampsia without fits ', this term is a misnomer, for the epileptiform convulsions are an essential feature of true eclampsia.

Incidence.—From hospital statistics the frequency of the disease is estimated at about one in every 200 pregnancies. These statistics cannot be considered altogether reliable, for women are often sent into hospital because they have exhibited warning symptoms or are admitted after convulsions have occurred. The frequency is probably not greater than once in 500 pregnancies.

Parity.—The disease is commoner in primiparæ than in multiparæ, from 70 to 80 per cent. of the cases occur in first pregnancies or labours. It is commoner in multiple than in single pregnancies, and with hydramnios than when the liquor amnii is in normal amount.

Modes of Onset.—The symptoms are usually preceded by those of the kidney of pregnancy, which may be aptly termed 'the warning symptoms of eclampsia'. This term is preferable to that of 'pre-eclamptic toxæmia', for even when the patient receives no special treatment eclampsia by no means invariably supervenes. In exceptional cases the fit may be the first symptom of the disease, and may come upon the patient 'like a bolt from the blue'. Herman quotes a case in which three hours before the onset of acute symptoms the urine was free from albumen; such cases, however, are rare, and in the majority of cases warning symptoms are present for some days.

Warning Symptoms.

(*a*) *Headache* is common and is very persistent, it is usually frontal, less often occipital, and rarely unilateral.

(*b*) *Œdema* of the legs, hands, face, abdominal wall, and vulva are common. It often develops with great rapidity and may precede the appearance of albumen in the urine by some days.

(*c*) *Visual Disturbances.*—Dimness of vision and flashes of light before the eyes are not uncommon. Total blindness and hemianopia are rare but are occasionally present. In some cases no changes can be detected on ophthalmological examination, but, as with the kidney of pregnancy, intense œdema of the disc, partial detachment of the retina, and yellow areas of degeneration around the macula may be

discovered. Stephenson has collected and analysed the published cases of visual disturbance without recognizable lesions, and draws the following conclusions :—

(1) That a form of amaurosis or amblyopia, not accompanied by ophthalmoscopic signs, or at least by none adequate to account for the condition, may supervene during pregnancy, parturition or the puerperium.

(2) That rarely it may assume the form of an hemianopic defect or of a central scotoma in the fields of vision, and still more rarely of hemeralopia.

(3) That it is often associated with such signs and symptoms of toxæmia as headache, œdema, convulsions, and scanty urine containing albumen, casts, and blood.

(4) That it appears to form one of the rarer manifestations of toxæmic poisoning.

(5) That it is not proved to be dependent upon uræmia, although it has usually been confounded with 'uræmic amaurosis'.

(6) That it recovers, as a rule, completely within a few hours or days.

(*d*) *Acute Epigastric Pain.*—Acute pain in the epigastrium is a striking feature in some cases, and usually indicates that convulsions are imminent. It is probably associated with the hepatic lesions, and is sometimes accompanied by vomiting.

(*e*) *Dyspnœa* is not a common symptom, but in some cases it simulates the 'renal asthma' of uræmia.

(*f*) *Giddiness and Drowsiness* are not uncommon, the drowsiness sometimes deepening into a state of profound coma. Hallucinations are met with occasionally.

(*g*) *Muscular Twitchings* may precede the fits by some hours.

Eclampsia may occur during pregnancy, during labour or during the puerperium, that is, may be ante-partum, intra-partum or post-partum. Of these the intra-partum cases are commonly regarded as the most numerous; it must, however, be remembered that eclamptic convulsions often

excite uterine contractions, and probably a considerable number of cases recorded as intra-partum would be more correctly described as ante-partum, the convulsions causing the onset of labour. The post-partum variety is undoubtedly the rarest. In Olshausen's series of cases 40 per cent. were ante-partum, 46 per cent. intra-partum, and 14 per cent. post-partum. In the ante-partum series the symptoms usually develop during the last two months of pregnancy, but the condition has been seen as early as the end of the third month. The cases associated with hydatidiform mole occur in the earlier months. In a few of the ante-partum cases the patient has recovered from the attack, and after an interval of weeks or months has given birth to a living healthy child; more often labour has supervened, or if the pregnancy has continued the child has been born in a macerated condition. In the post-partum series the disease usually manifests itself within forty-eight hours of delivery.

It is worthy of note that eclampsia has developed in cases of ectopic gestation.

The Convulsions.—In an eclamptic convulsion we recognize three stages, (*a*) the rigid or tonic stage, (*b*) the convulsive or clonic stage, (*c*) the stage of coma.

(*a*) *The Tonic Stage.*—The patient loses consciousness and becomes very pale, the pupils are usually dilated and fixed. The limbs are rigid and held stiffly in an attitude of extension. The back is sometimes arched, and exceptionally there is marked opisthotonos.

(*b*) *The Convulsive Stage* follows quickly, the eyes are rolled from side to side, and muscular twitchings commence in the muscles of the face and spread rapidly so that the whole body is thrown into violent convulsions; the muscles of the jaws work violently, the teeth are clenched and unclenched, and unless precautions are taken to avoid the accident the tongue may be severely bitten. Injury may also be inflicted upon the limbs by violent contact with the bed-posts. The muscles of the chest are involved, the patient becomes deeply cyanosed and foams at the mouth.

(*c*) *The Stage of Coma.*—The convulsions gradually subside and the patient remains for a longer or shorter interval in a condition of unconsciousness, breathing stertorously, and incapable of being roused. The duration of this stage varies from a few seconds to several hours, and the patient may pass from convulsion to convulsion without regaining consciousness in the intervals. There may be a single fit or many—in one case 160 were counted—ten to twenty are not uncommon, but the period during which they occur seldom exceeds forty-eight hours.

The Pulse.—During eclampsia the blood-pressure is high, the peripheral arterioles are constricted, and the pulse tension is increased. In the earlier stages the pulse is moderately frequent and of full volume, in the later stages when the patient is becoming exhausted the volume is small, the tension falls, and the frequency is increased. An increase of frequency, particularly if associated with irregularity, and combined with a fall of tension, is a sign of grave prognostic import and indicates cardiac failure.

The Temperature is usually raised; temperatures of 102 or 103 are not uncommon—just before death in fatal cases 107 or 108 F. may be registered; such high temperatures are probably due to a terminal infection, but may possibly be caused by direct stimulation of the thermal centres by the toxins. When the patient dies with gradually deepening coma the temperature may be subnormal for some hours before death.

Jaundice develops in a considerable number of cases, a fact easily understood when the gravity of the hepatic lesions is considered. It is sometimes present during the attack but is more often noticed a day or two after the cessation of the fits.

The Urine.—The most marked feature is a diminution in the amount of urine excreted, amounting in severe cases to absolute suppression. On microscopical examination hyaline, granular, and epithelial casts are found, and blood may be present in considerable quantity. On chemical examination albumen is present in almost all cases, its amount varies,

but it is not uncommon to find as much as 2 or 3 per cent., and in one case seen recently it reached 4·5 per cent.; both serum albumen and paraglobulin are present, and as paraglobulin is a less diffusible body than serum albumen its presence in large quantity is considered by some pathologists to indicate the gravity of the lesion. There is a marked fall in the total nitrogen excreted, and a marked variation from the normal in the proportions in which the various nitrogenous substances are present. The percentage of urea is diminished and may fall as low as 40 per cent. instead of the usual 88 per cent., such a marked variation as this is, however, unusual, and as a rule from 60 to 70 per cent. of the nitrogen is excreted as urea. Corresponding with this fall in the percentage of urea there is a rise in the percentage of undetermined nitrogen, which instead of the normal 4 to 6 per cent. may reach 12 to 14 per cent. The amount excreted in the form of ammonia salts varies, sometimes there is a great increase in the ammonia coefficient which may reach 20 instead of the normal 4 or 5, but in many cases there is but little change. Albumoses, amido-acids, lactic acid, formic acid, and other products of the disintegration of proteins have been found occasionally, and, particularly in cases associated with jaundice, leucin and tyrosin have been detected.

The proportion of chlorides in the urine is often diminished without diminution in the excretion of other inorganic salts; this observation is of interest because it has recently been suggested that œdema is closely associated with the retention of chlorides in the tissues.

If the patient recovers from the attack there is within a few hours of delivery a marked increase in the out-put of urine. During the first twenty-four hours the amount is usually very great, in two cases recently under my care it reached 180 and 220 ounces; this post-critical rise is a marked feature of the disease. After the first twenty-four hours the daily output gradually falls, and within 8 or 10 days has again reached the normal. After delivery the amount of albumen diminishes with great rapidity, but

a small quantity often persists for days or weeks, and is apt to be increased by alterations in the diet or when the patient resumes her ordinary mode of life.

The Influence of the Death of the Fœtus upon the Course of the Disease.—There is no doubt that when eclampsia develops during pregnancy the death of the fœtus is often followed by cessation of the fits and a rapid improvement in the patient's condition. This, however, is by no means invariably the case, for in some instances eclampsia has developed during labours which have terminated in the expulsion of a macerated fœtus evidently dead days or weeks previously. This, together with the fact that the symptoms sometimes do not appear until forty-eight hours after delivery, demonstrates clearly that the convulsions are not always checked by the death of the fœtus or by its removal from the uterus.

Prognosis: (*a*) *To the mother.*—Eclampsia is always a grave disease, its mortality is from 15 to 25 per cent. The prognosis depends upon the severity of the toxæmia, and the course of the disease is notoriously difficult to foresee. Generally speaking the prognosis is graver when the condition supervenes upon an old kidney lesion, and when labour is long and delivery difficult. Signs of ill-omen are—(i) fits of great severity occurring at short intervals; (ii) deep coma, so prolonged that the patient does not regain consciousness between the fits; (iii) great diminution or total suppression of the urine; (iv) frequency of pulse rate combined with low tension and imperfectly filled vessels; (v) a temperature raised above 103 or 104 degrees F.

The immediate causes of death are many. The patient may die from asphyxia due either to cessation of respiration during the paroxysms, or to the entrance of saliva into the larynx during the stage of coma; she may die from œdema of the lungs, from acute bacterial infection, from gradually deepening coma with either a very high or a subnormal temperature, or from cerebral hæmorrhage. Should she survive the acute stage there is still danger of death from a general septic infection or from septic broncho-pneumonia.

If the patient escape these accidents her recovery is likely to be rapid and complete. The œdema quickly disappears, the amount of urine excreted is increased, the albumen diminishes and convalescence is established. She never remembers anything of the fits and usually fails to realize that she has been gravely ill.

A question of great importance is 'what will happen in subsequent pregnancies'? The attacks are seldom repeated; cases are recorded of eclampsia reappearing during the next pregnancy but such cases are rare.

(*b*) *To the child* is even more unfavourable. Forty per cent. of the children are born dead or die within a few hours of delivery. They may die from asphyxia due to interference with the placental circulation during the convulsions, or may be killed by the direct action of the toxins; in the latter case the liver and kidneys will show lesions similar to those of the mother. If born alive the child may develop convulsions within a few minutes of delivery.

Sequelæ.—The gravest sequelæ are those depending upon septic infection. Septicæmia, sloughing of the pelvis tissues with the formation of fistulæ, and broncho-pneumonia are the commonest. Puerperal insanity is twelve times as common after eclampsia as after normal labours, and is probably to be regarded as a result of the action of the toxins upon the cerebral tissues. Hemiplegia from cerebral hæmorrhage occurring during the stage of convulsions is a rare sequel.

Treatment.—The preventative treatment of eclampsia is of the highest importance, and has been fully discussed in the section on 'The Kidney of Pregnancy'. It is established beyond all doubt that if such treatment be adopted the threatened attack can often be warded off. We are concerned here with those cases in which a fit has already occurred; the treatment in such cases may be conveniently discussed under three heads:—

(i) The prevention of further convulsions.
(ii) The treatment of the patient during the fit.
(iii) The elimination or neutralization of the toxins.

(i) The Prevention of further Convulsions.—The patient should be put to bed if not there already, all tight clothing should be removed, and she should be disturbed as little as possible. The room should be a quiet one, it should be darkened by drawing down the blinds, and no one but the nurse and the doctor should be allowed there. The fits are often excited by sensory impulses, by mental excitement or emotion, therefore, vaginal examinations, the administration of enemata, and the passage of a catheter should be avoided as far as possible. If vaginal examinations are necessary they should be made under chloroform. Various drugs are employed to lessen the violence and prevent the recurrence of the fits, chloroform, morphia, chloral, thyroid extract, and veratrum veride are amongst the more important.

Chloroform.—It is generally agreed that chloroform should be administered when vaginal or intra-uterine manipulations are required during eclampsia, for with the patient under anæsthesia there is less liability of exciting convulsions. It is usually advisable to administer chloroform also during the fits, not with the idea of anæsthetizing the patient, for the fit will be over long before anæsthesia is produced, but because clinical experience shows that by this means the fits are often rendered less violent and the interval between their recurrence is lengthened. Whether prolonged administration between the fits is desirable is open to question, for it is well known that lesions similar to those of eclampsia may be produced in the liver by the action of chloroform.

Morphia.—In many cases morphia is a drug of high value. It retards protein metabolism and so may help to diminish the quantity of toxins formed; it allays restlessness, diminishes arterial spasm, and has a marked effect in lessening the severity and number of the fits An objection to its use is that it tends to inhibit uterine contractions and so to delay labour, its value is therefore greater in cases of ante- and post-partum than in intra-partum eclampsia. It should be administered combined with atropine, because of its depressant action on the respira-

tory centre, and should be given in moderately large doses commencing with half a grain and if necessary continuing with quarter-grain doses every hour until 2 grs. have been given.

Chloral.—Chloral acts in much the same way as morphia, but the effects are not so rapidly produced nor so long sustained. It is best given by the rectum in drachm doses, combined with starch mucilage.

Thyroid Extract.—The use of thyroid extract in eclampsia has been strongly advocated by Nicholson and others on the assumption that the disease is due to thyroid insufficiency. Nicholson gives doses of 70 to 80 grs. daily during the attack and claims that a marked improvement usually follows its administration. Whatever beneficial effects it may exert are probably due to the fact that it is a powerful vaso-dilator and diuretic.

Veratrum Viride is a vaso-dilator and diuretic, but its use is not devoid of danger for it is a powerful cardiac depressant. When used it is administered hypodermically in 15-minim doses every half hour until the pulse rate falls to 60 beats per minute.

(ii) Treatment during the Fit.—The three chief dangers to which a patient is exposed during the fit are: that she may bite her tongue severely, that she may become asphyxiated by saliva trickling down into the larynx, and that she may injure herself by knocking her limbs against hard objects during the convulsive movements. The first danger may be avoided by placing a cork or the handle of a spoon wrapped in some soft material between the teeth; the second by turning the patient's head on one side so that the saliva runs into the cheek; and the third by gentle restraint if the muscular movements are violent.

(iii) Elimination of the Toxins.—(*a*) *The Bowels.*—In view of the fact that eclampsia may be in part an intestinal auto-intoxication it is rational to secure a free evacuation of the contents of the lower bowel. It is of little moment what particular aperient is used provided it be efficacious and act quickly. Calomel, jalap, senna, and castor oil have all been

recommended as the best, but it may be said that for any particular patient that drug is best which acts most quickly and efficiently. If the patient be unconscious 2 or 3 minims of croton oil may be given; croton oil is a mechanical irritant, and if the patient be unconscious its passage into the larynx may cause œdema, for this reason it should be mixed with castor oil or a little butter.

Besides removing toxic matter, aperients act beneficially in other ways; the arterial pressure is lowered, and scybalous masses which might act as mechanical irritants are removed from the rectum.

(*b*) *The Kidneys.*—The patient should be given large quantities of bland fluids by the mouth; distilled water, barley water, and milk are all diuretics when taken in considerable quantity. The most valuable diuretic measure of all is the infusion of normal saline solution to which sodium acetate has been added (one drachm to the pint of normal saline solution). The sodium acetate serves a double purpose, it increases the diuretic properties of the saline solution and increases the alkalinity of the blood. In eclampsia the alkalinity of the blood is always diminished, but there are wide variations between individual cases. The average alkalinity of the blood in normal pregnancy is 0·202 grammes of Na.OH in 100 cm. of blood, the average in eclampsia is 0·153 and it may fall as low as 0·048. The greater the diminution in the amount of urine passed the greater is the amount of acids retained in the blood, and although the symptoms of eclampsia are not to be attributed merely to the retention of acid substances in the blood there is evidence that the violence and frequency of the fits is diminished when the alkalinity of the blood is increased.

(*c*) *The Skin.*—The excretions of the skin may be increased by hot air or vapour baths, but no attempt should be made to excite secretion by the administration of pilo-carpin. Pilo-carpin increases the bronchial secretions and in an eclamptic patient pulmonary œdema is a danger always present.

(*d*) *Bleeding.*—Venesection is a valuable method of treat-

ment in some cases; it is generally recommended that it be employed only in cases of cyanosis combined with high arterial tension; in such cases it doubtless affords relief to the right side of the heart. It has, however, another and wider application, for if eclampsia be due to the presence of a toxin in the blood, by bleeding the patient freely we remove some of the poison. From 12 to 15 ounces of blood may be withdrawn and its removal followed by the intravenous infusion of an equal quantity of normal saline solution containing a drachm of sodium acetate; in this way the total amount of poison may be diminished and the alkalinity of the blood increased. I have employed this method in several cases in which the convulsions persisted after delivery of the child, and have noted an immediate improvement in some of them; but it has not as yet been given a sufficiently extended trial to allow of dogmatic statements.

Lumbar Puncture has been employed in a number of cases, but its results have not been encouraging.

Decapsulation of the Kidney has been employed in cases of total suppression of urine with a view to relieving the intra-renal tension and stimulating the kidneys to secrete; the value of the procedure has yet to be demonstrated.

Obstetric Treatment.—A great divergence of opinion still exists amongst obstetricians with regard to the Obstetric Treatment. One school urges the necessity of immediately emptying the uterus by the most rapid possible method, another holds that the interruption of pregnancy is not necessary and in many cases undesirable. It is true that patients have recovered from an eclamptic attack, and after an interval of weeks or months have borne a living child, but such cases are rare, and since there are strong reasons for believing that the placenta is the source of the toxins it seems reasonable to induce labour.

The particular method to be adopted will not be discussed here, such operations as Cæsarian section, vaginal section and rapid dilatation of the cervix by Bossi's dilator may have their place in the treatment of exceptional cases, but

generally speaking it is not advisable to adopt any operative measures which immediately endanger the life of the mother.

In pernicious vomiting and acute yellow atrophy the renal lesions are of secondary importance only, and a description of the clinical course of the diseases would be out of place here.

CHAPTER XXI

PREGNANCY AND CHRONIC NEPHRITIS

By Herbert Williamson, M.D., F.R.C.P.

Pregnancy in a patient the subject of chronic nephritis is fraught with grave danger. It is not uncommon in hospital practice to find a young primipara seeking advice about the fifth month of her first pregnancy because of headache and œdema of the legs. On examination albumen and casts are found in the urine, and at first it is doubtful whether the case should be classed as one of toxæmia or of chronic nephritis in which the symptoms have become aggravated as the result of pregnancy. On inquiring into the patient's past history it is ascertained that some years previously she suffered from scarlet fever followed by an illness in which œdema was a marked symptom ; as far as she is aware she got quite well and remained in good health until she became pregnant. Investigation discloses some degree of cardiac hypertrophy with an unusually high blood-pressure and sometimes it is possible to ascertain that the quantity of urine passed has been above the average, that its specific gravity has been low, and that it has contained a trace of albumen.

If all these data are available the case becomes clear, the kidneys have been damaged by the attack of scarlet fever, but have been able to perform their functions so long as no increased strain was thrown upon them and the symptoms of renal insufficiency, if present, were so slight that the patient was unaware of their existence. In pregnancy the kidneys are called upon to excrete the waste products of fœtal as well as maternal metabolism, if they are healthy they are

able to perform this function as they possess a certain reserve force which can be called upon when increased work is required from them, but if damaged, even to a comparatively slight extent, they may possess no reserve power whatever, they are then working at their highest possible level in excreting the waste products formed in the course of the ordinary daily metabolism, and when called upon to excrete the products of fœtal metabolism in addition are unequal to the task.

Pregnancy complicated by chronic nephritis must be studied from two points of view :—

(1) The effects of the pregnancy upon the chronic nephritis.

(2) The effects of the chronic nephritis upon the pregnancy.

(1) The Effects of the Pregnancy upon the Renal Condition.—Granular contracted kidneys may be affected by pregnancy in two ways: (*a*) They may be affected by the poisons which give rise to the symptoms of pregnancy toxæmia ; (*b*) They may prove unequal to the task of excreting the products of metabolism of the fœtus in addition to those of the mother.

(*a*) From clinical evidence it is clear that a damaged kidney is more susceptible than a healthy one to the action of the pregnancy toxins, and, as already pointed out, the lesions of an acute toxæmia may be grafted on to those of a chronic nephritis. The condition produced is distinguished by the term ' nephritic toxæmia '. The symptoms may occur at any stage of pregnancy, I have seen them prove fatal as early as the second month, but in the majority of cases they are not observed until the second half. Their onset may be gradual or they may develop with striking suddenness. There is lassitude, general malaise and headache ; disturbances of vision are not uncommon, flashes of light before the eyes, dimness of vision or even total blindness are complained of and the ophthalmoscope shows albuminuric retinitis with hæmorrhage. Œdema is a marked symptom and affects the face, hands and legs, vulva, abdominal wall

and other parts of the body. The urine is diminished in amount or may be totally suppressed; in this event the patient rapidly passes into a condition of deep coma from which she never rallies or dies in convulsions. The post-mortem appearances of the kidneys in a case of this kind have already been described. Two distinct lesions are present: (1) the kidneys are contracted, granular, and contain an excessive amount of fibrous tissue, evidence of chronic long-standing disease; (2) in addition there is found the acute epithelial degeneration characteristic of a condition of toxæmia. In 'nephritic toxæmia' the patient's life is in grave danger; the treatment to be adopted is described in the section upon 'The Kidney of Pregnancy', but unless palliative measures are attended by a rapid improvement, the uterine contents should be evacuated.

(*b*) In many cases the toxæmic condition does not supervene, and the patient usually passes through the first half of her pregnancy without any serious disturbance of health, but between the fourth and fifth month the symptoms of renal inadequacy develop. Œdema of the face and ankles is noticed, the quantity of urine diminishes, its specific gravity becomes higher, the amount of albumen increases, epithelial, hyaline, and granular casts are present in large numbers and occasionally blood is found. Pulmonary symptoms, œdema of the bases of the lungs with breathlessness, cough, and bronchitis are common. Headache is often persistent and severe, albuminuric retinitis with flame-shaped hæmorrhages is not uncommon, but has not the same grave prognostic significance as in the non-gravid state. The œdema is usually very marked, and affects every part of the body, ascitic fluid may be present in large quantities in the abdomen and passive effusions into the pleural cavities are found occasionally.

Should the fœtus die an improvement in the symptoms may be noted but this is by no means invariably the case. In spite of treatment many patients become drowsy, muscular twitchings are noted, and finally uræmic convulsions develop.

When symptoms such as described above are manifested

by a woman known to be the subject of chronic nephritis there can be no question of the propriety of inducing labour or miscarriage ; if this be delayed too long a fatal termination is almost inevitable. The condition of the kidneys is markedly worse at the end of the pregnancy even if the patient survive, and the life of the child is so precarious that it is not right to allow the mother to run the risk involved by continuance of the pregnancy. The expulsion of the fœtus is usually followed by a marked improvement, the amount of urine excreted is increased, the œdema becomes less and the pulmonary signs clear up, but the damage to the kidney is permanent.

It is often stated that a woman with chronic nephritis should be forbidden to marry ; it is no part of the duty of the physician to forbid marriage. He should explain fully to the patient, to her future husband, and to her relatives the dangers involved, but the ultimate decision must rest with them. If the patient survive her first pregnancy it is with a renal lesion of increased gravity, and should a second pregnancy ensue, as a rule the symptoms develop earlier and are of greater severity than in the former one. Occasionally patients known to be the subject of chronic Bright's disease may pass through successive pregnancies and survive for many years. I had recently under my care a woman who consulted her doctor before marriage on account of swelling of the legs and was advised not to marry because she had Bright's disease. She disregarded the advice, and shortly after marriage became pregnant ; labour was induced in the thirty-sixth week because of great œdema, breathlessness, and persistent headache. A living child was born, and after delivery the symptoms rapidly improved, but three months later the urine still contained a heavy cloud of albumen with granular and epithelial casts. She was warned of the risks of another pregnancy but conceived again within six months of leaving the hospital. During this pregnancy there was an exacerbation of the symptoms less marked than on the former occasion and she was allowed to go to full term ; she has

subsequently borne two other children. During each pregnancy the symptoms have become more severe but have improved after delivery. The last pregnancy was complicated by a severe ante-partum hæmorrhage. French records a similar case—'The patient had had all the signs of chronic tubal nephritis for thirteen years and had been married for eight years, she had borne five children and bore a sixth alive at term in the hospital. This was not a case of recurrent acute nephritis but of persistence of both albuminuria and tube-casts ; it is more remarkable in that even without the additional strain of pregnancy, it is unusual for a patient with such a renal condition to survive so long.'

Cases such as these are the exception but they show how impossible it is to foretell with certainty the effects of pregnancy in any given case.

(2) The Effects of Chronic Nephritis upon Pregnancy.

Conception.—There is no evidence available to show that a woman who suffers from chronic nephritis is less likely to conceive than one who is healthy.

Miscarriages are common. In analysing a series of fifteen cases I find six of the patients were primigravidæ, amongst the nine multiparæ there had been fifty-eight pregnancies, twenty-two of which had terminated in miscarriages before the sixteenth week ; in this particular series 34·4 per cent. of the pregnancies had ended in spontaneous miscarriage.

Ante-partum Hœmorrhage.—Accidental hæmorrhage (that is, hæmorrhage due to the separation of a normally situated placenta occurring after the child has become viable but before its birth), is perhaps more often due to chronic nephritis than to any other cause. Statistics vary greatly on this point, but my own experience corresponds closely with that of Winter who found evidence of chronic nephritis in a considerable proportion of his cases. The presence of albumen in the urine in association with accidental hæmorrhage has been noted by many writers, but the majority attribute it to pregnancy-toxæmia rather than to a pre-existing nephritis. I am unable to accept this view for

observations upon my own patients have shown that the arteries are thickened, the arterial tension is high, the heart is hypertrophied, and that albumen and tube-casts are to be found in the urine weeks after delivery. The cause of the separation is probably to be found in the placental lesions which are usually well marked in chronic nephritis. White and red infarcts are scattered through its substance and are sometimes so extensive as to interfere seriously with its functions; areas over which the placenta is detached and separated from the uterine wall by old blood-clot are less commonly found.

Premature Labour occurs in a considerable proportion of the cases; according to Whitridge Williams, with the exception of syphilis, chronic nephritis is the commonest cause of spontaneous premature labour, but it is impossible to estimate accurately its incidence. In hospital practice the premature expulsion of the child occurs spontaneously in from 40 to 50 per cent. of the cases; the frequency, however, is probably not so great as these figures indicate, a large number of the slighter cases go to term, and many of the patients from whom the hospital statistics have been compiled sought advice and were admitted because of the severity of the symptoms.

Death of the Child.—The death of the child in utero is a common phenomenon and is to be attributed primarily to the placental lesions. The placenta is the organ of nutrition, of respiration, and of excretion for the unborn child, and loss of function must be attended by disastrous consequences. The areas of infarct formation and of detachment are sometimes extensive and so much placental tissue may be destroyed that the nutrition of the child suffers. It is probable, however, that toxæmia also plays an important part in causing the death of the child.

Pregnancy as a cause of Granular Contracted Kidney.

French (*Goulstonian Lectures*, 1908) has suggested that pregnancy may possibly be a cause of granular contracted kidney. He states:—'It is difficult to prove or disprove

this because if a granular contracted kidney in a given case owes its inception to renal trouble arising during pregnancy, the patient can still continue to live for many years without untoward symptoms, and by the time death occurs there will be nothing in the post-mortem examination to show either how long the renal mischief has been present or how this mischief first began.' He argues that recurrent obstruction to the ureter is a potent cause of fibrosis, and suggests that repeated pregnancies may, from the pressure exerted on the ureter by the enlarged uterus, lead to sclerosis of the kidneys. This theory is one of great interest, but at present no convincing evidence has been put forward in its favour. It has never been demonstrated that fibrotic kidneys are commoner in women who have borne many children than in those who have borne none.

CHAPTER XXII

Hæmaturia in Pregnancy.

By Herbert Williamson, M.D., F.R.C.P.

Hæmaturia in pregnancy may be due to any of the causes which give rise to the symptom in the non-gravid condition. If a pregnant woman be suffering from a new growth of the bladder or kidney, from stone in the kidney or from tubercle, hæmorrhage may occur in the course of the pregnancy. Apart from all such causes pregnant women are occasionally the subject of urinary hæmorrhages for which no cause can be found; the hæmorrhage is present during pregnancy, ceases on delivery, and may recur in subsequent pregnancies. Previous to conception the patients have usually been in good health, and examination has failed to reveal any lesion of the urinary tract which could be regarded as the source of the blood. The bleeding may commence as early as the second or third month, but in the majority of cases the blood has first been detected in the fifth and sixth months. Hæmorrhage may be present for a few days only or may persist for months with or without remissions, but ceases within a few days of delivery though it sometimes recurs if the patient again becomes pregnant. In some cases the bladder has proved to be the source of the hæmorrhage, and cystoscopic examination has revealed either a ruptured varicose vein or a slow oozing from the mucosa. Proust has recorded the case of a woman three months pregnant in whom vesical hæmorrhage was so severe as to necessitate supra-pubic cystotomy. After the bladder had been freed from clots a ruptured varicose vein was discovered from which the blood was escaping. In the majority of cases cystoscopic examination shows a healthy vesical mucous membrane, and ureteral catheterization proves that the blood comes from one or other kidney. In

one case Albarran performed nephrotomy but was unable to detect any anatomical lesion in the kidney. The cause of the hæmorrhage is difficult to explain and the suggestions offered are mere guesses. Chiaventone regards the condition as one manifestation of pregnancy toxæmia, Guyon attributes it to passive congestion of the kidneys due to the pressure exerted by the gravid uterus upon the large veins of the abdomen ; neither of these suggestions offers a satisfactory explanation.

The prognosis is usually good, but occasionally the hæmorrhage is sufficiently persistent and severe to render necessary the induction of miscarriage or premature labour.

Treatment.—Rest in bed, a restricted diet and dry or wet cupping over the kidney region usually reduce the hæmorrhage to so small an amount that it is possible to allow the pregnancy to continue. Should these measures fail labour should be induced. It has been suggested that the amniotic cavity should be tapped and some of the liquor amnii drawn off to diminish the volume of the uterus and lessen the intra-abdominal pressure. It is difficult to believe that such a procedure would be successful, and it would almost inevitably be followed by the expulsion of the fœtus. Grosse advocates decapsulation of the kidney.

CHAPTER XXIII

PYELITIS AND PYELONEPHRITIS

I. *IN PREGNANCY*

By Herbert Williamson, M.D., F.R.C.P.

Reblaub, in 1892, drew attention to a condition of the kidney, found occasionally during pregnancy, in which the renal pelvis is distended by a collection of purulent urine. Before the commencement of pregnancy the kidney is healthy, there is no stone, no tumour, no tuberculous lesion ; there is no retention of urine, no difficulty of micturition, in brief, none of the usual precursors of renal suppuration are to be found. To this condition Reblaub gave the name ' pyelitis in pregnancy '. The name, however, is misleading, for in many cases the kidney substance, as well as the pelvis, is infected, and for this reason the term ' pyelonephritis of pregnancy ' has been generally adopted.

Pathology.

Pyelonephritis in pregnancy, as in most other conditions, is preceded by an obstruction to the outflow of urine, with consequent dilatation of the ureter and pelvis of the kidney ; some degree of hydronephrosis is thus produced and the stagnant urine is subsequently infected by pyogenic organisms. In discussing the pathology two points require consideration, (1) the cause of the dilatation of the ureter and renal pelvis ; (2) the mode of infection of the stagnant urine.

(1) The Mechanism of Dilatation.—It has long been known that dilatation of the ureters and renal pelves is commonly found post mortem in women dying during the later

months of pregnancy. The condition may be unilateral or bilateral; when unilateral the right side is affected in 84 per cent. of the cases, and when both sides are dilated the dilatation is usually greater on the right than on the left. These facts were demonstrated by Olshausen and Halbertsma. As many of their autopsies were performed upon women who had died of eclampsia, it was believed for a time that a causal relation existed between the two conditions; it is now recognized that dilatation is equally common in women who have died of hæmorrhage, or of some complication of pregnancy or labour, other than eclampsia, and the phenomenon is regarded as physiological rather than pathological.

The portion of the ureter situated below the brim of the pelvis is unaffected, the portion above is dilated and elongated; the dilation may be uniform or a series of dilated saccules may be separated from one another by areas in which the calibre has remained normal. The degree of dilatation varies, in most instances the lumen of the ureter is not greater than that of a No. 10 catheter, in others it is as great as that of the small intestine; the renal pelvis may be only slightly distended or the distension may be so great as to lead to a marked degree of atrophy of the kidney substance. From the fact that dilatation occurs only in the portion situated above the brim of the pelvis whilst the part below is not affected, it is clear that the obstruction occurs at this spot. The explanation is found when we consider the anatomical relations of the ureters. From the pelvis of the kidney they run obliquely downwards and inwards on the anterior surface of the psoas muscle, and in front of the sacro-iliac synchondrosis dip downwards to enter the true pelvis, crossing first the common iliac artery and vein, then the external iliac artery. At the pelvic brim they are separated from one another by a distance of 9 centimetres, and below this level run forwards in the base of the broad ligament, gradually converging to enter the bladder. Above and below the brim they are in contact with soft structures, but at the brim they lie on bone and a comparatively small compressing force is sufficient to obstruct the on-flow of

urine. Halbertsma has shown by experiments on dogs that a weight of 5 grammes compressing the ureter over a surface of 8 millimetres is sufficient to prevent the flow of a volume of urine weighing 400 grammes. The compressing force is furnished by the uterus which, as it enlarges, rises out of the pelvis and becomes an abdominal viscus. The compression is probably caused by the uterus itself, not by the lowest part of the fœtus, for in the latter event the disease would be commonest in the last two months of pregnancy, whereas it commences most frequently during the fifth and sixth months, at a time when the largest circumference of the uterus occupies the pelvic brim. The frequency of dilatation of the right ureter is also to be explained on anatomical grounds. The uterus lies obliquely in the abdominal cavity with the fundus inclined to the right, and during pregnancy is rotated upon its long axis so that the left border looks to the left and forwards, and the right border to the right and backwards. The right border is thus brought into closer contact with the posterior part of the pelvic brim and the left border is rotated away from it; consequently, if one ureter alone is affected it is usually the right, and if both are dilated the dilatation is greater on the right side than on the left. The right ureter also lies farther from the middle line and is thus less protected by the sacral promontory. The liability to pyelonephritis is not increased in cases of contracted pelvis or of pregnancy complicated by uterine fibro-myomata, a fact not easily explained.

(2) The Route of Infection.—The manner in which the infecting organism reaches the kidney has been hotly debated. Three methods require consideration :

(*a*) By an ascending infection from the bladder.

(*b*) By the blood-stream.

(*c*) By the lymphatics.

(*a*) *Ascending Infection from the Bladder.*—In only a comparatively small number of cases can a clear history of a preceding attack of cystitis be obtained. Statistics vary on this point, and the question is further complicated by the fact that frequency of micturition in the early months

of pregnancy is a normal phenomenon, depending partly upon an increased degree of anteflexion of the uterus, and partly upon increased vascularity of the vesical mucous membrane. In the cases personally investigated a history of cystitis could be obtained in very few. It does not follow, however, that because there is no cystitis the urine is sterile. Barris recently examined bacteriologically specimens of urine from 50 pregnant women, none of whom had suffered from urinary symptoms; in 11 cases the urine contained a coliform bacillus; in a similar series of 45 cases Dudgeon found a coliform bacillus in 9. These observations prove clearly that in pregnancy infection of the urine without symptoms of cystitis is common and that the lack of such symptoms cannot be regarded as evidence against the ascending route of infection.

The aperture between the bladder and ureter is valve-like, and under normal conditions the urine is ejected into the bladder in intermittent jets, not continuously, the valvular aperture being closed except when the urine is actually passing; this mechanism to some extent acts as a safeguard against ascending infection. The experiments of Guyon and Albarran have shown that when the ureter is dilated and contains a column of stagnant urine there is a free communication between the bladder and ureter and that organisms can pass without difficulty. The passage of solid particles has also been demonstrated by injecting sterilized granules of indigo into the bladder and observing their passage through a ureteral fistula in the loin. It must be remembered that in the pyelonephritis of pregnancy the portion of the ureter nearest the bladder is not dilated, that the valvular mechanism is not thrown out of gear, and that there is no column of stagnant urine extending from the bladder to the renal pelvis along which organisms may ascend through the movements of their flagella. Such conditions are, however, not essential to the theory of infection from the bladder. Bond has shown that the organisms may travel upwards in the mucous membrane of the ureter, and the more recent experiments of Kenneth

Walker demonstrate that in such cases they pass by the lymphatics. Walker ligatured one ureter a short distance above its vesical orifice and injected into the bladder cultures of the *Bacillus coli communis*, pyelonephritis developed and the organisms were found in the lymphatics of the ureter below the ligature. Dilatation of the ureter usually precedes the onset of pyelitis and, as far as I have been able to ascertain, in every case of pyelonephritis of pregnancy in which the ureter has been seen either at operation or post mortem it has been dilated; nevertheless, it is not improbable that ascending infection may occur even when there is no obstruction, though the case reported by Barnard and often quoted as evidence of this is not convincing. The patient was a man, aged 27, whose first symptoms were involuntary passage of urine, scalding pain on micturition, and hypogastric pain; two days later severe pain was experienced in the right loin and the temperature rose. Nephrectomy was performed and the kidney was found to be riddled with small abscesses; no bacteriological examination was made of the pus from the kidney, the urine, or the blood, but it seems probable that the kidney suppuration may have been secondary to a systemic infection.

(*b*) *Infection by the Blood-Stream.*—The possibility of infection by the blood-stream is proved by the experiments of Reblaub. He ligatured one ureter in a series of four rabbits and injected into the veins of the ear of two of them a culture of *streptococci*, and into the other two a culture of the *Bacillus coli communis*; pyelonephritis developed in each case and the organism found in the pus from the kidney was identical with that injected into the blood-stream. Similar experiments have been performed upon dogs by Sampson of the Johns Hopkins Hospital, and his results confirm those of Reblaub.

It is possible that the *Bacillus coli communis* is constantly passing in small quantities from the intestine into the blood-stream, and that the presence of the bacillus in the urine of women without symptoms of infection may be due to the excretion of the organisms by the kidneys, but that

when the ureter is compressed, and the functional activity and resistance to infection of the kidney lowered by the strain of pregnancy their excretion may be prevented. The *Bacillus coli communis* can, however, seldom be grown from the blood of a pregnant woman. In 8 cases of pyelonephritis investigated at St. Bartholomew's Hospital the blood proved sterile, and in a series of 50 pregnant women without urinary symptoms Barris was unable to find the *Bacillus coli* in the blood, though some of the women had suffered from severe constipation and other gastro-intestinal disturbances.

The importance of constipation and diarrhœa as exciting causes of pyelonephritis is difficult to estimate; constipation is very common during pregnancy and if it were an ætiological factor of great importance we should expect to find the disease commoner than it is. A case reported by Jeannin and Cathala is interesting from this point of view. A pregnant woman was admitted to hospital in a state of stupor, suffering from severe headache, raised temperature, and rapid pulse; there was a history of complete constipation for fifteen days. The urine contained no pus or albumen, but examination of the disks revealed optic neuritis with several small retinal hæmorrhages close to the left papilla. After the administration of aperients a large quantity of fæcal matter with a particularly fœtid odour was passed. A week after admission incontinence of urine and fæces developed, and after a short interval the patient died of broncho-pneumonia. At autopsy the kidneys were large, and when the ureters were cut across a quantity of purulent fluid escaped; on section abscesses were present in both the cortices and pyramids, whilst the calices and pelves were dilated and contained purulent urine. The pus from the kidneys gave a pure culture of the *Bacillus coli communis*, but there is no mention of a bacteriological examination of the blood. The account of this case suggests the possibility of a general infection, and from the fact that on admission the urine contained no pus and the patient's condition was one of profound toxæmia it is probable that the kidneys were infected secondarily.

In several of the recorded cases a history of severe constipation or of diarrhœa is given, and under such conditions the colon bacilli may invade the blood-stream in considerable numbers; in the majority of the cases there was no gastro-intestinal disturbance, and this cannot be regarded as an essential factor in the development of the condition.

(*c*) *Infection through Lymphatics.*—The experiments of Walker afford direct evidence of infection through the lymph channels. The close anatomical relation between the colon and the kidney suggests that the lymphatics of the two viscera may be in communication, and if such a communication exists infection from the bowel may take place directly.

We conclude that the organisms do not necessarily reach the kidney by the same route in every case, and that the clinical and experimental evidence available point to the possibility of infection in each of the three ways discussed.

Bacteriology.

The organism most commonly found is a coliform bacillus. Amongst 56 cases collected by Ward this organism was found in 44, a streptococcus in 9, a staphylococcus in 2, and the gonococcus in one. Albeck found a coliform bacillus in pure culture 76 times in a series of 92 cases, and in 14 consecutive cases seen at St. Bartholomew's and the City of London Lying-in Hospitals a pure culture of a coliform bacillus was obtained in every instance. Under the term *Bacillus coli communis* are included a number of organisms differing from one another in virulence and in their reactions to indol, gelatine, and the sugars; the organisms isolated from cases of pyelonephritis show individual variations, and in many instances do not give all the reactions of the classical *Bacillus coli communis.* This fact is well illustrated in the subjoined table of reactions of the organisms isolated by Barris from four cases in St. Bartholomew's Hospital; the organisms were obtained directly from the kidney by ureteral catheterization.

COLIFORM ORGANISMS.

	Glucose.	*Lactose.*	*Saccharose.*	*Dulcit.*	*Adonit.*	*N. Red.*	*Milk.*	*Indol.*	*Gel. 22° C.*
Classical B. C. C.	*	*	−	*	−	+	+	+	+
Case 1	*	*	+	Gas + Acid −	−	−	+	+	Gas + Liq. −
Case 2	*	*	+	*	−	+		+	+
Case 3	*	*	+	*	−	−		−	+
Case 4	*	*	+	*	−	+		+	Gas + Liq. −

* = Acid + Gas. + = Acid.

The last three cases investigated at St. Bartholomew's Hospital, however, gave all the reactions of the classical *Bacillus coli communis*. In the tissues of the body the bacillus forms an endotoxin which is absorbed into the blood-stream and is the cause of the constitutional symptoms, headache, rise of temperature, furred tongue, and malaise. The presence of the toxins in the blood leads to the formation of bacteriocidal substances and agglutins, so that not infrequently cultures of coliform bacilli derived from the patient's urine are agglutinated by her serum.

Morbid Anatomy.

Comparatively few cases prove fatal and nephrectomy or nephrotomy are seldom required, consequently the material available for studying the morbid anatomy is but scanty. Fatal cases, with an account of the autopsy, have been reported by Reblaub and by Jeannin and Cathala (the latter has been alluded to already), the examination of a kidney removed post mortem is recorded by Cumston and a few other cases are described briefly.

The ureter is dilated and elongated, its walls are thin and the mucous membrane is hyperæmic ; the elongation is in some instances associated with kinking, particularly when there is marked mobility of the kidney. This is a point of some clinical importance, for in one case the kink was so

acute as to prevent the escape of pus from the kidney after the induction of labour.

The renal pelvis is dilated sometimes to so marked a degree as to form a large tumour, the walls are usually thickened and sclerosed, and the mucosa is either covered by purulent débris or completely hidden by a white adherent membrane. The kidney is pale and anæmic, the renal substance is sometimes markedly atrophied from pressure of fluid in the pelvis, the tubules of the medullary portion are dilated and their lumina obstructed by shed epithelial cells and masses of casts. In two cases small multiple abscesses were scattered through both medulla and cortex.

Ætiology.

(1) *Age.*—In 184 cases analysed by Ward the age incidence was as follows :—

Under 20 years	16 cases.
Between 20 and 30 years	121 ,,
,, 30 ,, 40 ,,	47 ,,

(2) *Number of Pregnancies.*—In a series of 30 cases analysed we have obtained the following results.

Primiparæ	13 cases.
1 previous pregnancy	3 ,,
2 ,, pregnancies	1 ,,
3 ,, ,,	4 ,,
4 ,, ,,	5 ,,
5 ,, ,,	2 ,,
6 ,, ,,	1 ,,
8 ,, ,,	2 ,,
9 ,, ,,	1 ,,

(3) *The Stage of Gestation at which the Symptoms are first noticed.*—Of 187 cases the statistics are as follows :—

Before the 4th month	16 cases
During 4th ,,	21 ,,
,, 5th ,,	40 ,,
,, 6th ,,	33 ,,
,, 7th ,,	27 ,,
,, 8th ,,	20 ,,
,, 9th ,,	13 ,,
,, 10th ,,	4 ,,
During Puerperium	13 ,,

(Ward.)

The onset of symptoms therefore occurs most commonly during the 5th and 6th months.

(4) *Relapses.*—Second attacks during the same pregnancy are of not infrequent occurrence. Ward estimates them at from 15 to 20 per cent. ; in our experience the proportion has been higher, viz. 25 per cent.

(5) *Attacks in subsequent pregnancies.*—The frequency of a return of the disease in subsequent pregnancies is difficult to estimate ; it is probably about 10 per cent.

Symptoms.

The symptoms of onset vary greatly, so that we may recognize several groups of cases :—

(1) Gradual onset with malaise and increasing lumbar pain.

(2) A sudden acute attack of pain in the lumbar region followed by the development of constitutional symptoms.

(3) High fever with at first no localizing symptoms.

(4) Onset with marked urinary symptoms.

(5) Onset with vomiting and abdominal distension simulating intestinal obstruction or peritonitis.

(6) Onset with symptoms suggesting pleurisy or pneumonia.

Group 1. In the first group of cases the earliest symptom is often slight intermittent pain over the loin ; the pain is probably due to distension of the renal pelvis. Stoeckel regards pain of this kind as the first manifestation of urinary obstruction, and by means of ureteral catheterization has proved dilatation of the renal pelvis in such cases. The pain is followed by a general condition of malaise, there is headache, pallor, constipation, and slight irregular rises of temperature. The tongue is furred ; anæmia, constipation, and night sweats are present, there is tenderness over the kidney region and often a sense of discomfort or of aching pain in the loin which gradually becomes more severe.

R. F., aged 23, was admitted to hospital in the 6th month of her first pregnancy. A month previous to admission she experienced slight pain ' like lumbago ' in the lower part of the back, associated with nausea, headache, and constipation.

The pain in the back had been gradually increasing and for the last two weeks before admission she had been unable to do her household work ' because she didn't feel fit for it '. The tongue was furred, the temperature 100·8° F., and the pulse rate 110, the urine contained a little albumen but no pus. On the night of her admission a rigor occurred, the temperature rose to 103° F., and on the following day a quantity of pus was present in the urine. The discharge of pus continued for four days and the temperature rapidly fell to normal. By ureteral catheterization the pus was found to come from the right kidney ; on bacteriological examination it gave a pure culture of a coliform bacillus.

Group 2. Without previous warning of any kind a woman may be seized with acute lumbar pain, followed quickly by a rise of temperature and pulse rate, rigors, vomiting, furred tongue, headache, malaise, and drenching sweats.

' A patient, aged 28 years, had had two children, aged now five and two years respectively ; she had had no miscarriage and was pregnant for the third time, when at the beginning of the fifth month she was suddenly seized with severe pains round the waist. The suddenness of the onset of symptoms may be gathered from the fact that she was preparing her husband's mid-day dinner when the pain seized her acutely in the loins ; she was unable to go on with the dinner preparation ; she took to her bed and remained there a fortnight under treatment before she was transferred to the hospital. The pains across the loins persisted all the time, waxing and waning to some extent, but not in such a way as to suggest colic. Vomiting had been frequent, especially after food, and this notwithstanding her diet being milk and soda-water only. In addition to the vomiting there had been severe headache, and on several occasions rigors. The skin was dry for the first five days, but since then there had been copious perspirations.' (French.)

Group 3. The onset may be with high fever malaise and other indications of a septic intoxication, but without any symptoms pointing to the kidney as the site of infection.

' In 1907 M. A. L. was admitted to Queen Charlotte's Hospital. She was in the 6th month of her pregnancy, and was very ill with severe hectic fever, the temperature rising at night to 102° F. or 103° F., and often falling in the

morning to 97° F., while the pulse-rate varied between 100 and 120. She was sent into the hospital with the diagnosis of septic endocarditis, for she had twice had rheumatic fever and there was a systolic murmur at the apex. No tumour could be felt in either loin, and there was no tenderness there even on deep palpation; the urine was acid and contained no albumen or pus. On August 30th she was transferred to St. Bartholomew's Hospital. The blood contained red cells 3,456,000, leucocytes 18,000, and on cultivation was sterile. This, however, does not, as we well know, exclude septic endocarditis, and on September 5th, having no other indication, I injected a dose of polyvalent anti-streptococcus serum subcutaneously. She had a violent rigor soon afterwards.

On September 7th she had another violent rigor and severe pain was felt in the right flank.

On September 8th the right kidney could be easily felt. She had passed 41 oz. of urine, which was acid, of specific gravity 1007, contained no sugar, no blood but some albumen, a few granular casts and motile bacilli in large numbers. These when cultivated and examined gave reactions almost identical with those of *B. coli communis*. They were at any rate of the coli group.

That night she passed a quantity of pus, her temperature fell, and she began to improve.

On September 11th she was prematurely confined and the baby died.

By October 25th the quantity of pus had diminished to only a few cells seen with the microscope. There was no pain or tenderness and she was discharged quite well.' (Herringham.)

Group 4. The symptoms first noticed may be frequent and painful micturition, followed after a longer or shorter interval by pain in the lumbar region and the manifestations of a toxæmia.

'E. S., 25 years of age, in the 4th month of her second pregnancy began to suffer from slight abdominal pain, pain in the vulva, and from frequent and painful micturition. After these symptoms had persisted for a fortnight she noticed that the urine was cloudy and deposited a sediment on standing. A few days later a dull continuous pain was felt in the loins, first on the right side, later on the left; in the course of a month the pain became much more severe, and the patient lost

flesh, rapidly became anæmic, and suffered from attacks of vomiting, constipation, and sleeplessness.

On admission to hospital there was marked tenderness and resistance in the right renal region, the urine was acid and contained pus, the abdomen was distended, the temperature raised, and the tongue furred. As no improvement took place under medical treatment labour was induced, after which the pain and tenderness in the right renal region disappeared, the temperature fell, and the patient made a good recovery.' (Potocki.)

Group 5. In rare cases the onset is sudden, with abdominal pain, persistent vomiting, absolute constipation, and abdominal distension.

' E. M., in the 8th month of her fifth pregnancy, was seized with severe abdominal pain ; in the course of a few hours persistent vomiting set in, the abdomen became distended, and no fæces or flatus were passed. A diagnosis of acute intestinal obstruction was made and it was proposed to perform laparotomy. When the catheter was passed as a preliminary measure the urine was seen to contain a quantity of pus, and on examination under anæsthesia the right kidney was found considerably enlarged. Operation was therefore abandoned, labour was induced, and the patient made a good recovery ; pus completely disappeared from the urine within three weeks.'

Group 6. Occasionally the symptoms resemble those of pleurisy or of pneumonia affecting the base of the right lung. There is pain over the posterior part of the lower ribs, worse on respiration, particularly on deep inspiration, associated with a rise of temperature, rapid pulse, vomiting, and hurried breathing.

' Mrs. D., aged 29, quartipara, pregnant five months, when away from home complained of sudden severe pain in the " right side ", as she expressed it, " at the bottom of her ribs behind " ; she had a rigor, temperature 102° F., pulse 100. There was some frequency of micturition, bowels constipated, nausea and vomiting ; abdomen slightly distended. The pain in the right side " caught her breath " and hampered her breathing. The diagnosis made was right basal pleurisy. When I saw her she was still complaining of the pleurisy pain, which was easier on some days, worse on others. On

physical examination I could find no evidence of pleurisy, but noted that the pain complained of extended well below the costal border, and that there was well-marked hyperæsthesia and tenderness over the whole kidney neighbourhood. There was no pain or tenderness complained of over the appendix area in front. A specimen of urine was examined and found to contain a small sediment of pus. The reaction was acid, the deposit showed pus cells, active leucocytes, and epithelial cells. The bacteriological report was *B. coli* present.' (Burnett.)

Of these various modes of onset, that described under Group 2 is the commonest; in 60 per cent. of our cases sudden pain in the lumbar region, sometimes of intense severity, sometimes comparatively slight, has been the first symptom to attract attention. But whatever be the mode of onset, the cases present certain symptoms in common, and these common symptoms call for closer study.

Pain is the most striking symptom of the disease; in some cases it is at first slight, felt in the back and often spoken of by the patient as a dull ache, like lumbago. In others its onset is sudden and acute, felt over a wide area and difficult to localize; sometimes it is felt most severely over the iliac fossa and may be attributed to appendicitis; sometimes in the lower part of the chest, and gives rise to suspicions of pleurisy or pneumonia, but in the majority of cases it is felt in the region of the kidney and radiates towards the groin of the affected side. Occasionally it is paroxysmal, like that of colic, but more often dull and continuous, though exacerbations and remissions occur without obvious cause. When both sides are affected the pain is usually more severe on one side than on the other.

Temperature.—The temperature is raised, irregular, and remittent; it usually rises at night to 101° F. or 102° F., and in one of our cases reached 105° F. When the pus is pent up in the kidney the temperature rises and the discharge of a quantity of pus *per urethram* is usually followed by a fall of temperature. Rigors are common and are sometimes of great severity.

Pulse.—The pulse-rate is increased and varies from time

to time with the pain, temperature, and constitutional disturbance. In the milder cases it may never exceed 100 beats per minute, but in the severe cases reaches 120 or 130.

Vomiting occurs commonly during the paroxysms of pain, and in some cases is a marked feature of the disease. In two of our cases a rise of temperature associated with severe vomiting preceded the onset of pain by two and four days respectively. Gastro-intestinal disturbances are often spoken of as precursors of the disease; it is doubtful, however, whether in many cases they should not be regarded as its earliest manifestations.

Other Constitutional Symptoms.—Drenching sweats are often noted and are of toxic origin. Anæmia, rapid loss of flesh, a sallow earthy complexion, furred tongue, headache, loss of appetite, and constipation are nearly always present when the condition has lasted some days.

Abdominal distension is often present; in most instances it is only slight, but in some cases has been so marked that, in association with persistent vomiting, it has led to the diagnosis of intestinal obstruction.

Urinary Symptoms.—Frequent and painful micturition are recorded in a relatively small number of cases. The urine at first is usually diminished in quantity, of dark colour and of high specific gravity; later the amount is increased, the colour is paler and the specific gravity lower; the increase in amount is probably the result of treatment, for all my patients have been encouraged to drink large quantities of bland fluids. Immediately after it is passed the urine is turbid, and on standing deposits a layer of flocculent material consisting of pus, mucus, flakes of lymph, leucocytes, and shed epithelial cells. As a rule it has no offensive odour, and the reaction is acid when the infecting organism is the *Bacillus coli communis*; in the mixed infections and in the rare cases of streptococcal or staphylococcal infection it is more often alkaline.

Chemical Examination.—Albumen is often present in small quantities before the pus is discharged. There is seldom any marked diminution in the output of urea, and

in the cases I have examined there has been no increase in the ammonia coefficient.

Microscopical Examination.—Active motile bacilli are found in large quantities. Pus cells are present in varying amount; epithelial cells, leucocytes, and a few red blood corpuscles are often seen, and, when the kidney substance is affected, epithelial and hyaline casts in addition.

There is nothing in the chemical or microscopical qualities of the urine to enable us to tell whether the pus comes from the bladder or the kidney. This can be determined with absolute certainty in one way only, namely, by catheterization of the ureters.

Blood Examination.—Pyelonephritis is usually associated with some degree of leucocytosis. It must be remembered that in pregnancy there is normally an increase in the number of white blood corpuscles, but during the fifth and sixth months (the time at which pyelonephritis is commonest) they seldom exceed 10,000 per c.mm. in uncomplicated pregnancies. The absence of a leucocytosis does not exclude the presence of pus in the kidney; a patient was admitted to St. Bartholomew's Hospital on January 15, 1909, with a temperature of 100° F., a pulse of 96, pain in the loin, pus and motile bacilli in the urine, but with a blood-count of only 8,200 leucocytes, although on the day previous to admission she had vomited and had a severe rigor. Such cases, however, are unusual, and we commonly find a leucocytosis up to 12,000 or 14,000 per c.mm.; in one of my cases it reached 22,000.

As previously stated, the *B. coli communis* can very seldom be grown from a blood culture. Agglutins and bactericidal substances are sometimes present in the blood, for in several instances the serum has caused clumping in cultures of a bacillus derived from the patient's urine or fæces.

Physical Examination.

The condition found on examination will depend upon the severity of the symptoms and the degree of distension of the renal pelvis. In acute cases the face is flushed and the skin

has a slightly yellow tinge, the tongue is furred, the temperature raised, and the pulse rapid. The abdomen is often distended, and the abdominal muscles, particularly upon the affected side, are held rigid. The presence of the pregnant uterus renders palpation of the kidney difficult, and the difficulty is increased by marked hyperæsthesia over the affected side, extending from the ribs above to the iliac crest below. This area of hyperæsthesia is very characteristic. There is usually tenderness over the right iliac fossa, often most marked at the outer border of the rectus on a line drawn from the umbilicus to the anterior superior iliac spine ; the great tenderness at this spot has in several cases led to a diagnosis of appendicitis. On bimanual palpation the kidney is tender, its mobility is often greater than the normal, and not infrequently a definite enlargement can be detected, though the tumour seldom attains a large size. On vaginal examination, in the majority of cases there is tenderness over the posterior wall of the bladder and the pelvic portion of the ureter is tender and thickened.

Cystoscopic Examination and Catheterization of the Ureters is a most valuable means of investigation. By the help of the cystoscope we may ascertain the condition of the vesical membrane and of the ureteric orifices, and further may watch the escape of urine from the ureter into the bladder. It is often possible to observe the escape of clear urine on one side and of thick turbid urine on the other, thus rendering certain a diagnosis which was otherwise more or less problematical. The urine from each ureter may be collected separately by means of Luy's separator, or still more satisfactorily by means of ureteral catheterization. In the investigation of our earlier cases we used the separator, but in the later cases we have employed ureteral catheterization, which enables us to obtain urine for bacteriological examination directly from the pelvis of the kidney. Ureteral catheterization should not be employed if the bladder is infected.

Course of the Cases.—It is necessary to remember that under suitable treatment the patients tend to get well, and

evacuation of the uterine contents or operations upon the kidney are seldom required. After the symptoms described above have lasted some days the condition begins to improve, the temperature falls, the pain ceases, the quantity of pus diminishes, and the patient becomes convalescent. The urine for some weeks after the symptoms have ceased may contain a small quantity of pus, and after all pus has disappeared the bacilli are still present, a fact which accounts for the frequency of relapses in the later months of pregnancy. The temperature may fall by lysis or by crisis; in the latter event the fall is often coincident with the evacuation of a quantity of pus. Relapses are common when the patient is allowed to get up; on two occasions patients have been discharged from the hospital apparently well and have been re-admitted within a week with a return of the symptoms. Generally speaking, the cases with an insidious onset run a longer course than those in which the onset is more acute. It is possible, as has been suggested by Bar, that many cases of coli infection do not progress to suppuration, but that there is a stage marked by the presence of coli in the urine associated with constitutional symptoms due to the absorption of toxins, and that the formation of pus implies an acquired resistance to the infecting organism on the part of the patient.

Although one kidney only is affected as a rule, the condition is by no means uncommonly bilateral. 'Of 187 cases where the side affected could be ascertained, in 107 the disease was confined to the right side; in 63 both kidneys were affected; and in 17 it was the left kidney alone. Translated into percentages this gives us roughly:

55 per cent. right kidney
35 per cent. both kidneys
10 per cent. left kidney.' (Ward.)

Complications.

The kidney may be converted into a pyonephrosis, a dilated thin-walled sac full of pus. Rupture of the pyonephrosis is a rare event, but an instance is related

by Matthews Duncan: 'I may mention a case lately in "Martha"—a woman pregnant about five months, and having pain in the right side, and a large tense swelling indistinctly felt there. Lying in bed made her comfortable and she left the hospital. In a few days she died almost suddenly. Post mortem it was found that a pyonephrosis had given way, a very small aperture transmitting the dirty pus into the peritoneal cavity.' (*Clinical Lectures*, p. 280.)

A pyonephrosis may also rupture extra-peritoneally and so lead to the formation of a peri-nephric abscess: this event is also rare.

Ureteritis and cystitis are common complications, and if the inflammation be very acute, hæmaturia with the passage of a considerable amount of blood may occur; in cases of uncomplicated pyelonephritis a few red blood corpuscles may often be found in the urine on microscopic examination, but the passage of a large quantity of blood is rare.

Respiratory Complications.—Pleurisy at the base of the right lung is not uncommon; in some cases it is accompanied by effusion, and in one instance a pure culture of a coliform bacillus was obtained from the fluid withdrawn by tapping. Pneumonia occasionally develops in the course of the disease, and empyema and pulmonary abscess have both been recorded. Cough is often present, associated with diminished chest movement, poor air-entry, and crepitations at the base of the lung on the affected side.

Vascular System. Endocarditis has been recorded by Ward and by Ruppaner. Thrombosis of the left femoral vein occurred in the course of the disease in one of our own cases.

Toxæmia.—The profound toxic condition met with in some of the cases has been already referred to; epileptiform convulsions like those of eclampsia have been described; such cases are probably instances of true eclampsia affecting a patient whose kidneys are already damaged. Uræmia does not often supervene, though some of the cases of profound

coma and of epileptiform convulsions may possibly be properly classed under this heading.

Prognosis to Mother and to Child.

(1) *To the Mother.*—It is difficult to estimate the mortality of pyelonephritis of pregnancy. For accurate knowledge on this point we require series of consecutive cases such as can be obtained only by a collective investigation. Amongst the 23 cases under my own personal observation, some of them very severe, there has been no death. Ward states that amongst the first 13 patients he saw 4 died, giving a mortality of 30 per cent., but that amongst the cases he collected from the literature the death-rate was 1·8 per cent. Ward's cases must have been of exceptional severity; no other writer records a death-rate approaching 30 per cent. It is probable that amongst patients who present severe symptoms the mortality may be as high as 5 to 7 per cent., but that if we take all cases together, mild as well as severe, it does not exceed 1 or 2 per cent., for I am convinced from my own experience that cases with but slight symptoms are much commoner than is generally believed.

Death may be due to a profound toxæmia, to exhaustion and cachexia following upon prolonged suppuration, to an acute general infection, or to an accident, such as the rupture of a pyonephrosis. Nephrotomy or nephrectomy are necessary in a small proportion of cases, and are called for more often in the streptococcal, staphylococcal, and mixed infections than in infections with the coliform group of organisms.

Whether the kidney is usually permanently damaged, and whether chronic interstitial nephritis is apt to develop or calculi to be formed in later years, are questions which for the present must remain unanswered.

(2) *To the Child.*—The prognosis to the child is grave in the extreme. In a considerable proportion of the cases abortion or premature labour occur spontaneously, and in many of the severer cases have to be induced in the interests of the mother. Ward quotes 131 cases: 70 children were

born at full term, of whom 3 died soon after birth ; in 61 cases the pregnancy terminated prematurely, though 21 of the children were born alive. There is no record as to how many of the premature children survived ; it is probable that the majority of them died within a month or two ; but even if we assume that half of them lived the fœtal mortality is 40·4 per cent.

Diagnosis.

Three cardinal symptoms are present in the majority of cases :

(1) Severe pain in the lumbar or iliac regions, sometimes paroxysmal in character, associated with tenderness on palpation over the kidney region.

(2) A raised, irregular temperature sometimes associated with rigors.

(3) The presence of pus and motile bacilli in the urine.

In addition to the three cardinal symptoms there are often present :

Vomiting.

Slight abdominal distension.

Rapid loss of flesh.

Anæmia.

Furred tongue.

Frequent or painful micturition.

Constipation.

Pain on deep inspiration over the base of the right lung.

A leucocytosis.

Diagnosis is usually easy, but in some cases the symptoms are so misleading and the physical signs so obscure that every means of investigation at our disposal has to be employed to elucidate them.

Differential Diagnosis.

Pyelonephritis of pregnancy has been mistaken for :

(*a*) Acute lesions of the alimentary tract :—intestinal obstruction, appendicitis, gastro-enteritis, and gall-stone colic.

(*b*) Diseases which lead to a condition of profound

toxæmia :—enteric fever, malaria, influenza, malignant endocarditis, and the toxæmias of pregnancy.

(*c*) Acute lesions of the respiratory tract :—pleurisy and pneumonia.

(*d*) Lesions of the kidney :—stone or tubercle.

(*a*) *Lesions of the Alimentary Tract.*—A case has already been quoted in which pyelonephritis simulated and led to a diagnosis of intestinal obstruction ; a much commoner error, however, is to mistake the condition for appendicitis. The pain is often referred in the first instance to the right iliac fossa, the abdomen is distended, the muscles are rigid, and there is marked tenderness over McBurney's point. Pyelonephritis is, however, distinguished by two features which are absent in appendicitis, pus in the urine and an area of marked tenderness and hyperæsthesia over the kidney region. The persistent vomiting which marks the onset of some cases has led to a diagnosis of gastritis, and the attacks of acute pain have been mistaken for gall-stone colic ; in all such obscure cases the urine should be examined daily for the presence of pus and bacilli, and the kidney region should be daily palpated.

(*b*) *Diseases which lead to a Condition of profound Toxæmia.* —Attention has been drawn to a group of cases in which the onset is marked by a raised temperature, rapid pulse, furred tongue, and malaise. There are no localizing symptoms and the diagnosis for some days remains in doubt, but malignant endocarditis, enteric fever, influenza, or other causes of continued fever are suspected ; if rigors are present, especially if the patient has lived abroad, a diagnosis of malaria may be made. In doubtful cases Widal's test should be applied, cultures taken from the blood, malaria parasites looked for, and the white blood corpuscles counted. In pyelonephritis the only abnormality detected will probably be a slight leucocytosis, but negative results under these conditions have a distinct value in diagnosis. It has been stated already that albumen is often to be found in the urine some days before pus is detected : in such cases the toxæmia

of pregnancy may be suspected ; daily examination of the urine and repeated exploration of the kidney region will eventually reveal the true condition.

(*c*) *Acute Lesions of the Respiratory Tract.*—Pain at the base of the right lung, worse on deep inspiration and associated with cough and raised temperature, give a clinical picture closely resembling that of pleurisy or pneumonia. Burnett, who has drawn attention to such cases, remarks :

'Trousseau's famous aphorism, "whenever an infant complains of pain in the abdomen carefully examine the chest," occasionally requires to be inverted when applied to the adult, for the diagnostic features of pyelitis, sudden onset with rigor, the acute costo-vertebral pain, high temperature and pulse, may readily be mistaken for an acute pneumonia where the consolidation has not yet so far advanced to the surface as to give the characteristic physical signs.'

(*d*) *Lesions of the Kidney.*—A renal calculus or tuberculous disease of the kidney may first give rise to symptoms during pregnancy. The diagnosis under these conditions is very difficult, and in most of the recorded cases has not been made until after delivery, when the persistence of the symptoms has led to the suspicion of a further lesion. In these cases bacteriological examination of the urine may afford help, for with tuberculous lesions or renal calculus we seldom obtain a pure culture of *Bacillus coli communis* from the urine. Pyelonephritis may closely simulate the passage of a renal calculus ; the sudden onset of the pain, sometimes with vomiting and abdominal distension, its distribution and severity, often suggest an attack of renal colic.

Treatment.

1. *Medical Treatment.*—It has already been stated that in the majority of cases medical treatment only is required ; this is easily carried out, and as a rule marked improvement is observed in the course of ten to fourteen days. In carrying out the treatment there are five essential points :

(*a*) Absolute rest in bed.

(*b*) Careful dieting.

(*c*) The administration of large quantities of bland fluids.
(*d*) Urinary antiseptics.
(*e*) Free action of the bowels.

(*a*) *Rest in Bed.*—Absolute rest in bed in the recumbent position must be insisted upon; it is a striking fact that patients are often free from pain and the temperature is normal so long as they remain in bed, but if allowed to get up, *although all other treatment is continued*, the pain returns and the temperature again rises. The patient should be instructed to lie in the semi-prone position and on the side opposite to that affected, so as to cause the uterus to fall away as far as possible from the pelvic brim, and so allow free drainage of the kidney. She should also be instructed to lie over on her face for a period of an hour once or twice daily.

(*b*) *Diet.*—A strictly milk diet is often insisted upon, and it is sometimes stated that such a diet diminishes the virulence of the organisms in the intestine; this, however, is very doubtful. A milk diet is monotonous and irksome to the patient, and apparently quite unnecessary; in my recent cases I have allowed boiled fish, bread and butter, custard, eggs, and cocoa: I am convinced that the more liberal diet has proved beneficial.

(*c*) *Fluids.*—Large quantities of fluids are necessary to flush the kidneys. Barley water or imperial drink to which potassium citrate is added in such quantity that each ounce contains five grains, is perhaps the form in which it can best be administered. Although the point is difficult of explanation, practical experience has shown that the citrates and acetates of potassium and sodium given in large doses have a marked effect in alleviating the symptoms and shortening the course of the disease; they should never be omitted from the treatment. Distilled water, Contrexéville or Vichy water may be substituted for imperial drink or barley water.

(*d*) *Urinary Antiseptics.*—Of urinary antiseptics those which liberate formaldehyde, namely urotropin and helmitol, have proved the best. These drugs should not be given in

tablet form, but five grains of the powder should be dissolved in two-thirds of a tumblerful of warm water and administered three times daily. Urotropin sometimes causes vomiting, in such cases helmitol should be substituted. Acid sodium phosphate is often added to render the urine acid ; whether it has this effect, however, is very doubtful, and in most cases of *Bacillus coli* infection the urine is acid throughout the course of the disease. Methylene blue and Salol are recommended by some writers in preference to urotropin.

(*e*) *Aperients.*—The bowels should be made to act freely, but what aperients are selected is a matter of no great moment. Senna, cascara, calomel, and the salines may all be employed.

Serum and Vaccine Treatment.

The results of treatment by sera have proved very disappointing. This is hardly surprising when we remember that *Bacillus coli communis* is a generic term and that the members of the group exhibit marked individual characteristics. It is probable that a serum prepared by inoculation of an animal with bacilli of one particular strain would prove inert in an infection due to organisms of another strain. Further, it is doubtful whether the *Bacillus coli communis* develops an anti-toxin ; its power to do so is denied by many bacteriologists.

It is difficult to estimate the value of vaccines ; they are almost always combined with other forms of treatment, and it is usually impossible to ascribe the improvement definitely to the vaccines. I have seen cases which showed but little improvement under the treatment outlined above improve rapidly after the administration of vaccines, and I have never seen any harm result from their use. I therefore now employ them in all cases. The injection of stock vaccines is useless : the vaccine must be autogenous, that is to say, it must be prepared from cultures of bacilli derived from the urine of the patient. The dosage is still to a large extent a matter of individual preference ; some commence with a dose of 4 million bacilli, others with 10 millions. The

injections are given every third day in increasing doses until 50 millions is reached.

During the period of administration of the vaccine the symptoms usually improve and the amount of pus diminishes; the bacilli, however, can still be found in large quantities in the urine and may be detected weeks after the disappearance of the pus.

Irrigation of the Renal Pelvis.

I have no personal experience of this method of treatment, nor do I think it likely to prove of great value. Stoeckel describes the method he employs as follows:—

'I force the catheter gradually as far as the renal pelvis and receive the flowing urine into a glass; then I connect the pavilion of the catheter by means of a gum elastic tube with a very easily worked 50 cm. capacity syringe, whose contents I pass up very gradually and with equable pressure into the pelvis of the kidney. The fluid returns to the bladder alongside the catheter, if the catheter is thin and the ureter-lumen not quite filled up. After removing the syringe a portion of the infected fluid runs out of the catheter into a glass and is again tested; a 1 per cent. solution of silver nitrate is the fluid I most commonly use.'

Obstetrical Treatment.

Once again I would emphasize the fact that induction of labour is necessary only in severe cases, and should not be advised until other methods of treatment have failed to bring about alleviation of the symptoms. Every case must be considered on its own merits; it is impossible to lay down hard-and-fast rules as to when pregnancy should be terminated. It may be stated generally that if after ten to fourteen days' treatment by rest, diet, drugs, and vaccines, there is no improvement, it will be right in the interests of the mother to evacuate the uterine contents. The best method to adopt is the introduction of a bougie between the membranes and the uterine wall. Contractions are usually excited within seventy-two

hours. If due aseptic precautions are observed the method is practically free from danger, and the fact that the patient is the subject of pyelonephritis does not appear to increase the risk of infection of the puerperal uterus. If the symptoms arise in the later months of pregnancy when the child is nearly viable, it may be possible to delay induction for a few weeks in the interests of the child, but it must be remembered that the infant mortality is over 40 per cent. in severe cases. The knowledge of this fact will make us careful not to allow the mother to run an undue risk.

Surgical Treatment.

Under very exceptional conditions the induction of labour fails to bring relief, and the operation of nephrotomy or nephrectomy has to be performed; a case has been mentioned already in which the ureter was so sharply kinked that emptying the uterus did not afford escape to the pent-up pus. There are circumstances in which it may be advisable to perform nephrotomy rather than induce premature labour, as for example, in the case of an elderly primipara who is not very likely to have more children. The operation implies the establishment of a fistula in the loin which will have to be kept open until delivery and may fail to close afterwards. Lennander records a case in which nephrotomy was performed on account of a permanent fistula, and the patient developed pyelonephritis of the remaining kidney in her next pregnancy. If these risks are explained to the patient and she wishes in the interests of her child to have the operation performed, she has a right to have her wishes respected.

Of the two operations nephrotomy should be selected—nephrectomy is required only when the kidney is completely disorganized, or for the cure of a fistula which has failed to close spontaneously.

CHAPTER XXIV

PYELITIS AND PYELONEPHRITIS (CONTINUED)

II. *IN CONDITIONS OTHER THAN PREGNANCY.*

To the above account given of pyelonephritis in pregnancy by Dr. Williamson it remains to add a few words on the disease as it occurs in other conditions.

It is found at all ages. It is common in children, uncommon in young adults, common again in later life. In children, the great majority of patients are female. In young adults, so far as I have seen, the numbers are about equal. In elderly people the majority of the cases are male. This varying liability of the sexes is not difficult to explain. In little girls there is great risk of infection of the vulva from the anus. The risk is much less in boys. Young adults are cleaner in their habits, and resist infection much better. In later life affections of the bladder are much commoner in men than in women, and they afford a fruitful source of infection for the kidney.

It is, as Dr. Williamson has remarked, very rare to find the blood infected by *Bacillus coli*, and, though the experiments he quotes show that when the bacillus is injected into the circulation the kidney may be infected from the blood, they do not go far to prove that this is a frequent method of invasion in man. Whether the infection can be conveyed directly from the intestine remains, I think, doubtful. Most cases are undoubtedly affected from below.

While in pregnant women the right kidney is more commonly affected than the left I do not find this reported by those who have written on the disease in childhood, nor is it the case in later life.

The *Bacillus coli* is at all ages by far the commonest infection, but staphylococcus, streptococcus, and gonococcus

occasionally occur, either as the only infection or combined with *Bacillus coli*.

In children the only predisposing cause known is diarrhœa, and this undoubtedly acts by increasing the risk of contamination of the vulva. In elderly persons disease of the bladder is the most frequent antecedent, and next in frequency are tumours in the pelvis or malignant disease in the vagina. These causes all act in the same way. In the first place, they obstruct the flow of urine and thus lead to its stagnation and to dilatation of the passages, both of which favour infection; secondly, either by their own nature or by the use of catheters which they occasion, they greatly add to the chance of infection from without.

Dr. Williamson has so fully described the symptoms of the disease that I need not repeat them in detail. I will, however, relate one or two typical cases in young adults which were published by me in the *Clinical Journal*.

Anna S., aged 22, in very poor and miserable circumstances, was hop-picking in August when she was seized with general pain which was worse on the right side and made breathing difficult. Three weeks later, on September 1st, she was admitted to St. Bartholomew's. She then had herpes on the lips, her tongue was dry and brown, and both liver and spleen were enlarged. There was no tumour in either loin, and the urine was natural. The temperature was between 102° and 103° F. I thought she had typhoid fever, but there were no spots, and the blood did not clump either the typhoid or the paratyphoid bacillus. She had violent rigors, the temperature rising on one occasion to 106·2° F. Both rise and fall were very rapid. The blood was sterile, but the urine contained a coliform bacillus. A few days later the right kidney became palpable, and five days after that a little pus was found in the urine. On September 14th a large discharge of foul-smelling pus occurred, and on September 16th the temperature fell permanently to normal. She was treated by injection of a vaccine made from her own bacilli, the doses rising to 200 million dead bacilli. She gradually improved, but on November 24th, when she was

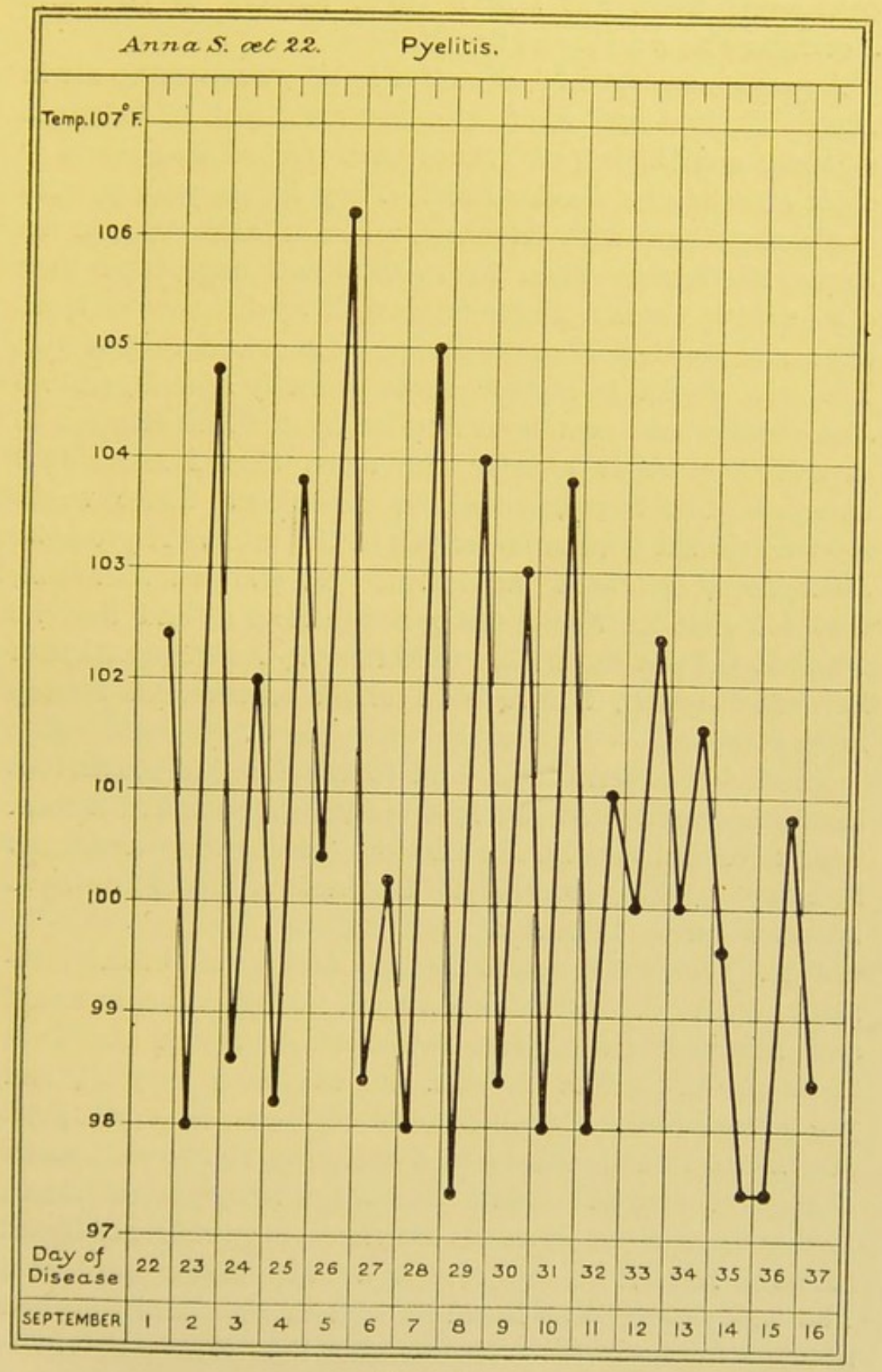
Anna S. æt 22.
Pyelitis.
Temp. 107° F.
106
105
104
103
102
101
100
99
98
97
Day of Disease
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37
SEPTEMBER
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

Chart I.

discharged, there was still a slight amount of pus, and a considerable number of bacilli.

A gentleman, aged 30, of active habits, was sent to me in 1898. He had had what he called an attack of influenza eighteen months before. Since then he had had seven or eight attacks of a similar kind. They began quickly, with chills, sometimes with shivering, and with acute pain in the back and bones. Then followed a hot stage, and then a drenching sweat. He felt knocked up for two or three days afterwards. I could find no disease of any viscus. The urine passed in my room was perfectly normal, and no abnormality had ever been noticed in it. The attacks, as described, were so exactly like ague, that I made that diagnosis, but I was completely mistaken. Three weeks later he passed a quantity of pus in the urine. A prostatic abscess was suspected, but Mr. Godlee, who saw him then, tells me that he found the prostate normal and that he believed the pus came from the kidney. As this gentleman has left England, I have been unable to trace his history further.

To this remittent form, and to the form of continuous hectic exemplified by my first case, may be added a form with a continuous high temperature, ending like pneumonia by crisis, or falling gradually. Instances of these forms have been related by Lenhartz.[1]

John Thomson,[2] describing the disease in infants, remarks upon 'the extreme severity of the general symptoms, and the very trivial and equivocal nature of the local manifestations. The children are obviously very ill, and yet there is nothing distinctive to be found, beyond a little pus in the urine.' He gives a summary of 25 cases under 2 years of age and many illustrative temperature charts. He lays great stress upon the diagnostic importance of rigors. 'I have never,' he says, 'seen a baby under two years who was described as having a regular rigor and who had not pus in the urine.' He remarks that this symptom is confined to girls. Boys, however, are very seldom attacked by the disease. The children are often drowsy or delirious,

and the onset is sometimes with convulsion. There is general tenderness and great distaste for food. In children as well as in adults leucocytosis is the rule.

Thursfield [3] describes the disease in children at a later age. He speaks of three types, an acute form resembling that in adults, a subacute form 'in which without pain or rigors, there is an unexplained fever and wasting, with anæmia, loss of appetite, and general malaise', and a remittent form with attacks of fever, vomiting, and headache, separated by intervals of health. He notices that this form closely resembles the cystic vomiting of children.

The morbid anatomy of the disease is not often studied. Thursfield describes the appearance of the pelvis in an early stage. It was opened under the impression that it contained a stone. 'The mucous membrane was thickened and œdematous, and was streaked with dilated and tortuous capillaries. The pelvis contained a slightly turbid fluid which was swarming with bacilli.' Thomson gives beautiful coloured illustrations of the kidney in a fatal case, and microphotographs of the parenchyma. The disease, however, seldom ends fatally except in elderly persons suffering from other antecedent disease. Under other circumstances recovery is the rule, and when a fatal case occurs it is found that the kidney is riddled, as in Thomson's picture, with small abscesses. I imagine that the parenchymatous suppuration is the exception, and that in most cases there is not more than a suppurative pyelitis.

In adults and in children beyond infancy the treatment usually pursued is to flush the urinary passages by copious draughts of water, and to give antiseptics such as urotropin (gr. v to xv). It is best given in several ounces of water as it has been known to cause pain in micturition. Helmitol and hetralin (gr. x to xxx) which are akin to urotropin are less soluble in water. The benzoates of ammonium (gr. v to xv flavoured with orange) and of sodium (gr. v to xxx flavoured with vanilla (Martindale)) are also useful. John Thomson says that in infants it is most important to render the urine alkaline. He gives citrate of potash

48–60 grains daily if the urine remains acid. This cannot, I should think, have any direct action upon the bacilli, for Box [4] says that they grow better in alkaline than in acid urine. The alkali must, therefore, act in some other way.

Vaccines have been recommended by Rolleston [5] and others. I treated the girl above mentioned persistently by this method. I do not believe it had any effect. Thursfield and Dudgeon are also sceptical. But though its power of removing bacilli from the urine is doubtful, it seems to have considerable effect in relieving the symptoms of *Bacillus coli* cystitis in elderly men. On the other hand, too great a reliance on this method has its dangers. I saw a case in which it had been pushed to extremes. I believe if the kidney had been removed in good time the patient would have been saved.

Dudgeon recommends an anti-colon serum.

These cases are so seldom progressive that the need for operation is rare. But where the general symptoms do not improve, or where, as in Barnard's case, they are extremely severe, the kidney should be exposed, and if it be found to be riddled with small collections of pus it should be removed. It is of no use merely to incise it, for the abscesses are so disseminated that they cannot be reached by any single incision.

Cases of pyelitis in which the collection of pus is sufficiently large to form a renal tumour, and has lasted a considerable time, become clinically cases of pyo-nephrosis, and are discussed in Chapter XXVI.

References.

1. Lenhartz, *Münch. Med. Woch.*, 1907, liv. 761.
2. John Thomson, *Quarterly Journ. of Med.*, 1910, iii. 251.
3. Thursfield, *The Hospital*, 1909, 453.
4. Box, *Lancet*, 1908, i. 77.
5. H. D. Rolleston, *Practitioner*, 1910.

CHAPTER XXV

RENAL TUMOURS

There are many kinds of renal tumour. Some are enlargements of the kidney itself, such as polycystic kidneys, others are formed by dilatation of the pelvis, such as hydro-nephrosis, hæmato-nephrosis, and pyo-nephrosis. Simple cysts and hydatid cysts occasionally, though very rarely, form renal tumours. It is usually impossible to distinguish by palpation a solid from a fluid tumour of the kidney. The diagnosis of polycystic kidney is discussed under that heading. Hydro-nephrosis and pyo-nephrosis usually produce characteristic symptoms. The other forms of fluid tumour are rarely recognized except at an operation or in the dead-house.

This is true also of the benign growths of the kidney. They are almost confined to the small fibromata which are seen as small white masses of about the size of a pea, and are most common, I think, in the medullary part.

There are, however, two cases on record of large lipoma, in which the tumours were removed under the impression that the growth was malignant. In Alsberg's case [1] there were numerous fatty tumours sprinkled all over the kidney, and enlarging it to the size of a child's head. Although Alsberg calls it a lipoma, he describes parts of it which were very like sarcoma tissue, and it may have been a mixed growth. The patient was alive and well two years later. Warthin's case [2] was a single large growth and did not anywhere resemble sarcoma. It was more like a fibroma with much fatty infiltration.

Perhaps this is the best place to mention the rare cases of retro-peritoneal and peri-renal lipoma, which have been studied and collected by Adami.[3] They grow from the fatty

tissue round the kidney, without pain or any marked disturbance, but they often produce emaciation, and, by obstructing the vena cava, œdema of the legs. They give

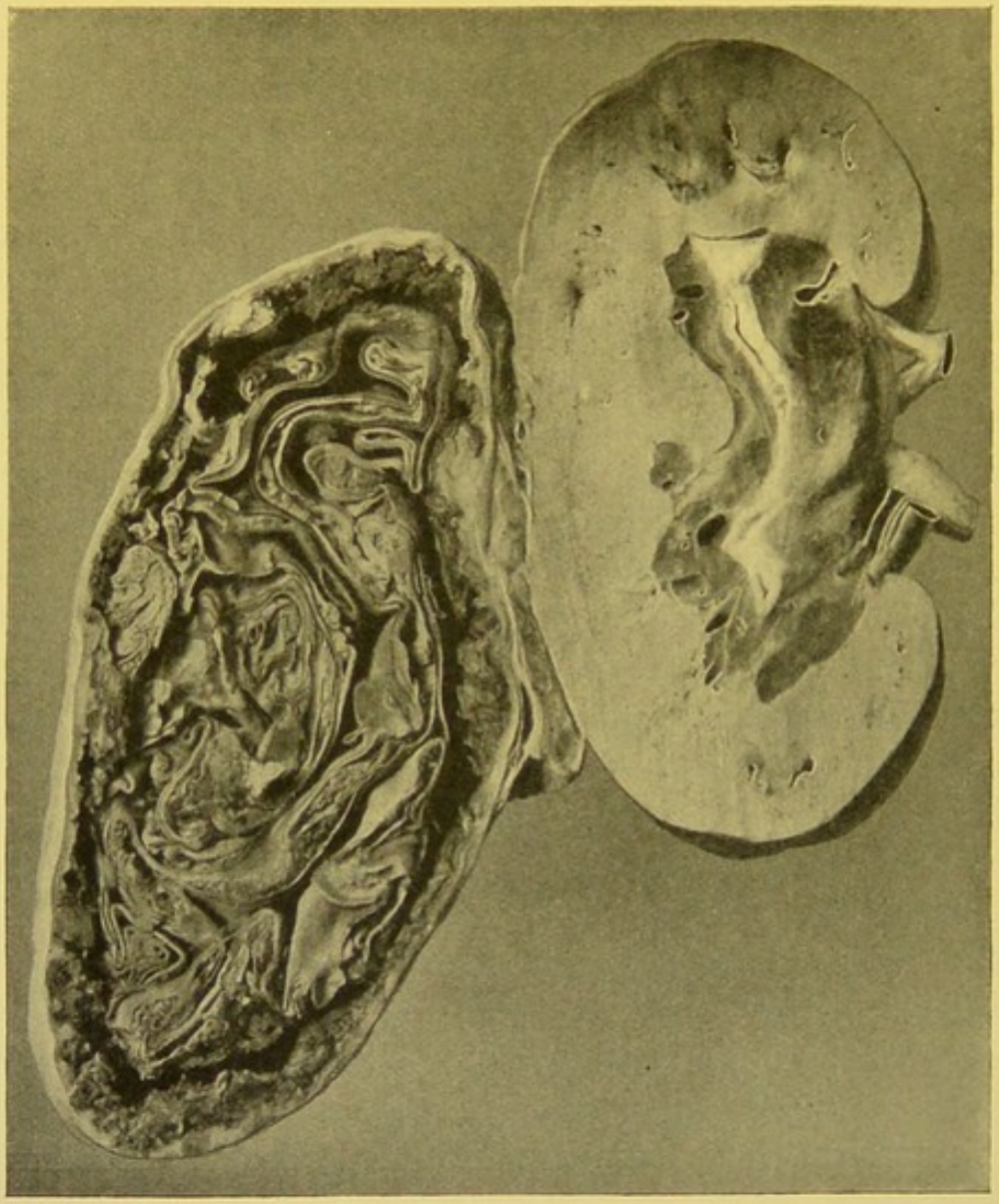

Fig. 22. A hydatid cyst in connexion with the kidney.
From the museum of St. Bartholomew's Hospital.

the sense of fluctuation. In structure they are myxo-lipoma.

In 1883 Grawitz [4] described small tumours, seldom discovered except on the post-mortem table, and of little clinical importance, which owing to certain characteristics he ascribed to misplaced remnants of adrenal tissue. They

lie just under the renal capsule, not in the middle of the kidney. The cells of which they are formed, both by their individual appearance and by their columnar arrangement, recall those of the adrenal cortex. They contain fat and glycogen. Lastly he found that amyloid change might be found simultaneously in the vessels of these tumours and in those of the adrenal cortex. To this fact he attached great significance. His hypothesis has been accepted by the majority of pathologists, though it is still disputed by some. But these tumours are of extremely uncertain character. Some of them are, as were the cases which Grawitz himself described, of an apparently innocent nature. Others, resembling them in other respects, have proved to be malignant and recurrent.

This uncertainty is shared by the adenomas. These are growths reproducing the type of the renal tubes, either small or large, sometimes dilated into cysts of considerable size (cystic adenoma), which may have papillary growths projecting into them. They are usually encapsuled, but sometimes the new formation abuts directly upon renal tissue. Sometimes the interstitial tissue between the tubes or in the capsule is formed by, or contains, masses of round or spindle cells permeated by blood sinuses, which resemble sarcoma (adeno-sarcoma), and sometimes alveolar spaces are seen crowded with cells like carcinomatous growth (adeno-carcinoma). But it seems to be acknowledged that the character of such a growth cannot be predicted from its histological structure. In 1895 Edgar Willett showed two specimens to the Pathological Society. The one, which he thought to be cystic adenoma, removed from an infant, recurred in eleven months; the other, which he thought a papilliferous cystic carcinoma, removed from a man aged 19, had not recurred one year and a half after the operation. Another tumour was removed by Malcolm [5] from a child under two years of age, and was described by Targett as malignant adenoma. The child was alive ten years later.

Lastly come tumours which are by some divided into sarcoma and carcinoma, but by Allen and Cherry [6] are

grouped entirely with sarcomas. Their paper is based on a histological study of twenty-nine specimens in the Melbourne pathological museum, and, though it does not contain a full description of all the cases, gives the authors' conclusions, some of which are as follows. Adenomas always originate from renal tubes, never from adrenal or Wolffian inclusions. All stages can be seen between simple tubes and papilliferous cysts. In the capsules of such growths are sometimes visible alveolar structures resembling now carcinoma, now alveolar sarcoma. Alveolar structure may form the chief part of such a growth, yet never pass into true carcinoma. Such growths may increase very rapidly, but their character does not vary with the amount of sarcoma tissue found in them. Some true sarcomas remain small and inactive. Active tumours may be pure sarcoma, or epithelioid growth. Typical adenoma and typical sarcoma both pass insensibly into these pseudo-carcinomatous structures. Even when most like carcinoma, infection takes place in the fashion of sarcomas. The renal epithelium so far as new growths are concerned behaves as a mesoblastic tissue.

Whatever may be held as to the last point, pathologists seem generally to agree on the atypical character of many renal growths, and Morley Fletcher [7] describes a case as carcinoma-sarcoma.

Allen and Cherry base their hypothesis on the fact that the kidneys are of mesoblastic origin, and they explain by this the occurrence of other mesoblastic structures, fatty, areolar, and connective tissue, cartilage, and muscle-fibre striped and unstriped. These, though, with the possible exception of muscle-fibre foreign to the kidney, occur in the surrounding muscles, bones, and other tissues, which are developed from the same somites. Some anatomists describe muscle-fibre as a normal constituent of the renal capsule.

Probably the majority of pathologists would not agree with Allen and Cherry, and would maintain that true primary carcinoma occurs in adults. But the subject is in such confusion that no statistics based upon the distinction of sarcoma from carcinoma of the kidney are of any value.

If we accept the division as it has hitherto been made we may say that the carcinomas are usually of the soft encephaloid kind, and that scirrhous cancer is much rarer. Villous carcinoma sometimes occurs in the pelvis. In a case described by Drew [8] such a growth was associated with simple papillomas of the ureter and bladder. A case from a woman aged 76 is figured by Dickinson.[9] The sarcomas are round and spindle-celled ; some of them are alveolar in structure. They include the tumours found in infants and young children, which from their contents are called rhabdomyoma, myo-sarcoma, myo-chondro-sarcoma, lipo-myoma, and by various other descriptive names. Some of these infantile tumours, and even some adult tumours of the kidney, grow to a very large size. In children they have been known to amount to a quarter of the weight of the child. Roberts and Dickinson give illustrations of enormous renal growths.

Taking all malignant growths together these infantile tumours are so common that more occur in the first five years than in any ten years during the rest of life. Morris gives the following table for 148 cases :—

From	birth	to	5	years	.	.	.	.	39	cases
,,	5	,,	10	,,	.	.	.	.	2	,,
,,	10	,,	20	,,	.	.	.	.	6	,,
,,	20	,,	30	,,	.	.	.	.	14	,,
,,	30	,,	40	,,	.	.	.	.	20	,,
,,	40	,,	50	,,	.	.	.	.	30	,,
,,	50	,,	60	,,	.	.	.	.	22	,,
,,	60	,,	70	,,	.	.	.	.	11	,,
,,	70	and	upwards		.	.	.	.	4	,,

The cases of carcinoma occur chiefly, if not entirely, after 40 years of age.

Of 42 adults, 32 were men and only 10 were women, but the preponderance of males is not so great in childhood (Roberts).

Out of 67 cases the disease was confined to one kidney in 60. The two sides were equally affected. In 7 cases both kidneys were affected, but in only 3 did the disease appear to be primary in both (Roberts).

Primary neoplasms of the kidney give rise to metastases which are most common in the abdominal glands, in the lungs, and in the liver. It is remarkable that they seldom occur in the lower parts of the genito-urinary system.

The kidneys are not infrequently the site of secondary growths, but these are seldom of clinical importance.

Lymphadenoma occurs in the kidney as in other organs, but does not produce a tumour that is recognizable during life. The growths take the form of yellowish gelatinous-looking patches about 1 cm. in diameter, sprinkled freely through the kidney.

Every one allows that some cases of renal tumour are exceedingly puzzling. When they grow to a great size they so displace the abdominal contents that all ordinary land-marks are lost. They may tilt the liver forward, or force it over to the left side. They may completely displace the spleen and the intestines, and they may descend so far as to resemble a tumour springing from the ovary or uterus. All that can be done is to give some rules that are applicable to the great majority of cases.

A renal tumour grows forwards. Though it sometimes fills up the slight hollow that is seen below the ribs in the back, it never causes a swelling there. It is accordingly felt more easily by the front hand in bimanual examination. It appears first just below the ribs outside the rectus muscle, but may grow inwards, and downwards. It can be easily pushed backwards and forwards between the two hands. It usually moves with respiration, though not so freely as an enlarged liver or spleen. If it has formed adhesions it may not move at all. If on the right side, it pushes the colon in front of it and to its inner side. If on the left, the last part of the transverse colon crosses it obliquely on its way to the splenic flexure, which is attached to the diaphragm opposite the tenth and eleventh ribs, and the descending colon lies in front of it, sometimes on its inner, sometimes on its outer side. The transverse part can be felt even when empty, and rolled under the hand over the tumour. By waiting a little peristalsis can often be seen, and gas

felt to pass through it. I do not remember that I have ever felt the colon on the right side, but others have, and in one of Bright's cases the small intestines were felt over a right-sided pyo-nephrosis. When the patient lies on his back with relaxed muscles the kidney tends to drop backward, and then the fingers can usually be inserted between it and the ribs in a way which is not possible when the tumour is due to enlargement of the liver or spleen. The shape of the tumour is rounded in every direction, which is not the case with an enlarged spleen, nor usually with enlargement of the liver. An enlarged spleen, which it must be remembered may lie either vertically or almost horizontally, has an inner, or upper, sharp edge, on which a notch can usually be felt. The local enlargement of the right lobe of the liver, called a lingual or Riedel's lobe, also has in most instances a well marked edge somewhere.

When there is overlying intestine with gas in it, there is resonance to percussion over the tumour, which, if it can be found, may be held to exclude a hepatic tumour. When the muscles are relaxed so that the tumour drops back, resonance may sometimes be found between it and the liver. Auscultatory percussion is useless anywhere, but it is, if possible, rather more misleading in the abdomen than in the thorax.

In one of Roberts's cases the stomach lay in front of the upper and inner part of the tumour, the colon ran down in front of its inner margin, the spleen lay loose over its lower part in the iliac fossa, and the tail of the pancreas lay in front of it also. In a child who was Dickinson's patient the liver was pushed into the left hypochondrium. In Bridges's patient (Dickinson, iii. 717) the liver was wedged out below the ribs and its edge could be felt. It was pressed forward by the renal tumour. The colon was pushed away from the tumour as it increased in size.

A renal growth sometimes compresses the vena cava, in which case there is œdema of the lower parts and a development of new venous circulation in the abdominal wall. Sometimes it is adherent to the vena cava or aorta, so that

nephrectomy has to be abandoned; sometimes it invades the renal veins and produces thrombosis in them which may spread to the vena cava. Sometimes, also, it grows into the vertebræ, producing great pain in the course of the lumbar and sacral nerves, with paraplegia (Dickinson's case).

A renal tumour may pulsate. A man aged 58 was admitted with a tumour in the left hypochondrium and another along the line of the eighth and ninth ribs on the right side. Two years before he had had hæmaturia, with an attack which was thought to be influenza. He had continued to work, though in failing health, until six months before admission. He had lost a great deal of flesh, and his weight had fallen from 15 st. 5 lb. to 10 st. 2 lb. in the two years. The abdominal tumour, which reached from the ribs to the level of the umbilicus, and to within $1\frac{1}{2}$ inches of the middle line, was firm, rounded, and of the size of half a cocoa-nut. A bruit was heard over it and it pulsated with the heart-beat. The thoracic tumour measured $3\frac{1}{2}$ by $1\frac{1}{2}$ inches and had an expansile pulsation. A systolic bruit was audible over it. There was blood in the urine. This fact and the presence of the second tumour led to the diagnosis of a pulsating renal sarcoma with a secondary growth in the right pleura or lung. This proved on post-mortem examination to be correct. It was of alveolar structure. There were small growths in the right kidney also, and the splenic and left renal veins were thrombosed. Cases of pulsating renal tumour are recorded by Holmes [10] and Langstaff.[11]

The symptoms of renal tumour are pain and hæmaturia. The pain is not always present. It is often nothing much more than a dragging feeling. In some cases it increases to aching, and in a few it is constant and severe. In these it has the distribution of renal pain from any cause, shooting down to the groins, and down the inner side and occasionally the back of the thighs.

Hæmaturia is very common. It occurs at one time or another in fully three-quarters of the cases. Morris declares that it is the first symptom in at least 50 per cent. of them,

but Roberts does not place the number nearly so high. It has certain unusual characters. It is spontaneous, often copious, and recurrent. It is not affected by exertion or repose, but when it once starts continues perhaps for a fortnight though the patient remains in bed. It may occur as a single symptom, and nothing further be noticed for two or three years, when it reappears, and on examination a renal tumour is found. It is not uncommon for worm-like clots to be passed. They cause great pain.

It is very uncommon for any recognizable cancer products to be found in the urine. In the rare cases of villous growth small processes have, however, been found, and have been diagnosed microscopically as cancer (Drew).

The urine usually, though not always, contains albumen, and its natural constituents are often decreased in amount. But in one case of sarcoma the diseased kidney secreted considerably more urea, though less water, than the other, in the same space of time. The urine contained neither albumen nor blood. In some cases albumen is absent at one time and present at another. In some pus cells are found. It must not be forgotten that sometimes an abscess, either renal or peri-renal, forms in connexion with neoplasm of the kidney.

In children it is common for even a large tumour to cause neither pain nor hæmaturia. Except for the visible swelling, and the emaciation, the child seems in good spirits and in fair health.

It is impossible by physical examination to distinguish between adrenal and renal neoplasms. Adrenal tumours occur sometimes in the adult, but more commonly in children. In the latter they are of two kinds. One class is characterized by metastases in the skull and extreme anæmia. There is often ecchymosis about the eyelid, and the cases might then be mistaken for infantile scurvy. A good paper on these cases, with many photographs, was published by R. Hutchison.[12] A second class is remarkable for producing premature obesity, sometimes with abnormal muscular development, the 'infant Hercules' type, and precocious

growth of hair and of the organs of generation. These cases have been studied by Bulloch and Sequeira,[13] and by Guthrie and d'Este Emery.[14] In both papers full references will be found. In many of the cases the tumour was palpable during life. In adults abnormal hairiness sometimes occurs in females as in a case of Malcolm's quoted by Guthrie and Emery. But usually there are no special symptoms except weakness and sometimes pigmentation of the skin. The latter symptom has been noticed twice in cases of adrenal tumour at St. Bartholomew's in the last five years.

The difficulty of these cases is well shown in a case of my own. In July 1909 a butler aged 54 was admitted to my wards with a large abdominal tumour. He had known that he had a lump in his left side for four years. When it first appeared he had considerable pain and vomiting, and the tumour was thought to be a cancer of the stomach. When he came under me he was a healthy-looking man, with a good colour, and had no gastric symptoms. The tumour was superficial, and could be seen to move with respiration. It came out from under the left costal margin and lay so close to the ribs that the hand could not be passed up between them and it. Just beneath the ribs there was a boss on it three inches in diameter, the rest of it was smooth and hard. The absence of intestine over it, and its superficial position, led us at first to think it was an enlarged spleen. But two facts told against this opinion. It had no sharp edge or notch to it and there was no alteration of the blood such as leucocythæmia, or the anæmia and leucopenia of splenic anæmia. The red cells were 5,880,000, the hæmoglobin 95 per cent., the white cells 5,600, and the differential count natural. We next thought of hydatid, and there actually was divergence of complement when the serum was tested with hydatid fluid. But there was no thrill. There were no glands to be felt anywhere. The tumour grew and eventually reached from the ribs above to the iliac fossa below, and from the left flank to a point 5 inches to the right of the umbilicus, whence its inner margin ran obliquely up to the xiphoid cartilage. The diagnosis of malignant

disease probably of renal origin was made, though the urine showed no alteration, and an operation was carried out in September. Then it was found to be an adrenal tumour of sarcomatous nature. The patient did not long survive the operation.

Renal tumour is sometimes thought to be ovarian. Such a case is related by Bright. On the other hand Morris mentions a case where an ovarian cyst with a long pedicle was thought to be a hydro-nephrosis, and a sudden attack of pain and collapse due to torsion of the pedicle was taken to be renal colic. There was resonance over the front of the tumour. It was tapped in the loin, when the fluid was found to be full of cholesterine crystals, squamous epithelium, and neutral fats, which showed the tumour to be a dermoid cyst. Usually an ovarian tumour springs from the pelvis, and lies in front of the intestines. It is only accidentally, as from the formation of adhesions, that the intestine lies in front of it.

A malignant growth of the colon may occupy just the place of a renal tumour. There is usually diarrhœa or hæmorrhage from the bowel, or perhaps on the contrary obstruction to the passage of fæces, which will help to clear up the difficulty. If not, the diagnosis is most obscure. A mass of fæces has often been mistaken for a renal tumour, and the effect of purgatives is not so marked as might be expected. Such a mass is only cleared away by degrees. If there is marked constipation, and if the mass can be indented by the fingers, its fæcal nature should at least be suspected.

In the chapter on hydro-nephrosis a case is given where a retro-peritoneal cyst was mistaken for a renal tumour.

Dickinson records cases in which enlargement of the lumbar and vertebral glands were the cause of error.

The progress of these cases is, necessarily, to death. But their course is less rapid than in that of malignant disease in any other internal organ. Morris states that the duration is 3 or 4 years in carcinoma, 4 to 6 years in sarcoma. As the two are extremely difficult to distinguish it is best

not to lay too much stress on these numbers. But taking the average at between 4 and 5 years, it is clear that the expectation of life is better than it is when, for instance, cancer is discovered in the stomach, or liver, or lung.

No treatment is of any use except nephrectomy. The possibility of operation depends of course upon the existence of secondary growth and the patient's general condition. The operation as now practised has a mortality of 25 per cent., which is itself a heavy handicap, and recurrence is frequent and early. In a large number of cases it cannot be said to prolong life.

References.

1. Alsberg, *Arch. f. Klin. Chir.*, 1892, xliv. 458.
2. Warthin, *Journ. of Pathol.*, 1897, iv. 404.
3. Adami, *Montreal Med. Journ.*, xxv. 529–620.
4. Grawitz, *Virch. Arch.*, xciii.
5. Malcolm, *Clin. Soc. Trans.*, xxvii. 94, xxxvi. 233.
6. Allen and Cherry, *Intercol. Med. Journ. of Australasia*, 1896, i. 274.
7. Morley Fletcher, *Trans. Path. Soc. Lond.*, 1901, lii. 199.
8. Drew ibid., 1897, xlviii. 130.
9. This is de Morgan's case, ibid., xxi. 239.
10. Holmes, ibid., xxiv. 149.
11. Langstaff, *Medico-Chirurg. Trans.*, viii. 294.
12. Hutchison, *Quarterly Journ. of Med.*, i. 33.
13. Bulloch and Sequeira, *Trans. Path. Soc. Lond.*, 1905, lvi. 180.
14. Guthrie and Emery, *Clin. Soc. Trans.*, 1907, xl. 175.

An exhaustive paper on Adrenal tumours is published by Glynn, *Quarterly Journ. of Med.*, v. 157.

CHAPTER XXVI

HYDRO-NEPHROSIS, HÆMATO-NEPHROSIS, AND PYO-NEPHROSIS

Hydro-nephrosis.

When from any cause there is an obstruction to the flow of urine, the pelvis of the kidney and its calyces tend to become distended, and the parenchyma to be thinned, flattened, and atrophied. The process may continue until the organ becomes little more than a membranous sac. The fluid contained in it is generally urinous, but, as is the case with all glandular organs under pressure, the secretion is much more dilute than ordinary urine. It generally contains a little albumen and sometimes blood or pus. Occasionally it has been found to be viscid. When only one kidney is thus affected, the other commonly hypertrophies. The compensation may be sufficient to prevent any symptoms of disease.

The condition is not uncommon in the post-mortem room, and statistics upon the subject are usually gathered from post-mortem records. Morris found that of 142 cases no less than 116 were due to cancer of the pelvic organs and ovaries, and when by adding a second series he raised his total to 381, there were only 5 in which the disease was due to the impaction of a calculus in the ureter. Statistics from this source, however, are of pathological rather than of clinical interest. Morris remarks that, though the cases due to pelvic tumour form the great majority, he is not aware of a single instance in which this cause produced a renal tumour which was recognized during life. Roberts's collection of 52 cases is drawn mostly from literature, and it is not, therefore, surprising that it should include a large number of cases remarkable by their origin or course. Of the total

number 20 cases were due to congenital malformation, 32 were due to causes acquired in later life, of which calculous

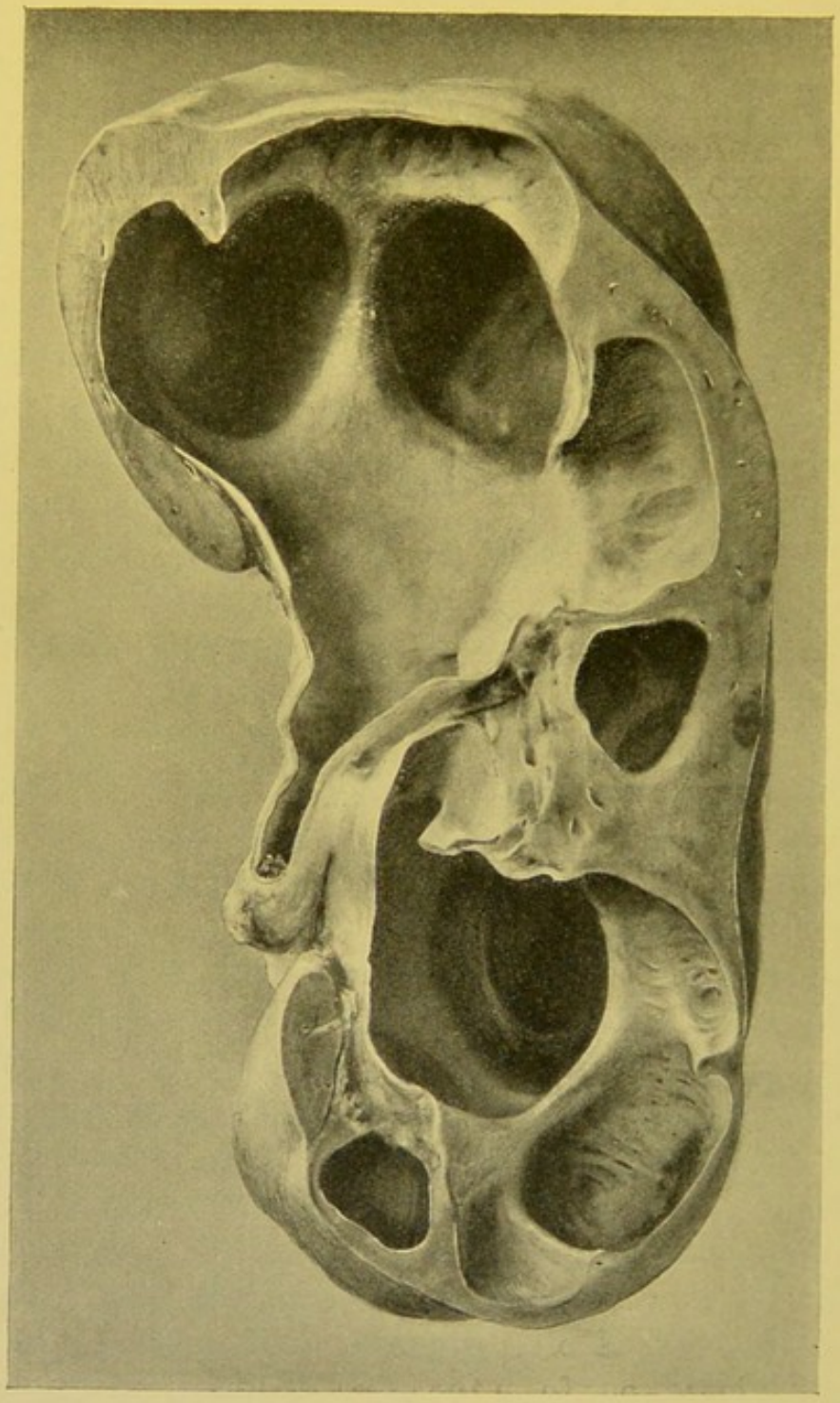

Fig. 23. A hydro-nephrotic kidney with a calculus in the ureter. From the museum of St. Bartholomew's Hospital.

impaction in the ureter amounted to 11, and only 6 were due to pelvic tumours. The two series are not comparable.

Among Morris' cases 98 were double. These bilateral cases are hardly ever recognized clinically. To the physician hydro-nephrosis is practically always an affection of one side alone.

Dickinson gives a table which corresponds more nearly than either to the facts of clinical practice. Of 43 cases in which the disease was on one side, 11 were due to calculus, 2 were due to congenital causes, 8 were due to peculiarities of the ureter which may or may not have been congenital, and in 9 the cause could not be ascertained at the post-mortem.

I have before me the notes of 19 consecutive cases from our wards at St. Bartholomew's, none of which were fatal, and as they differ somewhat from the series above given I will mention a few facts about them. The diagnosis was confirmed in 15 cases by operation, and in 4 the tumour subsided spontaneously, with a recognizable increase of the urine. Of these 19 patients only 6 were males, and, looking back over a series of years, I find in our statistics 55 females to 19 males. Morris and Roberts do not mention the proportion of the sexes to one another, and Dickinson, using only post-mortem records, makes them about equal. But the clinical facts are as I have stated.

The ages of the patients were as follows :—

Under 10	2 males	0 females
10–20	2 ,,	4 ,,
20–30	5 ,,	14 ,,
30–40	6 ,,	15 ,,
40–50	2 ,,	11 ,,
50–60	1 ,,	8 ,,
60–	0 ,,	1 ,,

In a few instances I cannot recover the age.

As may be supposed, the cause was much less frequently discovered in our cases than where a post-mortem examination was made. Out of the 19 cases a calculus was found in 3, in another gravel had been passed, in 1 a kink was found in the ureter which was held to account for the obstruction. In the remainder no cause could be established.

It will be rare, therefore, for us to be able to satisfy the curiosity of a patient on this head with certainty. We can say, however, that a one-sided obstruction is almost certainly situated above the bladder and is therefore in, or pressing on, the ureter. A tumour might do this, but not one of our cases owned such a cause. In rare instances a peritoneal adhesion has been the source of pressure. Usually, however, where there is no calculus the cause is either undiscoverable at operation or after death, or is one of four things, a congenital stricture of the ureter, an acquired stricture, a faulty connexion with the renal pelvis, or an abnormal vessel.

The ureter is apt to be ill-developed in two spots, at its exit from the pelvis and at its entrance into the bladder. At either place it may be extremely narrow. A stricture in other parts of the duct is usually an acquired condition. In one of the specimens in our museum there is a stricture in the middle of each ureter, and in life there was an impermeable stricture of the urethra. It is highly probable that they were all due to the gonococcus. This was a bilateral case, but we have another from a woman which is only on one side. In several cases after death, and in one of my clinical series, the ureter has been found to open obliquely into the dilated pelvis, thus causing obstruction by making the opening valvular. I suspect that this is in many instances produced by, rather than the cause of, the dilatation. Lastly, an abnormal renal vessel running across the ureter to the lower end of the kidney is a recognized, though a rare, cause.

Displacement of the kidney may, by kinking the ureter, produce obstruction, and the number of female cases is rather suggestive of such a cause. But if this was frequently the case, the right side would probably be affected much more often than the left (see chap. I).

A curious variation is worth noting. Some kidneys have two ureters, and in that case may, from the blocking of one of them, show a partial hydro-nephrosis, the remainder, which is served by the other ureter, remaining healthy. There is in our museum a single horseshoe kidney with two ureters, of which the left half alone is hydro-nephrotic.

Experiments have been cited to show that in order to produce hydro-nephrosis the obstruction must be inter-

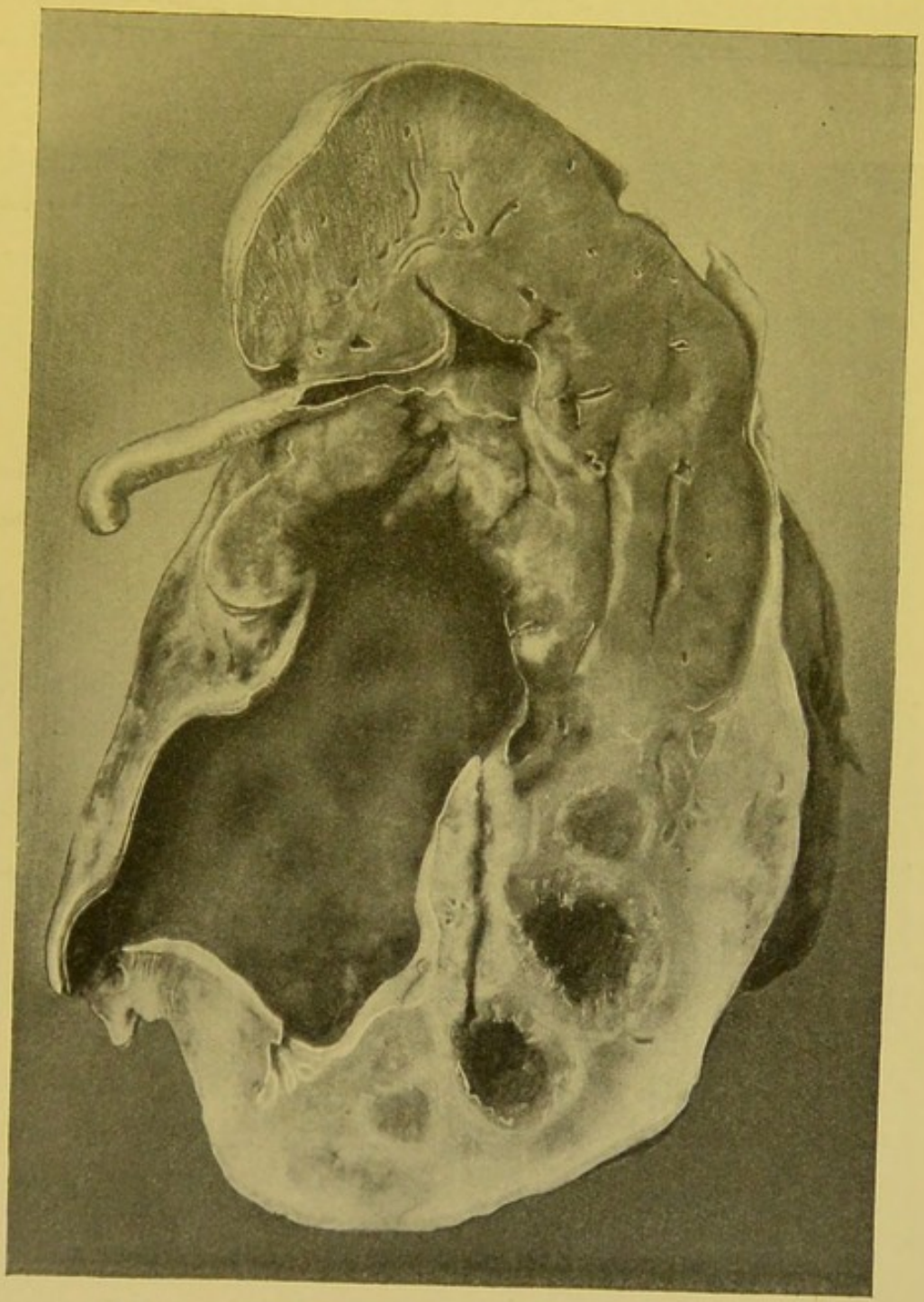

Fig. 24. A kidney with two ureters; the part drained by the one is hydro-nephrotic, while that drained by the other is natural. From the museum of St. Bartholomew's Hospital.

mittent or gradual. We have, however, a beautiful specimen from an experiment by H. W. Wilson, in which a typical

hydro-nephrosis was produced in a cat by a ligature which completely obstructed the ureter. The cases in which the ureter is blocked by a calculus in man are in some cases both sudden and complete. Many such cases lead, no doubt, to atrophy rather than to hydro-nephrosis, but we do not yet

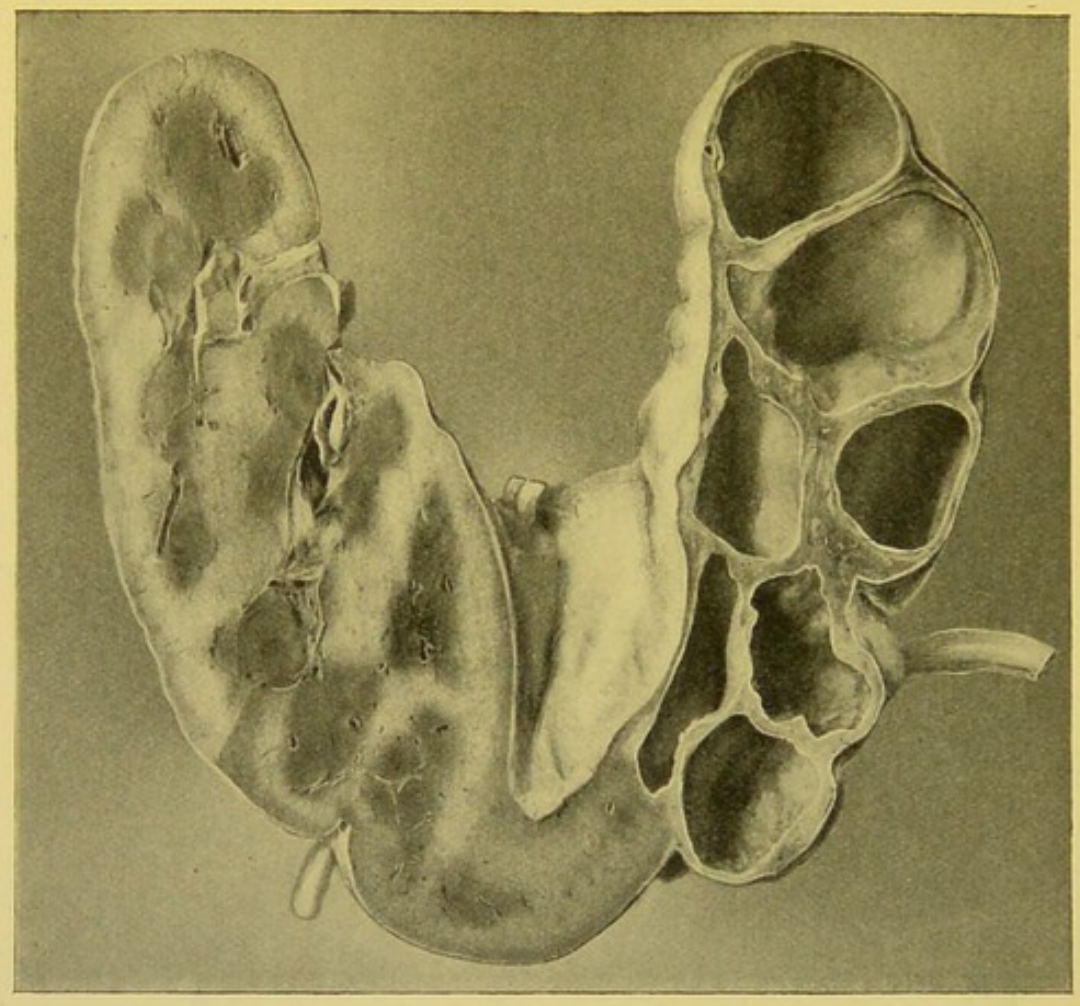

Fig. 25. A horseshoe kidney, with two ureters, of which the left half alone is hydro-nephrotic. From the museum of St. Bartholomew's Hospital.

know why in one case distension and in another atrophy should follow.

Bilateral hydro-nephrosis is produced by pressure affecting both ureters. The commonest cause is a pelvic tumour, occasionally within the bladder, and other causes are enlarged prostate, urethral stricture, and phimosis. In this last group, the immediate cause is probably the hypertrophy and contraction of the bladder itself, which any distal obstruction produces.

In a certain number of our cases of unilateral hydro-nephrosis the disease was latent, and the tumour discovered

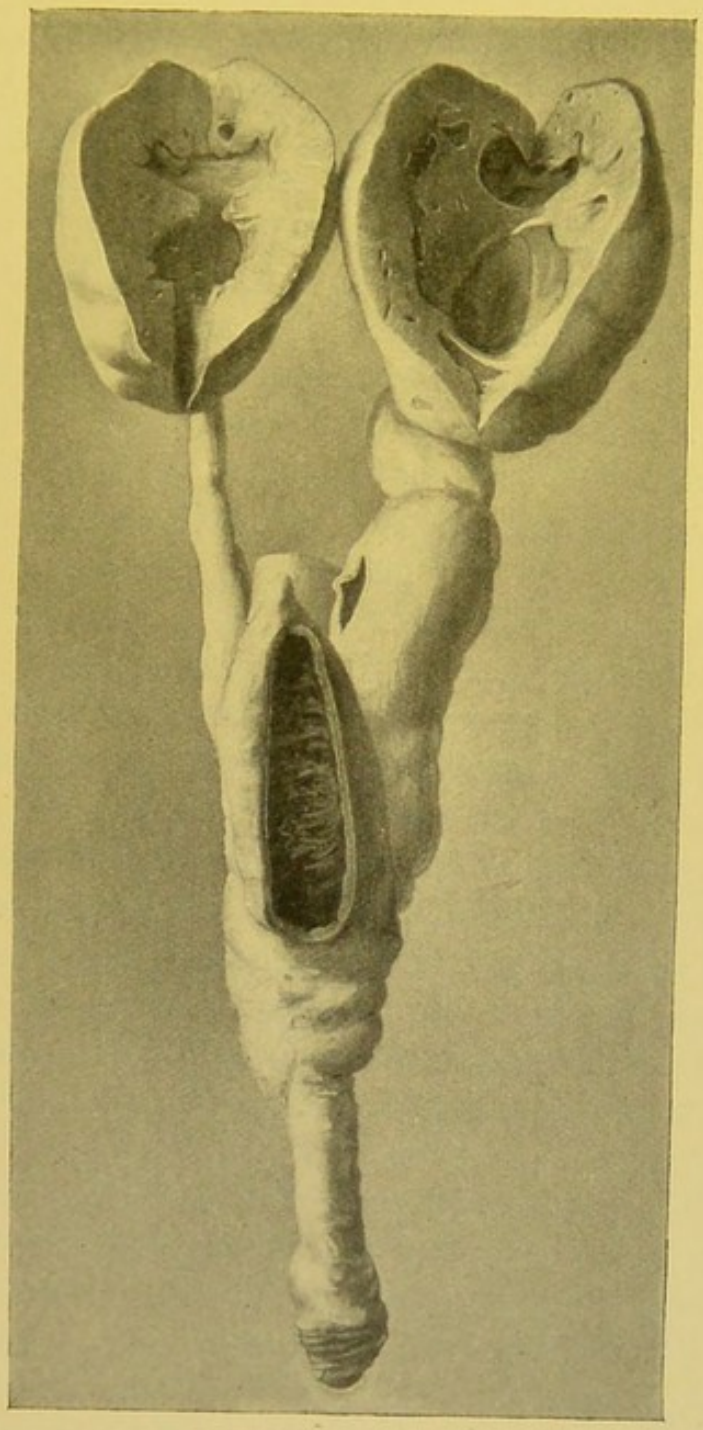

FIG. 26. Double hydro-nephrosis with dilatation of the ureters due to phimosis. From the museum of St. Bartholomew's Hospital.

accidentally. But the majority complained of pain in the side or back. In several there was a constant aching interrupted by acute accesses causing vomiting and, in one instance, fainting.

This sort of attack was followed in some cases by the passage of a large quantity of water, which coincided with the subsidence of the tumour. In more than one case there were symptoms of nephritis, and this was proved by microscopic examination in one kidney that was removed. Hæmaturia had been noticed by a few patients and was seen in the youngest case, a boy 4 years old. New growth was suspected in this case, but none existed. One patient, a man of 34, in whom the condition was due to calculi, complained of nothing but recurrent attacks of vomiting.

The tumour had the characters common to tumours of the kidney. The colon lay in some cases to the inner, in one left-sided case to the outer side. Usually the swelling was not tender, and was hard, elastic or fluctuating, and sometimes lobulated though broadly globular. In one or two cases no definite tumour could be felt, though operation proved the existence of a hydro-nephrosis.

The patients were not febrile, except in a case with nephritis. In the boy 4 years old the leucocytes numbered 15,000, and in another boy aged 11, 34,000.

The urine of the two kidneys was segregated in several, and the secretion from the affected kidney found to be less in quantity than that from the other. In two cases, on the other hand, in which the secretion was equal, the tumour disappeared. A trace of albumen, and a few pus cells, were not infrequently found. Cholesterin was found in the fluid from one case.

The kidneys removed were for the most part useless. The dilated pelvis formed the greater part of the tumour and the renal tissue was thinned out over part of it. In one, an intermittent case however, the renal substance showed much less change.

When hydro-nephrosis is unilateral the prognosis depends upon the health of the opposite kidney. There will always be danger lest the active kidney should be put out of action by a calculus, or be impaired by inflammation. Apart from this, however, such a tumour occasionally ruptures, and it may by its size interfere greatly with other organs.

In a few cases massage has caused the urine to escape and the tumour to disappear. In several instances a cure of hydro-nephrosis has been effected by tapping the sac. After one, or more often after several tappings, the tumour has in these cases failed to recur. The points for tapping are, on the left side, just anterior to the last intercostal space; on the right, midway between the last rib and the iliac crest, between 2 and $2\frac{1}{2}$ inches behind the anterior superior spine of the ilium (Morris).

Neither of these methods is, however, free from danger.

As a rule, therefore, when there is a hydro-nephrotic tumour an exploratory incision should be made, and the subsequent proceeding should be determined after kidney and ureter have been thoroughly examined.

Hæmato-nephrosis.

In 1904, a labourer, aged 31, was admitted under me for pain in the loin of a fortnight's duration. It began suddenly and was severe enough to make him vomit three times. It lasted a week and then gradually lessened. For the first four days he had passed blood with his urine. He said he had been subject to such attacks since he was a boy, that they were becoming more frequent, and that he had never passed a stone or gravel.

He looked ill and his temperature was 100·6° F. There was a slight serous effusion in the left pleura. The urine was of average quantity, neutral, sp. gr. 1023, and contained no albumen or blood. Two days later the temperature was still slightly raised and a tumour was felt in the left loin. The tumour, which had all the characters of a renal tumour, grew until it at last reached beyond the mid-line above the umbilicus. By this time the temperature had fallen to normal. The skiagram showed no shadow. On November 1st the urine amounted to 59 ounces, and was otherwise natural. Mr. Lockwood operated through the abdomen. The tumour was a distended kidney. A trochar drew off 3 quarts of altered blood. No stone or other cause for hæmorrhage was discovered. The edges of the

opening were united to the abdominal wound. A thin, clear discharge followed, and lasted till the man left the hospital. I heard from him in 1910 that the sinus had been healed for two years, that he had had no further attack, and that he was able to do light work.

In 1898 Rose Bradford reported a case of a large hæmatocele of a kidney which was the subject of hydronephrosis caused by calculus (*Trans. Path. Soc. of Lond.*, xlix. 171).

In our museum is a kidney from a case of hæmorrhagic variola, in which the pelvis is completely filled with blood-clot. A similar specimen is from a patient who died of purpura. In neither of these cases was the kidney enlarged. When, as in Bradford's case and mine, a large, solid, and perhaps growing tumour is found, it will almost certainly be mistaken, as both of ours were, for new growth.

Pyo-nephrosis.

A pyo-nephrosis is a collection of pus within the pelvis which is sufficient to produce a tumour that has lasted a considerable time. It is usually secondary to hydronephrosis. But in some the affection seems to be primary, like an empyema.

Of 24 cases of which I have the notes, 9 are males, 15 are females.

The ages are as follows :—

10–20	2 males	0 females
20–30	2 ,,	4 ,,
30–40	1 ,,	3 ,,
40–50	3 ,,	6 ,,
Over 50	1 ,,	2 ,,

Two cases occurred after confinement, one of which was tubercular ; in one case, a man of 18, there was a stricture in the course of the ureter, one case was secondary to cystitis caused by traumatic paraplegia, another to traumatic urethral stricture, eleven were due to calculus, two to cancer of the prostate or bladder. Six cases were unexplained. One which died was dissected without any cause being

discovered. In five of the calculus cases there were calculi in both kidneys.

Many cases are found post mortem which are not detected during life, and of these, as in hydro-nephrosis, a large number are bilateral.

In the majority of these cases there is a history of pain for a long time, and perhaps of frequent micturition, pyuria, or hæmaturia. But in a certain number the onset is more rapid, and occasionally it is sudden. Some, for instance, are cases of pyelitis during pregnancy with retention of pus. Two of this series are of that nature. One case in a woman began quite suddenly, while she was at work, with violent pain and vomiting.

The tumour of pyo-nephrosis is like a hydro-nephrotic tumour in most points. But it is generally much more tender. It is apt to give rise to a peri-nephritic abscess, as happened in four of this series.

The symptoms are generally much more severe than in hydro-nephrosis. The patients are more wasted and exhausted. There is often a marked hectic fever. It is by no means common to find any large quantity of pus in the urine, and when it can escape freely there is usually no fever. Sometimes even when the pus is pent up the temperature is not raised, and then the diagnosis is very difficult. There is not always a leucocytosis, though it is found in most cases. Cystoscopy and segregation of the urine will show that the affected side is not excreting, but may not reveal anything further. Usually, however, there is either pyuria or hectic fever, and these distinguish the condition from hydro-nephrosis.

Pyo-nephrosis is in itself an exhausting disease and is usually due to serious causes, such as calculus. It often leads to peri-nephritic abscess, which is a dangerous condition. The prognosis is therefore doubtful. Seven of these patients died. Four of them were calculous cases. I watched one case for five years. When first seen she was 24 years of age and then had calculi in both kidneys. She had always, however, free passage for the pus, and though thin and

delicate, and occasionally suffering much pain, she had hardly any fever throughout. A man who died at 26 had suffered with paraplegic cystitis after a fall seven years before. His legs had recovered, but there was dilatation of both ureters, and double pyo-nephrosis. He died of uræmic coma. A man aged 32 had had an operation on his kidney seven years before. He died of collapse after nephrotomy. The kidney contained 2 quarts of pus. A man aged 44 had an operation for renal calculus two years before and had passed calculi since. He died the day after admission. No post-mortem examination could be made. Four cases whose history was deficient had double calculus, and two cases had cancer. Probably six or seven years is a common duration of pyo-nephrosis.

When bilateral there is little to be done beyond palliative measures. When unilateral the kidney should, if the opposite one is sound, be removed. Occasionally the second will turn out to be diseased, even though it was thought to be sound at the time ; and occasionally the symptoms are so severe that the patient will have a better chance with one kidney, even though this is known not to be quite sound, than with two.

CHAPTER XXVII

PERI-NEPHRITIS AND PERI-NEPHRIC ABSCESS

In many, perhaps in most cases of chronic nephritis with fibrosis, the capsule is unduly adherent to the surrounding parts, which are themselves indurated by fibrous tissue, and the fat of the renal pelvis is increased. This change, partly an adiposis, partly a fibrosis, is so common as to leave no doubt that the peri-renal tissues react in much the same way as the kidney itself, and that a chronic peri-nephritis coincides with a chronic nephritis. This condition is seldom of clinical interest. In the chapter on hæmaturia I have, however, related a case in which at the operation for suspected calculus nothing was found but chronic peri-nephritis. It is possible that in some instances pain in the kidney such as this patient suffered may be found to depend upon this condition.

Sometimes peri-nephritis is found on one side only. A man, aged 45, died of ascites in the course of tertiary syphilis. He had gummata in the skull and in the liver. The right kidney was natural. The left was small and firmly imbedded in a coating of fibrous tissue about half an inch thick. There was no obstruction to the ureter, no dilatation of the pelvis, and no appearance of gumma in the kidney itself. It seemed probable that the mass of fibrous tissue was of syphilitic origin (Fig. 27).

Other processes occur acutely. Injury may produce almost any damage to the structures. There may be hæmorrhage into the pelvis of the kidney, into its substance, between the capsule and the gland, into the peri-nephric tissues independently or through a rent in the renal capsule. The kidney may be bruised, or lacerated, or torn right across, or reduced to a pulp. The renal vessels may be ruptured, or aneurysms may form on them later at the seat

of some slighter injury. Such cases cannot as a rule be accurately diagnosed, but the history of the injury, the

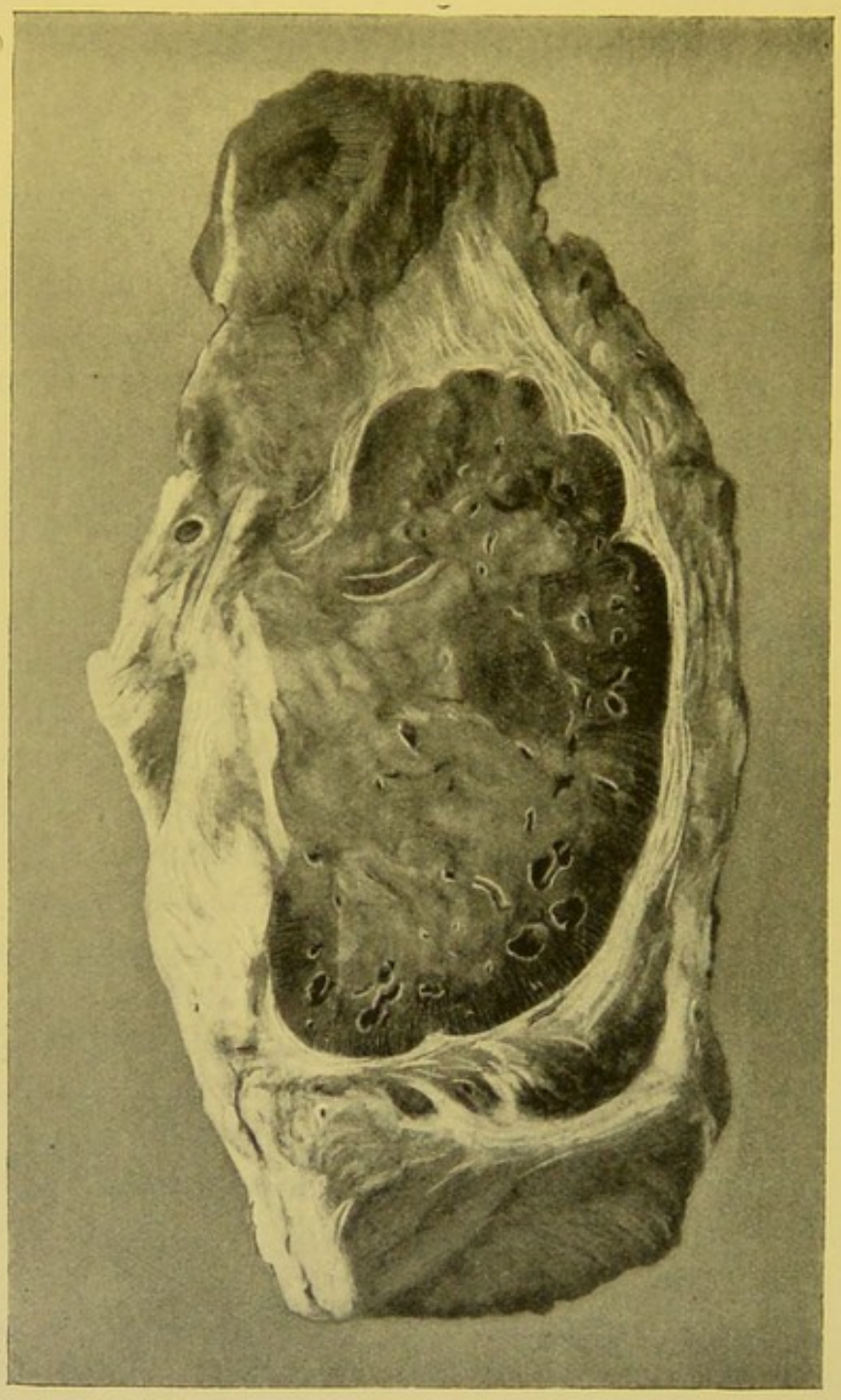

Fig. 27. The left kidney imbedded in a mass of fibrous tissue—perinephritis—from a man who was the subject of severe tertiary syphilis. From the museum of St. Bartholomew's Hospital.

symptoms and the signs are usually sufficient to show that some serious damage has been done. The symptoms are

hæmaturia and renal pain. Both are usually present, but neither is constant. Exceptions are met with in which there is hardly any pain, and others in which no blood is passed. The signs are those of a tumour, perhaps increasing in size under our eyes, spreading from the renal region. When a large artery is torn, the blood will pass behind the peritoneum upwards, downwards and toward the opposite side, until perhaps the patient may die from internal hæmorrhage.

The presence of the tumour depends upon the amount of extravasation, and when the blood is confined within the capsule of the kidney it may be impossible to discover any tumour.

Cases recorded by Sir Henry Morris[1] show that effusion of blood within the renal capsule may be caused by muscular strain alone.

Injury may again cause abscess in the peri-nephric tissue, and the same result may be produced by infection from within. It is not uncommon for pyo-nephrosis to infect the surrounding tissue. Suppuration in or around the bladder or rectum or female pelvic organs may spread up along the ureters. Appendicitis or cholecystitis on the right side and ulceration of or abscess round the sigmoid flexure on the left may also infect the cellular tissue in the loin. In many cases the exact cause cannot be traced.

Of 29 consecutive cases treated at St. Bartholomew's, 14 were male, 15 female. The ages were as follows :—

Under 20	1 male	1 female
20–30	4 males	3 females
30–40	5 ,,	6 ,,
40–50	0 ,,	3 ,,
50–60	4 ,,	2 ,,

The 4 male cases over 50 years of age, and one of those between 30 and 40 were secondary to disease of the perinæum, urethra, or bladder. Two of the former, a man aged 26, and a boy aged 7, were the subjects of calculus. In a man, aged 33, a whitlow was followed first by a perineal abscess, and a month later by a tender lumbar tumour, which gradually

subsided under fomentations. The remaining male cases were sudden in onset, and no cause was discovered.

Both the females above 50 years and two other women aged 47 and 37 respectively had calculus. A woman, aged 46, had cancer of the bladder. In two cases the symptoms began after confinement, and in one after typhoid fever. In three there was a long history of attacks of pain, reaching in one patient to 12 years, on the affected side. In only two female cases was the onset sudden.

Almost all of these cases were verified by operation. The disease occurred with equal frequency on each side of the body.

The symptoms are local and general. Hectic fever, rigors, sweats, malaise, emaciation, and anæmia are among the latter. Pain in the loin, radiating in the directions common to renal pain, and some alteration of the urine, albuminuria, or hæmaturia, or pyuria, among the former. Pyuria may however be due to a coincident pyo-nephrosis or cystitis. In our cases the commonest thing was to find a trace of albumen, and to see a few pus cells under the microscope. The local signs are induration of the lumbar region with rigidity of the muscles and tenderness. Since much of the peri-nephric tissue lies behind the kidney, the swelling has a greater tendency to spread backward than in the case of a renal tumour, and the hollow of the loin is obliterated or there is bulging there. There may be hard œdema, or even reddening of the surface. But the effusion when pus is found may spread forwards too and then a tender tumour is palpable from the front. It is usually fixed and does not move with respiration, but resembles a renal tumour in its relation to the intestine. Sometimes the kidney is thrust forward, and is easily palpable from the front.

The relations of such an inflammatory swelling to the fasciæ covering the psoas, the quadratus, and other neighbouring muscles, which fasciæ themselves become inflamed, produce great pain on extension of the thigh or when the trunk is held upright. In consequence the thigh tends to

be partially flexed, and the trunk is bent to the affected side. In two of our cases pain was felt in the knee.

The diagnosis of a case of this kind is always difficult and varies according to the presence or absence of a palpable tumour. Where such a tumour exists it has to be distinguished from other tumours in that region. It is often the result of injury and therefore an extravasation of blood might be present. But in practice there is not much difficulty on this score. An extravasation forms within the first day after the injury and the symptoms are those of collapse rather than of suppuration. If the patient live and the extravasation is not evacuated it is likely to become infected and to form an abscess. An injury to the loin may result in a traumatic aneurysm. The distinction from abscess will be the same as in extravasation, and there will in most cases be pulsation to be felt and a bruit to be heard.

Renal or adrenal new growths do not give the general symptoms of abscess, and though the relation of an abscess to the intestine and other organs may be the same as those of a renal tumour, bulging in the loin, and brawny induration of the tissues are absent in the case of renal tumour.

Pyelitis or pyelo-nephritis produces a tender swelling and the general symptoms of suppuration, but in those that I have seen there has not been any question of a peri-nephric abscess. The tumours have been circumscribed and movable, and there has been no lumbar bulging or induration. Even when the peri-nephric abscess is secondary to suppuration within the kidney there is little difficulty in diagnosing the former though the pyo-nephrosis may remain undiscovered.

Where there is no tumour evident, and the disease has not yet gone beyond inflammation, the difficulty of diagnosis is much greater. Sir Henry Morris points out how hard it may be in such cases to exclude vertebral caries, hip disease, and even lumbago and renal neuralgia. Most of us have seen a good many cases of pain in the back which we have not been able to explain. Some of them are severe and persistent, and I suspect that the possibility of peri-nephritis

is not often enough discussed. An abscess too small to be felt may produce marked symptoms.

In the early stages, or the slighter forms of this condition, cases which complain chiefly of pain, and do not present definite symptoms of suppuration or the signs of a tumour, it would not be right to perform any operation. Rest and fomentations or poultices are the first things to apply. Pharmacologists tell us now that the skin is impermeable to anodyne liniments. It may be so. Judging from the effect on patients I should doubt it. Belladonna and laudanum have both seemed to me effective and I shall continue to use them. Aspirin can be given by the mouth, and if necessary morphia. The bowels must be well opened, and the general treatment should be that of a patient acutely ill.

If the symptoms do not subside suppuration will be suspected. It must be remembered that a small abscess is often impossible to feel, and on the other hand that it is very important to operate early. It is right, therefore, to explore as soon as reasonable grounds exist for suspecting pus. In some cases exploration may seem at the time to have failed, but afterwards pus will break through into the wound that remains. Exploratory puncture with a syringe is not to be recommended. If exploration is done at all it had better be done through a free incision. The pus is often very foul.

It is dangerous to leave any such abscess alone because it tends to spread. It may pass upwards and either perforate the diaphragm, or set up an empyema by infection without actual perforation. If the lung has become adherent a pulmonary abscess may be formed. Or again it may pass downwards along the psoas and open in the groin, or in the thigh, or into the pelvis.

The treatment should, therefore, always be to explore and drain. When this is done the majority of cases which are not dependent on incurable disease of the kidney, or other organs, recover. The sinus, however, takes a long time to heal. Of our cases eight proved fatal. Four of these were old-standing cases of calculous pyo-nephrosis in which

a secondary peri-nephric abscess had formed. In one instance it caused general peritonitis. In a fifth case, a man aged 26, there was also a calculus in the kidney and pyo-nephrosis, but there had been no symptoms of these, and he had been suddenly taken ill only two weeks before admission. The sixth case, in a woman, was secondary to cancer of the bladder. One patient, a woman aged 35, died with a very large abscess which had invaded the psoas, and a man, aged 55, died with a peri-nephric abscess and pyelo-nephritis on the left side which was apparently secondary to severe cystitis. How the latter was produced there was no evidence to show. It was an acute and rapid case.

REFERENCE.

1. Morris, *Surgical Diseases of the Kidney*, i. 150.

CHAPTER XXVIII

SYPHILIS, TUBERCULOSIS, AND LARDACEOUS DEGENERATION

Renal Syphilis.

We do not hear much in England of the connexion between renal disease and syphilis. As before mentioned, some authors have ascribed cases of chronic nephritis with fibrosis, occurring in children, to congenital syphilis. Abroad, the question has been studied in stillborn or premature children.

Massalongo [1] reported the case of a syphilitic infant which died six months after a premature birth. The appearances found were those of diffuse nephritis, and included glomerular changes, endarteritis, and fibrosis. The same conditions were observed by Seldowitsch, by Pawlow, and by Hecker.[2] Karvonen [3] laid stress upon the delay in development which occurred in these infants, producing kidneys which at full time were embryonic in character. The same observation was made by Störk.[4] Cassel [5] found extensive disease in the tubules and glomeruli, and changes rather slighter in degree in the connective tissue and blood-vessels. Cellular infiltration around the vessels, and endarteritis are mentioned as the chief vascular changes by several of these authors. Herxheimer [6] gives a review of the whole subject.

Some French authors speak of albuminuria as common in the secondary period. When present it appears to be symptomatic of a diffuse nephritis not distinguishable from the usual form. Lancereaux only remarks that 'it is met with' at that period. Mr. H. J. Paterson writes to me, 'In my experience (at the Lock Hospital) a temporary albuminuria is not uncommon in the secondary stage, but a subacute or acute nephritis is very rare. I have seen three bad cases.

I have also seen a good many cases of subacute or acute nephritis in the tertiary stage.' The prognosis appears to be favourable as a rule, but Fordyce's[7] patient died of uræmia, and he mentions one or two other fatal cases.

At a later stage syphilis produces two changes in the kidney, a gummatous deposit, and lardaceous degeneration. Gummata in the kidney are certainly rare. Of ten cases of visceral syphilis (gummata in the liver or spleen or both) at St. Bartholomew's, not one showed gummata in the kidneys. In one of them the kidneys were marked by numerous scars, which might have been the result of former gummata. In five the kidneys were granular. In the remainder they were either lardaceous or natural. Spiers in 147 cases of syphilitic disease found lardaceous degeneration of the kidneys 42 times, and gumma only 7 times. Wagner[8] found lardaceous kidney 35 times, gummata only twice, and granular contraction much more frequently. Lancereaux in 20 cases of visceral syphilis only once found gummata in the kidneys.

A very remarkable case was reported by Bowlby.[9] The patient, a woman, aged 40, was treated in 1893 for a movable kidney. A year later the kidney had grown much larger and was painful. The urine was 45 to 55 ounces in quantity, and contained a trace of albumen, but no blood or casts. There was no history of hæmaturia, but a distinct history of syphilis 21 years previously. The kidney was thought to be affected by new growth and was excised. It weighed 17 ounces and was practically nothing but a mass of gummata. It must have been useless, for the urine remained just about the same after as before the operation. Four years later the patient was well and the urine normal in all respects. The specimen is in our museum.

In the preceding chapter is related a case in which a fibrous peri-nephritis, on one side only, was probably the result of syphilis.

It appears to me to be at once impossible to deny, and difficult to prove the existence of a chronic nephritis due to acquired syphilis. There is nothing in any of the accounts

given of it to distinguish it from the ordinary form. The latter is so common that it necessarily occurs in a large number of persons who have had syphilis. The natural incidence is probably even greater in the syphilitic than in ordinary persons, for, while it would be untrue to say that every syphilitic person is a reckless liver, it is true of the mass, and this tendency would naturally increase the incidence of renal disease. I do not, therefore, consider that any direct connexion is established between syphilis and nephritis, except in cases where albuminuria and other symptoms of true nephritis appear for the first time in the course of active secondary or tertiary syphilis.

There are a few such cases, and when they occur they usually recover under anti-syphilitic treatment.

In the great majority of cases I think the coincidence is fortuitous. In them anti-syphilitic treatment is only of use for the symptoms of active syphilis. It has no effect for good upon chronic nephritis and many have thought that it was harmful. It would be a great misfortune for patients if we began to give mercury, iodide of potassium, or arsenic, to patients with nephritis, merely because they have had syphilis.

Renal Tuberculosis.

Cases of tuberculous infection of the kidney from some old focus elsewhere in the body, are usually but a part of a miliary tuberculosis affecting many organs. In such cases the kidney is not the most important part involved. Meningitis, or miliary tubercle of the lungs are such severe diseases that the urine may be difficult to collect, and a trace of albumen, or even a little blood, may be laid to the charge of the fever or cyanosis which they cause. After death there are seen tiny transparent specks just projecting from the surface of the kidney, or minute white dots in its substance, which have been distributed there by the blood-current.

Sometimes, if the disease which proves fatal is of a less rapid nature, the tubercles have time to develop and begin to caseate. I remember a man, aged 39, who had had chronic

tubercular disease of his serous membranes. Pleuræ, pericardium, and peritoneum, were all affected, and he died of strangulation of the base of the heart. There were yellow tubercular deposits in the pyramidal portion of each of his kidneys.

This method of infection usually affects both kidneys, and the deposits have not time to grow very large.

But there are at least two other ways in which we see the kidneys attacked by tubercle of a more massive kind.

In some cases the affection is certainly primary in the kidney. A woman of 29 died of pneumonia. There were found in the right kidney several deposits of caseating tubercle, chiefly at the upper pole, of which the largest was an inch in diameter. They were each surrounded by a zone of intense congestion, and were entirely confined to the cortex. They had not opened into the pelvis, which, together with the left kidney, the ureters and the bladder, was quite free from tubercle. The lumbar glands were caseous, and there were small deposits in other abdominal viscera, but nowhere else.

When one kidney and ureter, and the bladder are found infected, but the other kidney is not, it is again probable that the disease has started in the kidney.

And again both kidneys may be the subject of advanced tubercle, or in one the disease may be advanced and in the other recent, and yet the bladder and other organs be free.

In all these cases there has been a primary deposit in the kidneys, which no doubt has come from the blood, and in the last mentioned there can be little doubt that the second kidney has been infected from the first, perhaps, through the lymphatics.

In other cases again the kidney is infected from the bladder. It is usual to find both kidneys attacked and for the ureters and pelvis to be diseased also.

Dickinson states that both kidneys are affected together in about as many instances as one separately. It is not quite clear whether he is referring to primary renal tuberculosis alone or not. But I do not think that his statement

is true, at the time it can be verified, namely, after death, even if it be so restricted. The second kidney is unfortunately diseased in much more than half the cases.

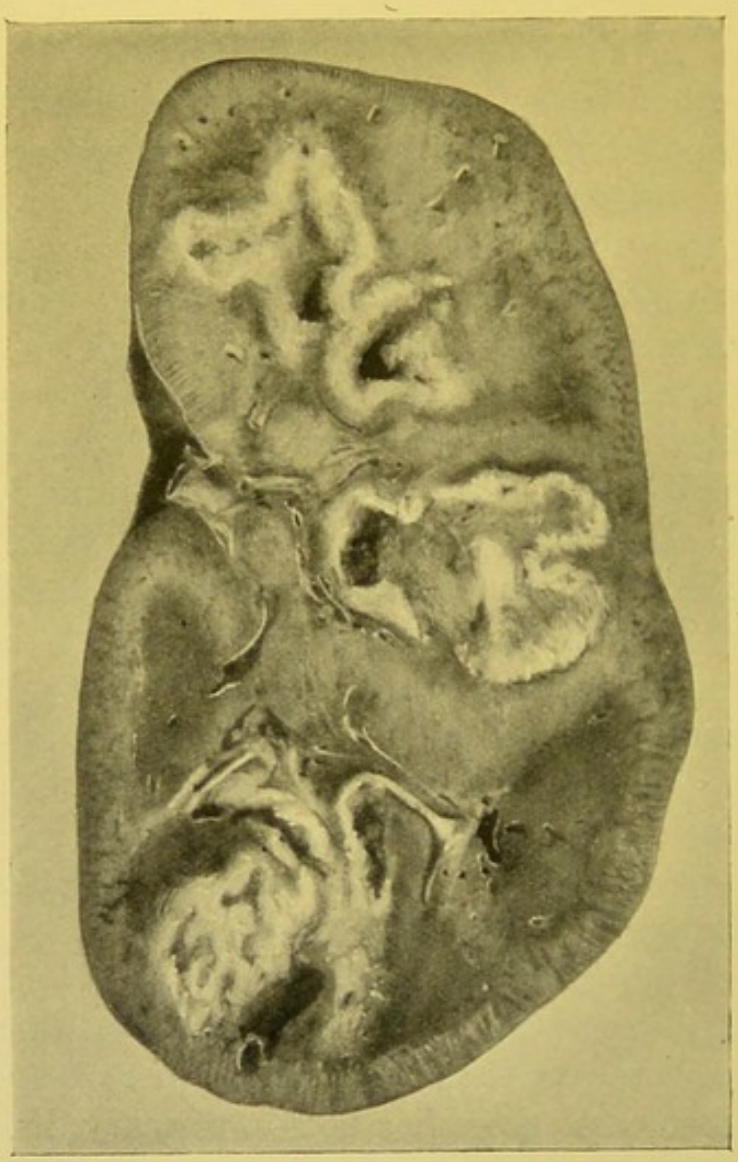

Fig. 28. Tuberculous deposits in the kidney. From the museum of St. Bartholomew's Hospital.

The sexes are equally affected. Of 20 consecutive cases whose notes are before me 10 are male and 10 female. The cases are distributed over the ages as follows:—

Under 10	5	cases
10 to 20	2	,,
20 ,, 30	5	,,
30 ,, 40	5	,,
40 ,, 50	3	,,

The symptoms differ greatly in degree. I have quoted above a case in which the disease was confined to the cortex

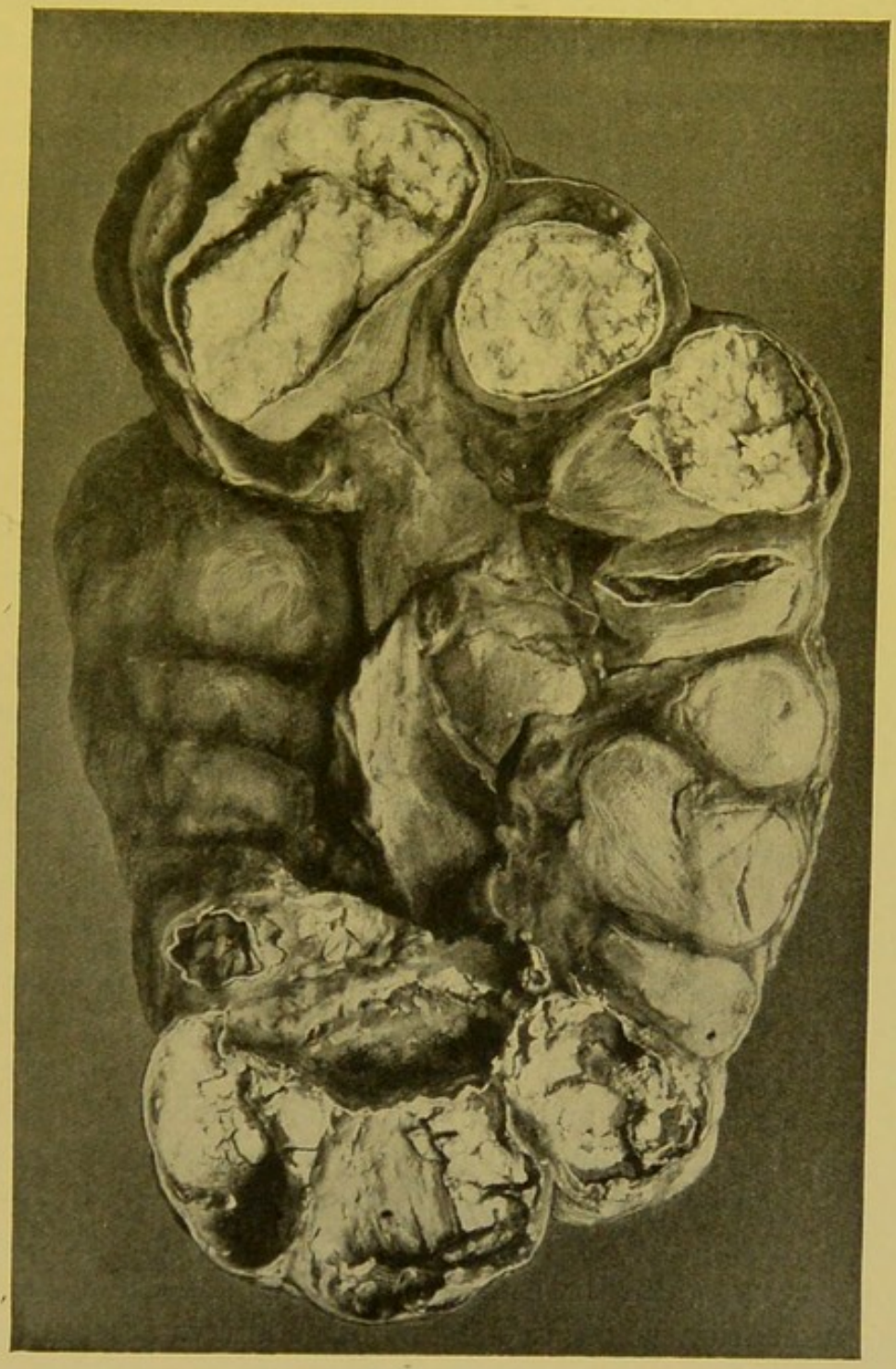

Fig. 29. Tuberculous deposits in the kidney. From the museum of St. Bartholomew's Hospital.

of one kidney. In that instance it was quite latent. There was no lumbar or abdominal pain and the urine showed

nothing abnormal. The woman was only in the hospital five days, during which she had a high fever, and she died of pneumonia, but she gave a history of ill-defined illness for two months previously and was much wasted. She gave the impression of a case of typhoid fever.

As a rule the first symptoms are lumbar pain and frequency of micturition. The pain is sometimes severe like renal colic, at others it is a mere aching. One patient referred the pain to the front of the chest, and complained chiefly of continual vomiting after food. Hæmaturia is not infrequent. In another case micturition was difficult. The patient felt the desire, but could not pass urine. When she micturated the act caused pain.

A tumour was felt in several instances. In most of them the pelvis of the kidney was invaded, and there was a certain amount of dilatation, but in at least one case the tumour was nothing but the kidney itself enlarged by tubercular masses.

Examination per rectum will sometimes reveal tubercular disease of the prostate and of the vesiculæ seminales. In the female a thickened ureter can be felt through the vagina.

A cystoscopic examination should always be made. It will decide whether the bladder is itself affected, which is always to be suspected when there is pain in micturition. The presence of disease in the bladder or prostate or vesiculæ is of importance if there is any thought of operation.

The urine generally contains a trace of albumen, and under the microscope pus cells are seen. If there is much pus it may be taken to mean that the pelvis itself is affected. Mucus when present may be due to the same source, or to cystitis. The urine from the two kidneys should always be segregated and examined separately, in order to get some indication whether one or both kidneys are diseased. But it will be evident from what has been said that even if the urine of one be natural there may nevertheless be already deposits in the glandular substance.

It is not easy, when the kidney alone is affected, to find tubercle bacilli in the urine, even after centrifugalization.

When the bladder or prostate are diseased they can be found readily enough. When the microscope fails, a guinea-pig should be inoculated. They are so susceptible that if the inoculation fails to produce tubercular disease the evidence is worth a good deal. This method should be used in any case of doubt for the secretion of each kidney separately.

The general symptoms are usually well marked. Except in early cases there is commonly, though not always, an irregular temperature. In one of the above series the temperature was subnormal though both kidneys, the bladder, and the prostate were affected. The patients are anæmic, though here again there are exceptions. In one or two cases there was a marked leucocytosis. This is worth noting as it is not the rule with tuberculosis, and might be taken as evidence that a pyo-nephrosis was due to some other infection. Wasting and loss of appetite are common. In several cases vomiting was a prominent feature, and in one case was so severe that the patient was fed by nutrient enemata. Diarrhœa was present in some cases. In one or two this was due to intestinal ulceration, but in others no ulcer was present. Severe headache occurred in two cases. Secondary tuberculosis of the lungs is not uncommon ; small râles will then be heard over the chest.

Of these twenty cases only four went out of the hospital alive, and even they were not cured. It is not fair to make a general statement on the basis of hospital cases for they are severer than the average. Still it must be allowed that tubercle is more difficult to eradicate from the genito-urinary tract than from the lungs or intestines. Occasionally we see the results of a spontaneous cure where a caseating kidney has dried up, has become infiltrated with lime salts, and so remains a greasy or mortary body from which all renal, indeed all living tissue, has disappeared. It no longer gives rise to any symptoms, and in course of time shrinks to a small mass.

Apart from this unfortunately rare issue the disease, I believe, usually progresses until the patient dies, either from the loss of both kidneys, or from the exhaustion which

the disease of the lower passages causes. Occasionally by occlusion of the ureter a dilatation of the pelvis is produced, and a form of pyo-nephrosis results. Tubercle is, however, a rare cause of pyo-nephrosis, and the fluid found in the pelvis under these conditions is not quite the same as in that due to staphylococcus or *Bacillus coli*. It is less purulent and more caseous.

It is difficult to tell how long these cases may last, because the first appearance of symptoms may not mark the beginning of the disease. Two patients had had symptoms, in each case pain and frequent micturition, for six years. In one of them the bladder was not affected, so that the frequency of micturition was not due to cystitis. But the other cases were shorter. The shortest lasted only three months.

Patients usually die by asthenia, but in two cases death was quite sudden.

If the disease could be discovered while it is in an early stage, general treatment by fresh air, sunlight, abundant food and tonics might well be expected to have good results. But I have never seen at autopsies any evidence of healed tubercle in the kidney such as we are familiar with in the lung. It is not uncommon to see scars in kidneys, for which we cannot readily account. These, on microscopic examination, are found to be patches of fibrosis. But the small calcareous specks which mark obsolete tubercle in the lungs do not occur in the kidneys. If tubercle of the kidneys recovers it leaves nothing but fibrosis behind it, and its former presence cannot be proved. Belief in recovery must rest upon clinical evidence, and there is very little of that. The truth is that we cannot get proof of the disease until it is so far advanced that obsolescence is highly improbable.

When it has reached the stage at which we can recognize it, the stage at which urinary symptoms begin, it has not only formed caseous masses of considerable size in the renal tissue, but it has also broken into the pelvis. I do not believe that then the disease can be cured, and we cannot promise that any method of treatment will produce that spontaneous cure by massive desiccation which I have already described.

The chief question to decide is whether the disease can be removed. If it can be localized to one kidney and ureter, and there is no evidence of disease of the other side or of the bladder, nephrectomy is the right treatment. Every surgeon can report cases where the operation has been successful and the patient has survived for many years. These cases are cases of primary tuberculosis of the kidney. It is a very different matter when the kidney has been infected from below. The probability of bilateral disease is much increased, and the presence of tuberculous disease in the bladder almost precludes operation.

Vaccination with tuberculin should never be preferred when nephrectomy of a single diseased kidney is possible. It is only where this cannot be carried out that vaccination should be considered. It has been highly recommended by some surgeons. But it seems to me that the more familiar vaccination becomes the more hesitatingly are its claims put forward. Though it is no doubt at present the right treatment in inoperable cases we cannot rely upon its effect. It should be given in gradually rising doses and according to a certain rule. I myself begin with ·00001 of a mg. of human bacillary emulsion, and inject twice weekly rising at each injection. The series runs ·00001, ·00002, ·00003, ·00005, ·00006, ·00008, ·0001, ·0002, and so on. If the temperature rises more than one degree after any injection I miss the next time due, and the time after give the same dose as caused the rise. If the rise occurs again I give the next smaller dose. The treatment should be continued for several months.

In some cases I have known even these doses produce such pain in a tubercular bladder that they had to be stopped.

At the same time, of course, the patient should be put in the best possible conditions and palliative treatment given as well. Urotropin, tincture of belladonna or of hyoscyamus, liquid extract of pareira and infusion of buchu or bearberry leaves are useful. The best in my experience is buchu tea made fresh at the patient's house by pouring

a pint of boiling water on an ounce of the leaves and draining it off after standing for five minutes. Half a tumbler twice a day relieves the irritation more certainly than anything I know.

When there is pyo-nephrosis it is often advisable to open the kidney from behind and drain it even though there is infection of the bladder or other kidney.

Lardaceous (Waxy, Amyloid) Degeneration.

Lardaceous kidneys are large and hard; the capsule, unless there is chronic nephritis in addition, peels easily; the edges do not evert when the organ is cut open; the glandular substance is yellowish white in colour, and the separate parts are indistinct. If a solution of iodine is poured over the cut surface small mahogany-coloured streaks and points appear in it in a little while. In some cases this colour turns on the addition of a weak solution of sulphuric acid to a dirty green, a violet, or occasionally to blue. If a microscopic section be made and stained with methyl-violet, the same areas stain pink, while the rest of the tissues stain blue. The areas so staining are the connective tissue about and in the walls of the small arterioles, the capillary walls, and the glomeruli. Where this change takes place the nuclei and all cell structures disappear.

The change was first identified by Rokitansky in 1842. It seems that one of Bright's original specimens of large white kidney which he thought nephritis, was really lardaceous. Virchow gave it the name Amyloid under the impression that the colour reaction indicated the presence of a carbohydrate body. This appears, however, not to be the case. We call it lardaceous, as Rokitansky called it bacon-kidney, because it resembles boiled bacon fat.

Friedreich and Kekulé[10] showed that lardacein was a modification of protein, and they were confirmed by Pavy and Odling.[11] Oddi (1893) found that the material contains chondroitin-sulphuric acid. Neuberg[12] stated that the proportions of N, of S, and of S as sulphate, and of un-

oxydized S, differed in different organs. The most marked difference was between that in the aorta and that in the viscera. Green [13] believes that lardacein has often been confused with hyalin. The two have the same structureless appearance and affect the same tissues but there are differences in colour reaction between the two. Hyalin gives no true iodine reaction. Though it stains pink at first with methyl-violet the colour fades quickly even when mounted in glycerin, Farrant's solution, or normal saline solution. It also loses all pink colour when dipped in a 1 per cent. solution of hydrochloric acid. Lardacein retains the pink colour in all these conditions.

He figures both changes occurring at the same time in the same tissue, and believes that hyalin is probably a precursor of amyloid. Litten also has seen the two changes occurring simultaneously (discussion on Neuberg's paper). Lazarus-Barlow states that, by selecting specimens, a series of staining reactions can be produced passing gradually from those of typical lardacein on the one hand to typical hyalin on the other.

Lardaceous disease occurs in other animals besides man. It has been found in cattle, sheep, fowls, pheasants, and horses, as a product of natural disease whose cause is not in any case known.

The chief British statistics on its occurrence in man are those of Fagge and Pye-Smith from Guy's Hospital, of Charlewood Turner from the London Hospital,[14] of Dickinson, chiefly from St. George's, of G. A. Gibson from the Royal Infirmary of Edinburgh [15] and of Kenneth Pretty from St. Bartholomew's.[16]

At Guy's, of 546 cases

211 were associated with prolonged suppuration other than pulmonary phthisis.
188 ,, ,, ,, pulmonary phthisis.
119 ,, ,, ,, syphilis, in many cases combined with prolonged suppuration.
28 ,, ,, ,, other conditions, none of which were repeated sufficiently often to establish a causal connexion.

At Edinburgh, of 430 cases

110 were associated with prolonged suppuration other than pulmonary phthisis.
193 ,, ,, ,, pulmonary phthisis.
75 ,, ,, ,, syphilis.
20 ,, ,, ,, heart disease following rheumatism without any of the above causes.

At St. Bartholomew's, of 75 cases

50 were associated with prolonged suppuration.
14 ,, ,, ,, pulmonary phthisis.
11 ,, ,, ,, syphilis (2 with tuberculosis also).
1 ,, ,, ,, rheumatism and heart disease.

Beattie[17] relates four cases of the association with rheumatism and heart disease and without either tubercle or syphilis.

A case has been related to me by Dr. Hugh Thursfield in which lardaceous disease was found in the body of a girl, aged 9 years, who died with rheumatoid arthritis of seven years' duration at the Children's Hospital in Great Ormond St. There was typical disease of the liver which was enormous, of the spleen, of the kidneys, and of the intestines, and there was the adherent pericardium which Still noticed as not infrequent in these cases. I showed at the Royal Society of Medicine in 1909 a case which I now believe to have been of this character. The patient is still alive.

Cases of malignant disease occasionally show lardaceous change after death.

Sometimes, as in two cases of pulmonary phthisis that I remember, lardaceous disease is associated with true nephritis.

Occasionally it is found unexpectedly. Thursfield and I, while examining a series of kidneys, found it in the case of a woman, aged 67, who died of chronic nephritis, gout, and cardio-vascular-changes ; in a man, aged 50, who died of chronic bronchitis, emphysema, and fatty heart, and more curious still, in a man, aged 21, who died of typhoid fever. He had a few small caseous foci at one apex, but they were not, I should have thought, at all adequate to explain the

marked lardaceous disease of his spleen and kidneys. There was no evidence of syphilis in any of these cases.

Litten, in the discussion of Neuberg's paper, stated that both he and Wagner had seen cases of lardaceous disease in which no other lesion existed. Hansemann said he had seen the same thing.

It is not certainly known whether the lardaceous change is an infiltration into the organs from the blood, or a degeneration. The latter is the view generally accepted. The iodine reaction is occasionally observed in tube-casts passed in the urine and in plugs found after death in the tubes (see Dickinson, vol. ii, pl. xi, p. 501), which looks at first sight as if the material were derived from the blood. It is not, however, to be found in the blood itself. If the casts which stain brown with iodine really contain lardacein, which is, I think, doubtful, it is perhaps produced after the exudation has taken place. It is not a common phenomenon, and I have often failed to find it in cases of lardaceous change. I have also found casts which stained brown with iodine in the urine of a case of phthisis which after death did not show lardaceous change, but only hyalin, in the kidneys. Lardaceous degeneration has been experimentally produced by Krawkow,[18] Davidsohn,[19] and Green,[13] who all used cultures of staphylococcus pyogenes aureus, and produced suppuration in animals and fowls by injecting it under the skin. There is some discrepancy between their results, but they all agree in the possibility of its production by this means. Under these conditions the disease is rapid. Krawkow's rabbits all died within two months, and he found the change as early as eleven days. The organs, however, are not like those of ordinary human cases. They are soft, and have not the shiny look of the lardaceous organ in man. This is true of the spontaneous disease in horses also. It is said that this softness may be connected with the acuteness of the process. Acute cases have been seen in man. Dickinson relates one in which the change was found three weeks after the compound fracture which caused death took place, but he does not mention that the kidneys were different from the

ordinary hard, lardaceous kidney. Again, Krawkow and Green noticed that both water and alcohol dissolved out of such organs a body which when recovered by evaporation gave the reactions of lardacein, and left the organs thus macerated incapable of giving these reactions. But in the human subject lardacein is known to be very insoluble. Such properties are at least as important as staining reactions, and it cannot, therefore, yet be definitely concluded that the experimental change is the same as the spontaneous.

In a very curious case reported by Hadley [20] the organs had the microscopic appearance of lardaceous disease, but gave none of the staining reactions.

In any patient with long-standing suppuration, such as chronic phthisis with cavities, or an unhealed empyema, we naturally examine the urine systematically for albumen. Its appearance is usually an indication of lardaceous change. In such cases the urine is at first copious, and of low specific gravity. The albumen is in large amount, and casts are present. As already mentioned, the proteid quotient of these cases has been observed with much care, but with no certain or constant results. After a time œdema comes on, and may reach a severe degree. At this time the urine diminishes in quantity. The heart does not hypertrophy, the blood-pressure does not rise, and albuminuric retinitis does not appear. Uræmia is rare. The patients usually die rather of the exhaustion of their original disease than of their kidneys.

The lardaceous change has been found after death in cases which during life showed no albuminuria. A man, aged 20, was admitted under me with phthisis and tubercular meningitis of which he died in five days. The urine was of sp. gr. 1020 and contained no albumen, but after death there was slight lardaceous degeneration of the kidneys, and a considerable amount in the spleen.

It has often been questioned whether lardaceous disease is curable. In the absence of post-mortem examination the diagnosis of cured cases is not perhaps quite certain. Such cases are not likely to occur in medical wards, as in our

patients the disease which causes lardaceous change is usually, such as chronic phthisis, incurable. But surgical cases are different. Sir Anthony Bowlby, who is surgeon to the Alexandra Hospital for Hip Disease, writes to me, 'I have often seen the enlarged amyloid liver and spleen gradually decrease, and become practically normal. I have also seen the diarrhœa and albuminuria pass away, but I am sure that the kidneys are more slow to recover than the liver, and less certain to recover completely.'

By his kindness I have seen one of his cases illustrating this statement. A boy, then aged 5, was admitted in February 1905 with hip disease of four months' duration. There was no albuminuria until April 1906 when a trace was detected. In December 1906 the liver was found enlarged, reaching about two inches below the ribs. In 1907 albuminuria continued, sometimes rising to as much as one-twelfth of the volume of urine when allowed to settle in a test-tube. In November 1907 it was no longer to be found. In December the liver was much smaller, and was hardly palpable below the ribs. During this time several small operations had been performed on the sinuses that were discharging about the hip. In 1908 albumen was again found, but disappeared in November. The boy meanwhile improved greatly, the symptoms about the hip disappeared, the sinuses closed, and in January 1909 he was discharged. In June 1910 he was again seen. The liver was not palpable. He was walking about, though, since one leg was rather shorter than the other, he used a crutch. I examined him in October 1911. He walks without pain. The sinuses have remained healed since his discharge, and the liver does not extend below the ribs. The urine is clear, acid, sp. gr. 1020, but on boiling there is a faint opalescence just detectable when compared with the unboiled urine, and permanent on the addition of acid.

Where the process is due to syphilis the proper treatment is to use iodide of potassium in combination with arsenic and iron, or the Liq. Arsenici et Hydrargyri iodidi of our Pharmacopœia. In other cases the iodides are not likely

to be of use, but iron, arsenic, and cod-liver oil should be given. In all a nourishing diet, fresh air, and sunshine, are of great importance. If the case is one of long suppuration surgical measures may perhaps be taken, but often it must be recognized that operation is of no avail.

References.

1 Massalongo, *Archivio per le Scienze med.*, 1895, 215.

2. Hecker, *Deutsch. Arch. f. klin. Med.*, lxi. 1.

3. Karvonen, *Die Nieren-Syphilis*, Berlin, 1901.

4. Störk, *Wien. klin. Woch.*, 1901, 958.

5. Cassel, *Berl. klin. Woch.*, 1904, xli. 558.

6. Herxheimer, *Lubarsch-Ostertag. Ergebnisse der allg. Path.*, Jahrg. xii, 1908.

7. Fordyce, *Journ. of Cut. and Genito-Ur. Dis.*, 1897, xv. 151.

8. Wagner, *Lubarsch-Ostertag. Ergebnisse*, &c., Jahrg. xi, 1. Abth., 1906.

9. Bowlby, *Trans. Path. Soc. Lond.*, 1897, xlviii. 128.

10. Friedreich und Kekulé, *Virch. Arch.*, 1859, xvi. 50.

11. Pavy, *Guy's Hosp. Reports*, 1864, x. 315.

12. Neuberg, *Verhandl. der deutsch. pathol. Gesellschaft*, 1909, i. 19.

13. Green, *Journ. of Pathol. and Bacteriol.*, 1901, vii. 185.

14. Turner, *Trans. Path. Soc. Lond.*, xxx. 520.

15. Gibson Thesis, 1887, quoted by Beattie and Dickson, *General Pathology*, p. 62.

16. Pretty, Cambridge Thesis, 1911.

17. Beattie, *Brit. Med. Journ.*, 1906, ii. 1444.

18. Krawkow, *Arch. de Méd. expér. et d'Anat. pathol.*, 1896, viii. 106.

19. Davidsohn, *Virch. Arch.*, 1897.

20. Hadley, *Trans. Path. Soc. Lond.*, 1899, l. 134.

CHAPTER XXIX

RENAL CALCULUS

At St. Bartholomew's in ten years, 1896–1905, our clinical records show the following statistics for the occurrence of renal and vesical calculus.

	Males.							*Females.*						
Age	–10	10–	20–	30–	40–	50–	60–	–10	10–	20–	30–	40–	50–	60–
Renal	2	8	29	24	20	4	4	1	3	22	14	6	6	1
Vesical	26	14	7	10	5	15	13	3	0	1	0	3	1	1

The great difference between the two suggests that it would not be safe to suppose that the pathology of the one was the same as that of the other.

Our post-mortem records are different again. I have taken the renal cases alone, and those only who have died in the medical wards, so that I might obtain the morbid associations. In this I have been considerably disappointed.

DEATHS WITH RENAL CALCULUS

	Males.							*Females.*						
Age	–10	10–	20–	30–	40–	50–	60–	–10	10–	20–	30–	40–	50–	60–
No. of Cases	7	0	5	7	5	5	5	3	0	1	6	2	2	4

These cases comprise the total number in whose bodies renal calculi were found over a period of 41 years. Very few of them had symptoms of calculous disease in life.

There were five children under 2 years old with small calculi. In one case there were two in the right kidney, and one in the left. The patients died of broncho-pneumonia,

or diarrhœa, or tuberculosis. One boy of 5 years died with a cystin calculus. Both kidneys were granular.

One man died at the age of 37 with a stone in his right kidney weighing 76 ounces, and one in his left weighing 21 ounces. He had had gout from the age of 27.

There were 22 cases in which the right kidney alone, and exactly the same number in which the left kidney alone, contained calculi. In 9 there were calculi in both.

The stones when confined to one kidney were solitary in 32 cases, in 12 there was more than one stone.

The composition of calculi has been stated variously. Cadge of Norwich (1874) said that in his experience nine-tenths of all calculi were formed of uric acid or urates, Bence Jones put the proportion at three-fourths, Roberts at five-sixths. A table composed by Dickinson from all the museums in London gave different figures. He found 91 cases of renal calculus in which the stone had been chemically analysed, of which 52 contained only one ingredient, and 39 were compound. Where the stone was uniform it was made of uric acid or urates in 24 cases, and of salts of lime in 24 cases. Where it was compound, uric acid was found 19 times, urates 21 times, oxalate of lime 25 times, and other salts of lime 31 times. In the last year or two some analyses have been made at Liverpool which are very different. Rowlands,[1] analysing 22 cases that were operated upon by Mr. Thelwall, found that in 19 of them there was no uric acid or urates at all, and only traces in the other 3. Oxalic acid, usually combined with lime, was found in every one. Mackarell and Benjamin Moore [2] made quantitative estimations of 24 other calculi similarly obtained. Two of them were vesical calculi, and were almost wholly made of urates. The remainder were renal, and were all composed chiefly of calcium oxalate and phosphate, the former greatly preponderating, with in many cases a little uric acid in addition. Thus 44 renal calculi were found to be almost entirely composed of lime salts.

I dare say the great preponderance of uric acid stones in the old calculations was due to the fact that most of the

stones they saw were vesical. That does not, however, hold true of Dickinson's table of renal calculi. If the Liverpool analyses are corroborated in other parts of the country, we shall have to conclude either that the character of calculi has changed, or that the old analyses were wrong. I notice that 11 of Dickinson's cases came from our museum. In our catalogue there are 15 renal calculi whose composition is mentioned, but in none of them is the analysis made quantitatively. I should be sorry to rely on qualitative analysis when it was opposed by quantitative. We shall have to re-examine some of our old stones. I do not see why the character of calculi should have changed. There is no sufficient change in diet or habits, especially among the poor, to make this at all likely.

The Liverpool authors upset former ideas also in another way. Most of us are accustomed to rely on the physical qualities of calculi, and to say that a smooth red stone is made of uric acid, a hard mulberry stone is oxalate of lime, and a rough mortary stone is at any rate externally phosphatic. But both these papers insist upon the unreliability of such conclusions.

The clinical associations of renal calculus are interesting. Sydenham said it was especially common in the gouty: 'Hic porro notandum quod Podagrici fere omnes, postquam cum hoc morbo diu conflixere, calculo renum sint obnoxii.' Authors have repeated this ever since. The age-distribution of our cases from the clinical records does not bear him out. Gout is not commoner from 20 to 40 years of age than at other times, and the infrequency of calculus after 50 makes the connexion even more unlikely. I find that in the post-mortem cases the joints of the great toe were examined twelve times for this connexion. In 2 cases a deposit of urate of soda was found; one of them was the man mentioned above, the other was a man of 51 years of age who died of renal disease, and had a branched calculus in his right kidney. In 10 cases there was no deposit of urate in the joint.

Lesions of the kidney, chronic fibrosis, pyelitis, pyo-

nephrosis, and peri-nephric abscess occurred a few times in the post-mortem records. The majority, however, died of causes not connected with the kidney, and so various that no one of them seems to have any affinity to calculus.

Calculus was said by Cadge to be connected with hard water. But the curve of frequency, according to the number of deaths, does not follow the chalk ranges of England. I do not know that the deaths from Norfolk dumplings, which have been said to cause calculus, are numerous enough to allow of reliable statistics.

The pathology of calculus admits of a broad division. The phosphatic deposits are all of them produced when the urine is alkaline, especially when the urea is decomposed by fermentation into ammonium carbonate, and the conditions which occur in the body can be reproduced in the laboratory with very similar results. Alkalinity of the urine, which is the common result of chronic pyelitis or cystitis, sufficiently explains their precipitation.

Cystin calculi are, as already stated, a class apart.

In considering uric acid, urates, or oxalate of lime, we have first to decide whether their deposition is due to their excessive formation in the system. If so, the principal questions will be those of the metabolism of nucleins, and of calcium, and of the formation of oxalic acid. Of the last two factors the base is likely to be the more important. We have in our museum a specimen which in this connexion is of great interest. A boy of 17 years of age was admitted with fibrous ankylosis of several joints. The disease was, and remains, obscure. But after death it was found that the bones were the subject of some wasting process which had reduced the tibia, for instance, to a mere shell. He had hundreds of small stones composed of oxalate and phosphate of lime in both kidneys, and in one of them some larger calculi of the same formation. It seems probable that the lime salts which had been in the bones, had been absorbed, and that at any rate one of the causes of the calculi was that these salts were in excess in the blood, and in the renal excretion.

If the connexion of calculi with gout is real, and if such

calculi are formed of uric acid, it is probable that the excess of uric acid or rather of urates, in the blood, may be one of the factors in their formation.

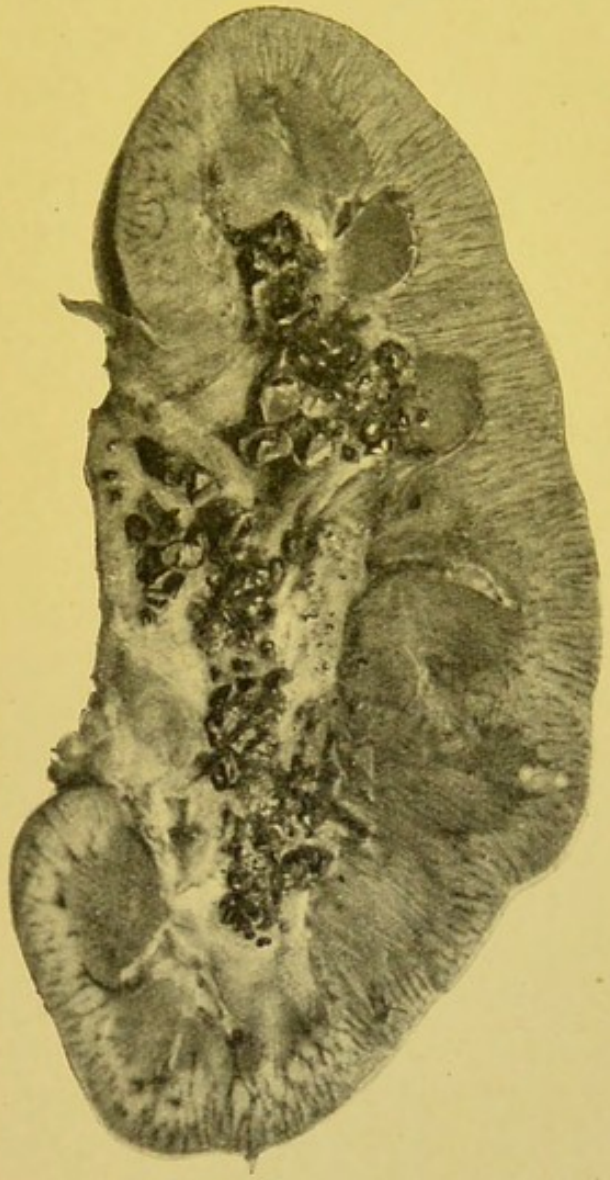

FIG. 30. A kidney with numerous small calculi of oxalate and phosphate of lime from a boy 17 years of age. From the museum of St. Bartholomew's Hospital.

A large number of uric acid or uratic calculi, however, are found in children. These are perhaps more plausibly connected with the deposits of these substances which are not uncommonly found in the tubules of infants. It has been suggested that they are due to a great amount of tissue change in the infant body, combined with a small intake of

fluid, which would render the urine highly concentrated. Such deposits when once formed would, it is supposed, attract

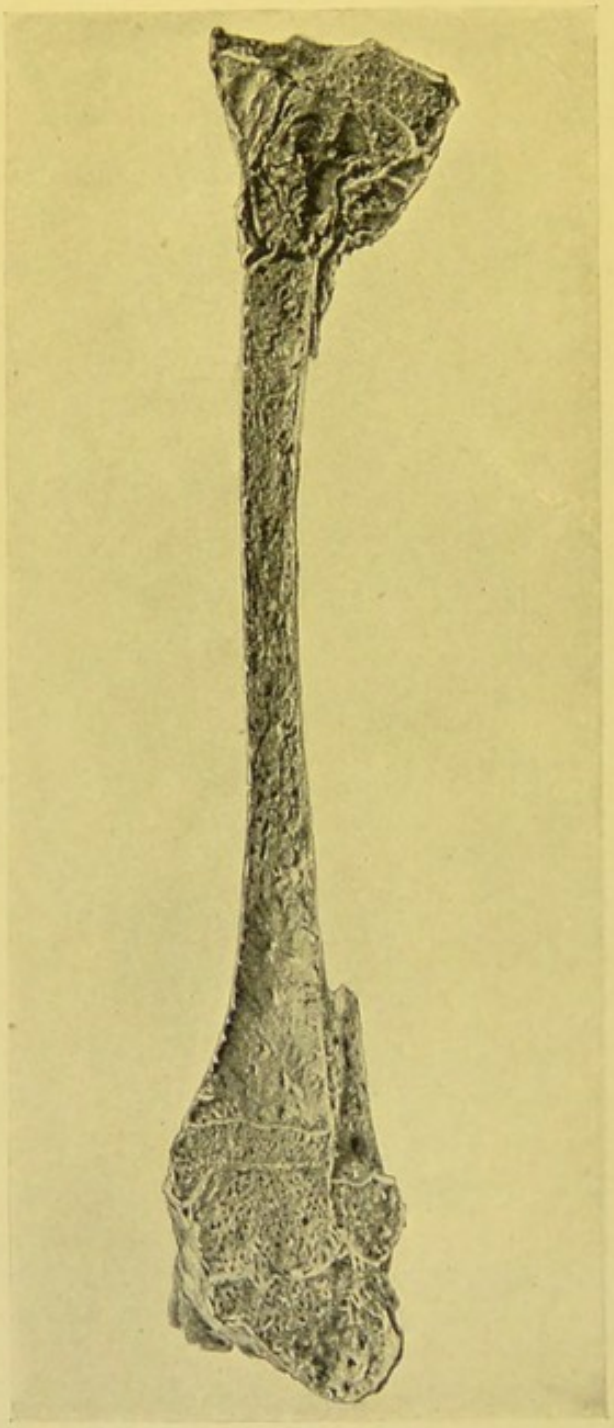

Fig. 31. A tibia from the same case showing wasting of the bone. From the museum of St. Bartholomew's Hospital.

fresh deposition, and lead gradually to the formation of calculi.

It is a remarkable fact that calculus in children is almost entirely confined to hospital practice. I have been told by many surgeons that they have never seen a case in the well-to-do, and that the late Sir Thomas Smith, who had a very large experience of children, never saw one. This looks as if the causation of calculus was connected with the feeding of the infant.

The above suggestion introduces beside the excess of the salt in the blood, a second factor in the kidney itself. It is possible that a third also comes into play.

Many years ago Ord applied Rainy's observations on the precipitation of salts in viscid fluids to the formation of calculi in man, and stated his belief that the presence of mucus or albumen was necessary to concretion. I have standing before me a 100 c.c. cylinder which I filled twenty-four hours ago with the urine of a strong healthy man, aged 40, who is in the habit of passing uric acid gravel. The urine was clear, neutral sp. gr. 1022, and contained neither albumen nor sugar. I added some acetic acid and left it to stand, wishing to see if any nucleo-albumen would separate. To-day it is perfectly clear. On the glass are many little colourless specks. There is no sediment. Each of these little specks is shown under the microscope to be some sort of colloid, probably mucus, full of uric acid crystals. This is just what Ord observed. The examination of calculi has shown that many contain a nucleus of organic matter, Fagge states that Bilharzia leads in Egypt to the production of large vesical calculi, and the recent observation that gall-stones are usually formed round an infective nucleus has led many of us to think that some such local inflammation is necessary for the formation of renal calculi.

When a stone has formed, it may cause no symptoms whatever. As a rule it gives rise to some whose severity varies greatly in different cases. Pain is the principal. It is of two kinds. There is often a dull aching, and this is interrupted by bouts of acute and violent, or even agonizing pain when the calculus is jolted out of place or, if it is a small one, becomes engaged in the ureter. The pain is often severe

enough to cause vomiting, and sometimes the patient faints. It is first felt in the loin and then, as any renal pain will, it radiates along the course of the last dorsal and upper one or two lumbar nerves, passing round the abdomen over the outside of the ilium and thigh (xii dorsal) or down the groin to the testicle, and down the inside of the thigh to the knee (i and ii lumbar). The second symptom is hæmaturia. It occurs with the pain, and is due to the injury which the stone by its movement causes to an already inflamed mucous membrane. It is not as a rule copious. Both pain and bleeding are lessened by rest and increased by movement. It is not infrequent for them to be obviously started by a bump or shake.

If the stone is small and slips into the mouth of the ureter the involuntary muscle of the duct catches it and passes it on. The contraction of the muscle against resistance, and the rough surfaces of the stone together can produce awful torture. The passage may last a week or even occasionally longer. When the stone reaches the bladder the relief is enormous. Frequently it is passed through the urethra shortly afterwards, but it may remain in the bladder and set up inflammation there.

Sometimes a calculus is single. A patient passes one, and never has any more symptoms. But frequently there are several in a kidney and often there are calculi in both kidneys. Sometimes a calculus is so shaped that it is easy to see the mark of another calculus upon it and to predict a repetition of the symptoms. Occasionally, as in the last case quoted, they may be very numerous.

A calculus which remains in the pelvis of the kidney generally sets up inflammation there. This is probably the cause of the aching pain. The stone can seldom be felt unless the kidney is much enlarged. There is, however, generally some tenderness in the loin. A stone can be sometimes felt in the ureter.

If it sticks in the ureter it may partially or completely block it. The first result is hydro-nephrosis and this is readily turned by infection into pyo-nephrosis. Even without leaving the kidney a stone may cause dilatation of

the pelvis. Sometimes it has another curious effect. We have a specimen in which complete fatty degeneration of the kidney has taken place. Microscopically, the greater part of the organ consists of nothing but adipose tissue intermixed with delicate connective tissue. In one or two places remains of gland structure can be seen. In another case the kidney has become sacculated, and the pelvis has then been obliterated by a dense growth of inflamed fat and fibrous tissue.

To hydro-nephrosis or pyo-nephrosis succeed peri-nephritis and peri-nephric abscess. The stone may ulcerate through into the colon, or an abscess may burrow in all directions.

When spasms of pain are accompanied by hæmaturia, calculus is the first thought that arises. Hæmaturia occurs also in renal growths, but there is often no pain in such cases and the bleeding goes on, it may be copiously, for long after the patient has been put to bed. In fact, it is not influenced by movement as the bleeding from stone is. Renal hæmaturia also occurs from many minor causes such as from a temporary oxaluria caused by eating rhubarb, from tubercular or pyæmic deposit, from 'essential' hæmaturia, and from granular kidney. When calculus is suspected, the urine should be searched for crystals of uric acid or oxalate or for those of the triple phosphate. In one of my cases oxalate crystals were found and the stone was rough with a thin coating of oxalates, but the main body of it was uric acid.

A skiagram should of course be taken. If the shadow can be clearly seen it is very satisfactory evidence. But in many cases no shadow is cast by a small uric acid stone, and I have known the same thing happen with a small oxalate calculus. In a good many cases doubt must remain. For instance, I saw a little girl, aged 14, who had had an attack of pain and hæmaturia. It had lasted a few hours only. The urine showed no abnormality, the skiagram was blank, and she had no return of the symptoms. I do not see what is to be said in such a case except that calculus is the most probable cause. In other cases an

essential hæmaturia may come with attacks of pain, and will deceive the very elect. Luckily, it apparently does these patients good to explore the kidney.

The treatment of renal calculus may, if the symptoms are slight, be simply preventive. In many cases there are only two or three, or perhaps only one small stone, and there is always the hope, especially if the skiagram is negative, that such is the state of things. In such a case a patient should be advised to live simply and drink copiously of water. Whatever the exact process may be, it seems certain that they are less likely to be deposited if the excretion is copious, and not only that, but also there is some ground for believing that a small stone, especially if of uric acid, can be gradually and slowly diminished by the passage of copious and watery urine. When hæmaturia has followed after eating special things, such as rhubarb, it is obviously right to forbid them, but we know too little about the pathology of calculus to be able to discriminate usefully between ordinary articles of diet. As regards oxalates at any rate it seems that the amount of lime in the food is as important as the amount of oxalic acid. We undoubtedly know that free living both in meat and drink tends to produce calculi, and any patient with symptoms should be temperate and moderate. I should certainly forbid any acid wine, or malt liquor, to a patient with calculus.

There are not any drugs which are of great value. When the urine is very acid it is easy to render it less so by the use of citrate or bicarbonate of potash, and it should be done. But the simple alkalies are the best for this, and there is no special virtue in lithia water. Piperazin (gr. v to xv) has been recommended as a solvent for uric acid, but appears to be without any real effect.

In the actual attack of renal colic the chief thing is to relieve the pain. Hot fomentations, and especially a very hot bath, often give great relief. An injection of morphia succeeds when these fail. Stones felt in the ureter have been helped onward by massage.

The question of operation must be settled for each case

on its merits. No one who has been through a severe operation, and operations on the kidney are severe, will lightly recommend a patient to do likewise. A young person in a first attack has a fair prospect of escaping for the future. An elderly person with damaged health, especially if there are signs of chronic nephritis, is a dangerous subject. It is also not improbable that there are stones in both kidneys. Still, even in some such cases, especially if there is pyo-nephrosis, the risk of operation is less than that of letting the disease alone. The cases in which there is least doubt are those in which there is no evidence of structural disease of the kidney, the patient is in good health, the skiagram shows a stone on one side but not on the other, and the patient has had several attacks of renal colic.

References.

1. Rowlands, *Bio-chemical Journ.*, 1908, iii. 346.
2. Mackarell and Moore, ibid., 1910, v. 161.

INDEX OF SUBJECTS

INDEX OF NAMES