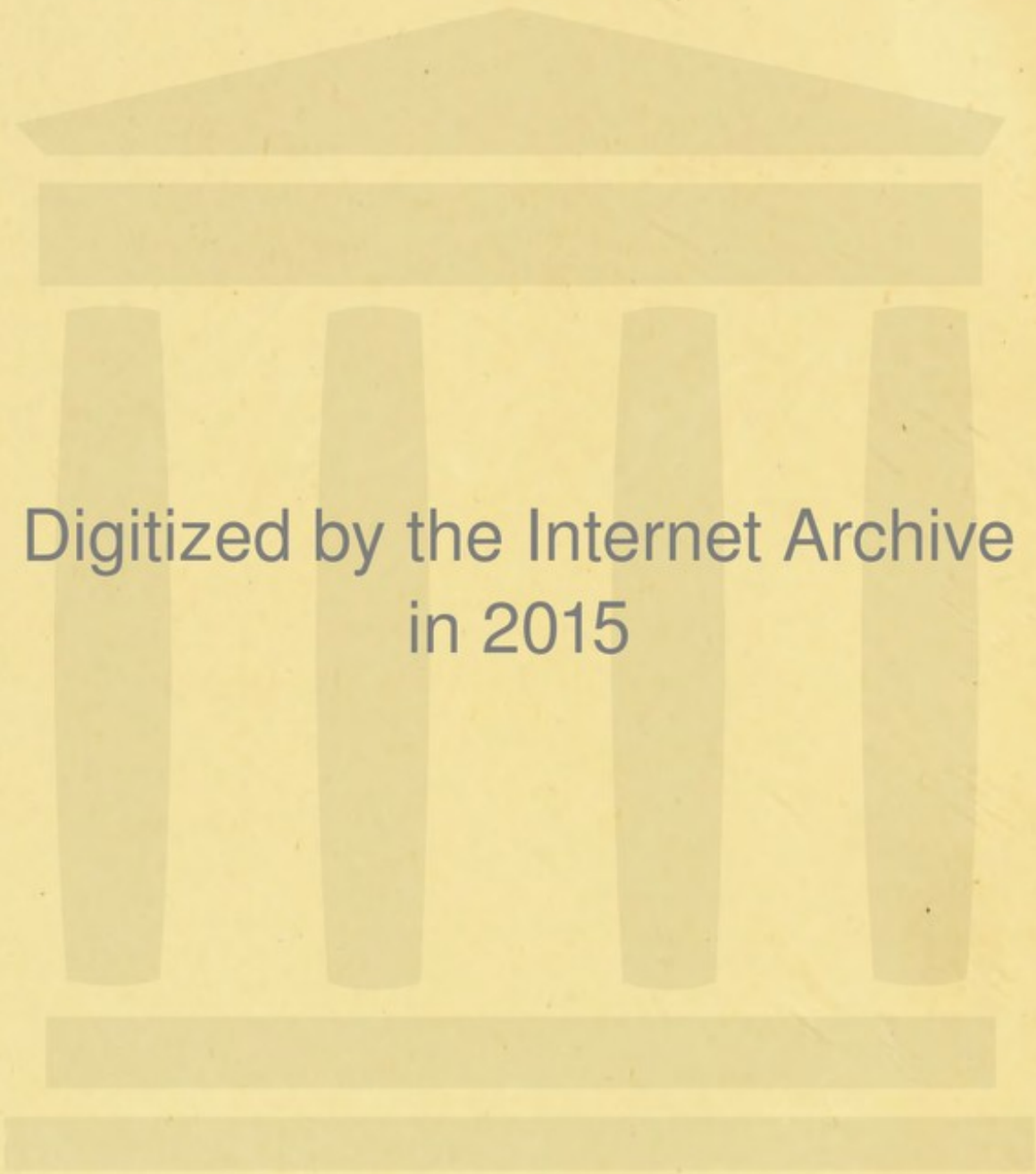
Bright's disease of the kidney / by Alfred L. Loomis.

MODERN TREATMENT OF BRIGHT'S DISEASE

ALFRED L. LOOMIS

Fig. 86.



BRIGHT'S DISEASE

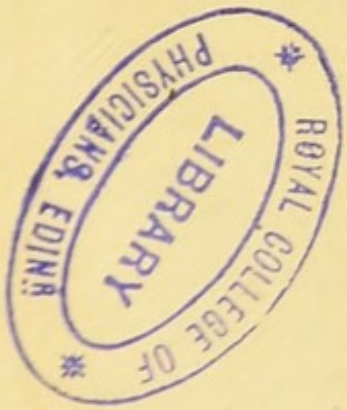
—OF THE—

KIDNEY.

—BY—

ALFRED L. LOOMIS, M.D., LLD.,

Professor of Pathology and Practice of Medicine, New York University Medical College; Visiting Physician to Bellevue Hospital: Consulting Physician to St. Luke's, Mt. Sinai Hospitals, Etc., Etc.



1888:
GEORGE S. DAVIS,
DETROIT, MICH.

BRIGHT'S DISEASE.

Scientific history of diseases of the kidney begins in 1827, when Dr. Richard Bright, Physician to Guy's Hospital, London, published the first systematic work on this subject based on accurate clinical observations. The scattered and solitary references to morbid states of the kidney of earlier authors, although in some cases accurate descriptions of the gross pathological appearances, were never so connected with clinical histories, either in the printed record or the mind of the observer, as to suggest any intimate relation between the two. Cruikshank, and later Wells, of St. Thomas' Hospital, and others had observed the appearance of albumen in the urine coincident with dropsy in various parts of the body, and had even seen the kidneys atrophied and cirrhotic, but failed to recognize any causal relation in the renal change, and regarded the dropsy as the primary condition, the albuminuria as dependent upon hæmic or other constitutional changes and the kidney affection as accidentally coincident. When, therefore, Bright pointed out the frequency of such renal changes, and not only their coincidence with, but pathological relations to albuminuria and dropsy, giving minute descriptions and drawings of the kidney changes, the application of the name Bright's disease to all conditions associated with albuminuria and dropsy, was an appropriate

recognition of his invaluable contribution to renal pathology. So long as the term shall remain, however, it will be impossible to formulate any satisfactory and comprehensive definition. It was early recognized that dropsy, one of the supposed cardinal symptoms, was often absent, and the name thus became synonymous with albuminuria even in the nomenclature of the College of Physicians. A second difficulty was encountered in the fact that the renal changes associated with both albuminuria and dropsy varied very greatly in character. Bright, himself, recognized three forms of kidney disease and was uncertain whether they should be regarded as distinct diseases or stages in a single process. Subsequent pathologists have taken opposite courses in their attempts to elucidate the matter.

Frerichs, in 1851, advocated the theory that the varied appearances presented by the kidneys formed successive stages of one process, in which the large white or fatty kidney represented the earlier or inflammatory stage, and the small granular or atrophic kidney was the final condition to which every case might come unless the processes were arrested, or interrupted by death.

Wilkes, Johnston, Traube and others, on the other hand, not only pointed out that the pathological changes found in the large white kidney, as well as those of the cirrhotic, constituted separate diseases, with characteristic and distinct ætiology, symptoms

and terminations, but thought it necessary to deny the position of Frerichs.

Later researches, while they establish the distinction clinically, as well as pathologically, between the large white and small hard kidney, also show that in some instances the former may possibly pass into the latter. The confusion and contradictions appear to have arisen largely from the attempts to define the disease and classify its forms and stages upon the basis of the gross morbid appearances. Upon a broad pathological basis we must recognize a unity of character in all forms of Bright's disease and learn to consider the various developments as varied phases of a single process.

Bright's disease may then be defined as non-suppurative inflammation of the kidney, with manifestations determined by its ætiology, the special elements affected and the inherited tendencies of the patient. While it is equally true of the kidney, as of other organs, that no one element is solely involved, yet a predominence of inflammatory changes can usually be recognized in the tubular or connective tissue element, so that Virchow's original distinction of parenchymatous and interstitial nephritis is not only clinically convenient but essentially true, as regards the two most frequent forms of renal disease.

Under a strictly pathological classification the term Bright's disease should be limited to these two forms of renal disease, but as the name still holds its

place quite as much from its clinical significance as from any generally accepted pathological significance, it is customary to include the so-called waxy, lardaceous or amyloid kidney under this head, a condition which were perhaps better described as one of the degenerations and a cause of Bright's disease, as it sooner or later induces both parenchymatous and interstital changes.

It must be recognized that all the pathological changes, except the amyloid, not only may be but usually are present in varying proportions in every case of Bright's disease, and that it is only the marked preponderance of one or the other, which determines the character of the disease. By careful examination it is also possible in most instances to determine in which anatomical element the primary changes were located. I shall describe Bright's disease under the following heads:

1. Parenchymatous nephritis, in which the tubular and functionating elements of the organ are primarily and pre-eminently affected. It is variously known as tubular, diffuse, catarrhal, croupous, desquamative or glomerular nephritis.

2. Interstitial nephritis, in which the inflammatory changes affect primarily and especially the connective tissue elements, both of the inter-tubular tissue and the vascular walls.

It is commonly known as the cirrhotic, hobnail, red granular, gouty or gin-drinkers' kidney.

3. Amyloid kidney, in which a peculiar development, appearing first in the walls of the arterioles, induces inflammatory changes of both cirrhotic and parenchymatous forms. It is also known as the waxy or lardaceous kidney.

While this classification represents better than any other the pathology of the disease, its clinical aspects necessitate a practical classification of simple, acute and chronic Bright's disease, since it is impossible in some instances to determine clinically the exact nature of the renal changes. Some authors have recently added the "cystic" kidney and consecutive nephritis to the forms of Bright's disease. As they do not differ materially, however, from those given, but are rather accidents of development or ætiology, I prefer to include them under the forms already given.

Before entering upon a detailed description of the clinical and pathological manifestations of Bright's disease, there are certain general questions which require consideration. The earlier history of medicine, as of all sciences, shows a tendency to differentiation rather than generalization, due in large measure to the fact that clinical phenomena of a necessity formed the sole basis of medical study while pathological knowledge was slight. At the time of Bright the anatomico-pathological basis was in vogue, with the anatomical element decidedly in the front. Bright's disease was therefore, at that time purely a disease of the kidneys.

A wider development of our knowledge, of

the pathological processes involved, the allied and dependent conditions both of cause and effect, and the intimate relations existing between all the organs of assimilation and excretion and the vascular system, has led to a gradual increase in the comprehensiveness of the term in both pathological and ætiological lines until the climax was attained by Mahomed in stating that we may have Bright's disease (of the kidney?) without lesions of the kidney. The essential point at issue is simply one of nomenclature—as to how much shall be included in the term. While freely admitting the ætiological relations of hepatic disease and hæmic conditions, and believing most fully that some forms of renal disease are often developed as a part of the fibroid diathesis, it still appears to me desirable to confine the term Bright's disease as heretofore to certain well defined lesions of the kidney. There can be no stronger reason for extending the term to include all the manifestations of the fibroid diathesis, than for employing cardiac hypertrophy in the same manner. Either one may be, but neither one is invariably dependent upon the constitutional condition. When the term is thus enlarged, however, acute Bright's must cease to exist and become acute nephritis for it certainly often occurs without previous hæmic or constitutional changes. While thus limiting the term we do not wish to deny, but rather to emphasize the relations which the disease is known to sustain to a general diathesis and to pathological processes, both

functional and organic, in other organs, especially the liver and blood. Putting aside acute Bright's, we have to recognize that both parenchymatous and cirrhotic kidney are often the local manifestations of a more general disease, and that the renal change is the evidence of an excessive functional activity, which has been developed as a conservative process and has become converted into a pathological condition secondarily. Without entering upon a discussion of the ætiology of Bright's disease in particular, or even attempting a resumé of the discussion upon this point, we think it may be stated generally and as covering the point in question, that cases of Bright's disease which are chronic from their inception will be found to develop in two classes of subjects. 1st. Those suffering from the fibroid diathesis in whom all forms of irritation tend to the induction of fibroid inflammation, not only under stimulation, which in other individuals would produce only healthy nutritive activity, but even in what would otherwise be considered purely physiological conditions. 2d. Those in whom, either through an inherited or acquired functional weakness of the organs of direct and retrograde metabolism, or on account of intemperance in food or drink, the kidneys are for a long time called upon to eliminate both an excessive quantity of the normal elements of excretion and products of faulty metabolism. Since tastes, habits and moral qualities are inherited equally with physical defects, we often

find individuals of the first class following those habits which place them also in the second class, until eventually a set of individvals is developed, who combine a marked fibroid diathesis with functionally weak liver, heart and mucous membranes, and for whom, barring accidents, we can predicate death from either apoplexy, cardiac failure or Bright's disease.

It is not germane to our present purpose to discuss physiological and chemical questions as to the nature of all those products of malassimilation or defective metabolism whose excretion by the kidneys so certainly results in fibroid or parenchymatous inflammation of the organ. The essential point which we wish to emphasize is a clinical one, that, while removal of the cause may possibly arrest further developments, injury once inflicted upon the organ can not be remedied. So that, while recognizing the kidney lesion, we should not forget those prior and still present constitutional conditions, which constitute the more important element of danger to the patient. Clinically, then, every diagnosis of chronic Bright's disease implies the recognition of a primary ætiological constitutional disease.

In connection with the general pathology of Bright's disease several common symptoms require special consideration.

1. Uræmia:—Very early in the history of renal pathology it was recognized that failure on the part of the kidneys to eliminate the solid elements of the

urine was sooner or later followed by marked cerebral symptoms which developed in the classical forms of nausea, vomiting and convulsions, indicative of cerebral irritation, or headache, drowsiness and coma, evidencing abolition of nervous irritability. Upon the theory that the nervous symptoms were due to the retention of urea within the system, and its poisonous action upon the cerebral centres, these conditions were called uræmic convulsions or coma, or in general uræmia, and it may be added that not only has the name been retained but that thus far no entirely satisfactory explanation has been given of the uræmic phenomena. Various experiments have been made upon animals to disprove the theory but little definite knowledge has been added. From the clinical side it may be said in support of this view, that uræmia never occurs so long as the excretion of urea by the kidneys remains free, but that failure in this excretion is attended not only by uræmic symptoms but a previous marked increase of the urea found in the blood.

When urea is fed to animals no toxic symptoms are manifest so long as water is supplied in abundance and the renal function remains unimpaired; when, however, through lack of solvent or from sudden injection of large amounts directly into the circulation of nephrotomized animals, the proportion of urea in the blood becomes excessive, symptoms resembling those of uræmia in the human subject are developed. The fact that other substances may induce similar symp-

toms tends to show that urea may not be the only cause of the uræmic attack, but offers no proof that it is not the most important element of urinary excretion which, when retained in the circulation in excess, induces the uræmic phenomena. Analyses of the blood of uræmic patients show not only an increase in the urea, which may reach even 0.6 or 0.8 per cent. from a normal average of 0.04, but also the presence of large amounts of extractives, creatin, uric acid, and various salts.

In connection with the somewhat negative experiments with urea, the presence of these products of tissue-waste has led to the belief that no one element of retrograde metamorphosis is the sole cause of the uræmic attack, but that the general accumulation of waste matter in the tissues, particularly the nervous centres, not only interferes with the normal nutritive process, but becomes a direct local irritant, thus inducing in its milder degrees the convulsive, and in more extreme grades the comatose manifestations of the uræmic state. Nor do those cases of somewhat persistent anuria without uræmic developments negative the above assumption. The uræmic seizure depends upon two very unstable factors. 1. Percent of urea in the blood. 2. Individual susceptibility.

The former of these factors is again dependent upon very variable conditions, the rapidity of tissue-waste and consequent formation of poisonous products, and the vicarious elimination of such elements by those organs so well known to assume excretory

functions in renal failure. Nor can those assumed clinical evidences of the excretion of urea by the intestinal canal, nausea, vomiting, and diarrhœa, be relied upon as accurate indications of the amount of vicarious action going on in any given case. Even carefully conducted experiments for determining the amount thus eliminated, as well as that thrown off by the skin, leave much to be desired.

It must be admitted, on the other hand, that many cases occur in which a large accumulation of urea in the blood is not attended by uræmic symptoms, and that such phenomena are developed in cases where the amount of urea in the circulation is but slightly if at all increased. Such facts have led various observers to consider some other single element as the materies morbi. Traube advanced the theory that the "uræmic" phenomena were due to mechanical effects of cerebral œdema and an anæmia, which was due partly to compression of the cerebral tissues and in part to diminution of the corpuscular elements of the blood, in varying proportions. In many cases of uræmia, however, the brain is shown to be abnormally dry, while in other cases the œdema has been shown to be secondary to the uræmic attack, rather than its cause, or the result of decrease in cerebral tissue from atrophic changes. The latter, of course, only in chronic cases.

Minute capillary hæmorrhages have not infrequently been found in cases of uræmia, and when

present may in a measure account for the convulsions or coma, but are not of sufficiently frequent occurrence to afford any satisfactory explanation of the uræmic seizure.

Of the theories offered in support of a chemical cause of uræmia, that of Frerichs was for a time quite generally accepted. He propounded the theory that the condition was one of ammonæmia rather than uræmia, the poisonous element being carbonate of ammonia, which was formed in the blood by decomposition of the urea. The essential point of this theory was not affected by the suggestion of Fritz, that the decomposition took place in the intestine, of urea which had been vicariously excreted, and that the ammonia was absorbed by the intestinal surfaces.

It has already been shown that, even when present in the blood during an uræmic explosion, the carbonate of ammonia is not found in sufficient quantities to account for the cerebral disturbance, while still further and quite conclusively the phenomena of ammonæmia, as developed when decomposing and ammoniacal urine in the bladder is undoubtedly the source of the poison, are characteristic and markedly distinct from those of the uræmic state. In the former the ammoniacal odor of both breath and excretions is alone sufficient to distinguish it from the state in which the odor of all the patient's exhalations is most distinctly urinous. The vicarious elimination of urea, which often, long before the uræmic seizure, may be

found in all the secretions and may appear in extreme cases during the uræmic paroxysm as crystals upon the skin, proves beyond question that it is an important, if not the sole, cause of the uræmic state.

One fact, which tends to show that certain products, intermediate between the primary products of waste in albuminoid tissue and urea, are largely the cause of uræmia, is found in the condition known as obstructive suppression. It is found that when the ureters are ligated, or when the ureter of a sound kidney, the other being functionally inactive from disease, becomes occluded by a calculus, the blood may contain a much larger proportion of urea without inducing an uræmic attack than is possible when the function of the organs is entirely abolished, and that the attack when developed presents characteristics which render it quite distinct, and allow of its pathological as well as clinical differentiation from uræmia. It would thus seem that these by-products of tissue metamorphosis undergo some change in the kidney which renders them less poisonous to the system, and that urea alone exerts a much less powerful as well as deleterious influence upon the cerebral tissue than do these intermediate products, which have been variously supposed to be kreatin, kreatinin, or leucin and tyrosin. This proposition has the support of so able an authority as Dr. Roberts.

Perhaps the latest experimental investigations of the nature of the uræmic poisoning are those of

Bouchard. While experimentation upon animals is subject to many sources of error and can never replace careful clinical and pathological investigation, yet the results obtained are of extreme value in pointing out lines of investigation. Bouchard's conclusions regarding the sources of the urinary poisons, divide them into four classes.

1. Aliments, and especially the potash salts.
2. Absorbable elements of products developed by putrefactive changes in the intestine.
3. Various secretions, as bile, saliva, etc.
4. Tissue disintegration.

Many interesting clinical facts are at hand which support the theory of a multiplicity of elements in the uræmic poison and which bear out the statement of Bouchard that this poison varies from day to day and even from hour to hour. The varied forms of the uræmic seizure and the several well recognized and yet distinct combinations of symptoms, offer a most forcible argument in favor of such a supposition. Dr. Carter in the Bradshaw lecture for 1888 also cites a remarkable case in which two persons, both accustomed to post mortem examinations, were made acutely ill, with nausea, faintness and diarrhœa, by the exhalations from the body of an uræmic patient who died in sudden collapse, and asks whether the same volatile element which prostrated the examiner was not also the cause of death. It is to be recorded that Feltz and Ritter also claim that the potassium

salts are the only real poisons of the urinary secretions.

While all these experiments have a direct bearing upon treatment which we shall note later, yet the clinical fact remains that urinary suppression, as related to the solid elements of the excretion is the first cause of the uræmia, whether that failure depend upon excessive demands made upon the kidney, or inflammatory changes in the functional elements of the organ.

Since the uræmic phenomena are not specifically associated with any one, but may occur in connection with all forms of Bright's disease, they may properly be described once for all.

Symptoms of Uræmia.—The typical manifestations of uræmic poisoning are convulsions and coma, which may appear singly or in succession. The rapidity with which accumulation of urea takes place, as well as the peculiar nervous condition of the patient determine in part the character of the seizure.

Aside from the general symptoms of renal disease, as œdema, usually about the face or ankles, a pale, waxy skin, and marked lassitude, the acute uræmic attack is usually preceded by symptoms distinctly indicative of nervous irritation. Marked restlessness or a distinct weariness and irresistable desire to sleep, nausea, vomiting, diarrhœa, and impaired vision may continue for days or even weeks before the final outbreak, or they may within a few hours be followed by intense headache and vertigo, which rapidly pass on

to delirium and convulisons. The last, which are not to be distinguished by the convulsion alone from epileptic attacks, may, rarely, be single, but more commonly are recurrent, appearing every few minutes or at intervals of several hours until they either terminate in uræmic coma or death, or are relieved through re-establishment of excretion by the kidneys, skin, or intestine.

During the convulsion the face becomes livid, the veins of the head and neck distended, the eyes rolling, staring and glassy, with contracted pupils, the teeth firmly clenched or grinding, the mouth filled with frothy mucus, which is often bloody from lacerations of the tongue, the nostrils tense and dilated, while the breathing is rapid, shallow, and often irregular and hissing.

The muscular spasms may be bi-lateral or unilateral with a paretic or distinctly paralytic condition of the other side, and may vary all the way from slight twitchings of some muscles to a tonic spasm of all the body with opisthotonos. The pulse, which, according to Wagner, may at times fall to 50 or even 40, is usually rapid and tense, rarely irregular, and the temperature is high, reaching in some cases 107° or 108° in the axilla, even when the convulsive manifestations are slight. In the aged and some few cases a low temperature and restless delirium may be the characteristic symptoms. Death may occur during a convulsion, but more commonly a condition of more

or less profound insensibility which intervenes between the attacks, deepens into absolute coma as the convulsions themselves decrease in intensity and finally cease. Less frequently, sudden coma may occur with the convulsions.

When not thus preceded by convulsions, uræmic coma may be either gradual or sudden in its advent. In the former case headache, giddiness, partial or complete loss of vision, great lassitude and sleepiness more or less rapidly lapse into partial or complete coma. The patient may remain for some days in a condition of stupor, rousing sufficiently to drink or possibly answer questions in an uncertain and far off manner or become so deeply comatose as to resist all attempts to excite consciousness. Less frequently without premonitory stupor or convulsions, coma develops so rapidly as to resemble an apoplectic attack, not only in the loss of consciousness but in the development of paresis or paralysis. Such cases are more frequently developed in connection with the capillary cerebral hæmorrhages, already noted as occasionally present. During the coma, the face loses its turgid appearance and becomes pale and dingy, the eyes are often drawn to one side, the pupils dilated, rarely irregular, and respond but slowly if at all to light, the jaw is relaxed and the sterterous breathing is marked by a peculiar sharp hissing sound not found in apoplexy. The respirations, at first rapid and shallow soon become deeper, slow, labored and often ir-

regular. The pulse is rapid, but weak, and may be irregular or intermittent. Aside from the typical forms the uræmic seizure may present various irregular forms. Rarely the convulsion is unattended by any loss of consciousness, or again the first light spasms may suddenly be followed by cardiac asystole and death.. Again the spasm may be confined to single muscles or pairs of muscles, in a limb, about the eye, face or jaw. Charcot reports cases which simulated the tremors of paralysis agitans. The delirium also, which is usually a short stage preceding convulsions or coma, may be persistent for days, and perhaps be the only as well as prominent symptom of the uræmic poisoning.

When the failure of renal function is gradual, and the accumulation of urea and waste products in the blood is slow, the nervous centres may become "acclimated" to a large excess of urinary poisons, such as will produce symptoms of chronic uræmia not directly referable to nervous irritation. Of such symptoms dyspnœa without cardiac complications, which is usually paroxysmal, resembling asthma, is doubtless primarily of nervous origin, though it is at times associated with more or less œdema of the lungs and larynx. When purely nervous it is apt to be especially expiratory in character. Of less distinctly nervous origin are disturbances of the gastrio-intestinal tract, of which vomiting and diarrhœa are the more constant. The latter especially is believed to be due to local irrita-

tion, either primarily from excretion of urea, or secondarily from decomposition of urea already thrown into the intestine and the formation of ammonia carbonate. Doubtless œdema of the mucous membrane and transudation upon its surface are elements promoting the watery discharge. Persistent intractable vomiting, even unattended by œdema, is at times the only symptom of the uræmic poisoning. Irregular at first, it soon becomes quite constant whenever food is taken. Such persistent vomiting should always lead to an examination of the urine. The cases, which are most typical of chronic uræmia, often present no localized symptoms, but exhibit the results of that malnutrition which is the most characteristic symptom of chronic Bright's disease and failure of renal function. Such cases follow a persistently downward course, with gradually developing emaciation, weakness, mental and physicial lassitude, and general decay, despite every effort at relief. Tonics are of no avail, oil is useless, iron impotent, or even harmful; food is taken, but not assimilated, and the poison-soaked tissues struggle on with failing function, until malnutrition, which is shown in every fibres of the body, causes cardiac failure, arterial rupture or cerebral paralysis. Such patients often die without apparent cause. The steadily progressive weakness slowly invades the nervous centres. Lassitude urges into a mild wandering of the mind, and the attendant mental torpor slowly lapses into low delirium or coma, and a final quiet

cessation of respiration and cardiac action. These patients are often said to have died from senile decay simply exhaustion.

ALBUMINURIA.—Within a comparatively short time albuminuria has ceased to be synonymous with Bright's disease, and pathologists have come to recognize a physiological and pathological albuminuria, the former including those cases of transient or recurrent albuminuria, in which we are unable to recognize any lesion of the kidney. It thus becomes an exceedingly important point to determine when albumen in the urine is significant of organic change, as well as to ascertain what relations so-called physiological albuminuria may hold to subsequent changes. It is well established that the passage of albumen or, strictly speaking, serum albumen and paragloblin, from the blood in the urine is dependent upon some functional failure on the part of the epithelium of the glomeruli. Such failure is readily understood when from inflammatory or degenerative changes there is also degeneration of this epithelium, but the question arises, upon the other hand, whether nervous influences may not so affect the tissue in question as to cause functional weakness without organic change, or again, if in certain individuals such excretion of albumen may not be physiological, and to maintain equilibrium in the nutritive elements of the blood. The answer can only be clinical.

Albumen is often present in the urine of other-

wise apparently healthy persons, usually at a particular time of day. A transient albuminuria may be produced in certain individuals by excessive indulgence in albuminous food. It is occasionally traceable very directly to mental distress. It may be induced by certain nervous or vascular shocks, as from cold bathing. Without entering upon a discussion of all the explanations which have been offered of these facts or the theories which have been deduced, it seems a safe clinical conclusion that, while albuminuria may in exceedingly rare instances be physiological, and even possibly conservative, in most instances it indicates failure in nutritive activity of the renal epithelium and to that extent organic change. Opinions are widely divergent as to the frequency with which such albuminuria leads to more palpable lesions. Although by far the larger proportion of such cases terminate in recovery in the sense that the albuminuria ceases, I can not but believe that they show a failure of cellular activity such as must strongly predispose to inflammatory and degenerative changes, and that, if neglected, they tend towards organic disease of the kidneys. Not infrequently cases are found which go a step farther towards distinct Bright's disease. In these the albuminuria is not transient and intermittent, but constant throughout the day, and often persists for a considerable period without other evidences of organic disease, and while the patient is in the best of health. Such cases are undoubtedly

due to a mild form of glomerular nephritis, and no sharp line of division can be drawn separating them from chronic nephritis. They must be regarded as incipient Bright's disease. Nor can the absence of casts be allowed to stamp them as functional, rather than organic conditions, for small hyaline casts may occur in connection with the most transient forms of albuminuria. Pathology has given no more satisfactory explanation of the albuminuria which occurs in connection with various diseases, without evident renal lesions. It is found

1st. In all the distinctly infectious diseases. It is doubtless then due to inappreciable nutritive lesions of the epithelium, a supposition which is not invalidated by the frequent occurrence of cloudy swelling of the renal epithelium unattended by albuminuria.

It is entirely undetermined whether this functional weakness is due to the high temperature, nervous irritation, vitiated blood, disturbed circulation, or the direct local action of the hypothetical bacillus of each case.

We are inclined to ascribe it, however, in accordance with the later developments of bacterial pathology, to those chemical products which result from bacterial growth, the various forms of ptomaines.

2nd. In connection with mechanical disturbances of the renal circulation, either arterial or venous, such as may result from cardiac or pulmonary disease, abdominal tumors, etc.

3rd. In certain diseases of the brain, cord and vaso-motor nerves, more especially such as are attended with organic lesions, as apoplexy and concussion, but also with tetanus, epilepsy, etc.

4th. In certain chronic diseases marked by peculiar changes in the blood.

Clinically speaking, albuminuria is regarded as a symptom of these various diseases, rather than of a complicating nephritis, so long as the amount of albumen is small and unattended by casts. Any considerable amount of albumen even under such conditions would indicate that something more than functional weakness was present. It must not be understood, however, that small amounts of albumen, either relatively to the amount of urine passed, or absolutely considering the entire amount excreted in 24 hours, are always indicative of functional rather than organic disease of the kidney. In cirrhotic kidney the amount may be not only small but absolutely nil for varying periods, a fact which suggests at least, that absence of epithelium from either the glomeruli or renal tubes is a less important factor in albuminuria than distinct inflammatory changes affecting the epithelial elements.

Plainly stated, however, we are unable to say whether or not the passage of albumen from the blood is especially affected by denudation of the convoluted tubes, though personally we are inclined to the belief that the tubular epithelium plays a prominent role in the pathology of albuminuria.

Dropsy.—The second symptom which Bright especially associated with disease of the kidney is dropsy.

None of the theories of its causation thus far offered afford a satisfactory explanation. While it is true, as noticed by Bright, that the density of the blood serum is often reduced to even as low as 1015 or 1012, presumably by the extraction of albumen, it is equally true that the most extensive dropsies are often found in cases where, from partial suppression, but a small amount of albumen is lost. Moreover, in cases of prolonged albuminuria, the amount of albumen lost is seldom of such quantity, that were the general nutrition of the body unaffected, the normal processes of assimilation might not easily replace it.

Nor does the supposition that from failure to eliminate the watery portions of the urine, the fluid is forced from the vessels, find any stronger clinical support, for dropsy is occasionally excessive in cases of cirrhotic kidney, and usually in the later stages of parenchymatous nephritis, when the amount of urine passed is greatly in excess of the normal.

The supposition of Conheim is most nearly in accord with our own belief as to the nature of Bright's disease. As already intimated, we are inclined to regard all forms of the disease as at least secondary to, and often directly dependent upon previous disturbances in the general processes of assimilation and retrograde metamorphosis, or as excited by some blood poison. Every form of the disease is directly

traceable to an irritant brought to the kidney by the blood, or to mechanical disturbances of the circulation, which affect other organs as well. With the direct evidence that such irritants induce changes in the renal epithelium of an inflammatory and degenerative nature, it appears reasonable that similar processes may be caused in the endothelial lining and walls of the systemic capillaries, changes which may allow a passive transudation of the blood serum. Nor does this supposition seem negatived by the fact that the anasarcous fluid differs from that of inflammatory œdema. Pathology has thus far failed to draw the line between conservative physiological processes following stimulation and inflammatory changes which are strictly pathological. We too often fail to recognize that many processes which we call pathological, and which in their fullest development tend directly to death, are in their inception strictly conservative and should be recognized as Nature's remedial measures. Viewed from such a standpoint, and remembering that the solid constituents of the anasarcous fluid are principally inorganic salts among which urea is prominent, it is not impossible that the dropsy of Bright's disease may be in its natural purpose a conservative measure; Nature's method of relieving the blood of its burden of poisons.

Admitting (for the argument) that the dropsy is conservative, it is by no means true that its absorption must be a source of danger. Upon this point Dr. Carter's

arguments (Bradshaw lecture) appear to us unsound. Briefly stated they are: 'If dropsy is conservative, then (1) convulsions and coma should not occur while it is increasing, and (2) symptoms of uræmia should develop during absorption of the dropsical fluid.' In support of his denial of the hypothesis he instances a case in which under rapidly increasing dropsy convulsions developed and a second in which it was rapidly absorbed without untoward symptoms. Such argument is based upon the assumed propositions, both of which are untrue, 1st, that, if dropsy is intended to remove poisons from the blood, it will develop with sufficient rapidity to accomplish this, and 2nd, that its reduction must return poisons to the blood more rapidly than they can be eliminated by the kidney. It is self evident, however, that dropsical effusions, even though removing poisonous elements, may fail to keep pace with the production of such elements. Conversely it is equally an axiom that absorption of dropsical fluid, even if it contain poison factors, may be rapid in many instances without transferring to the blood an amount larger or even equal to that removed by kidneys which are resuming their functional activity.

It is a well established clinical fact, bearing directly upon this point, that renewal of renal function results in a much more rapid subsidence of dropsy, than an amount of catharsis and diaphoresis which removes from the blood a far larger quantity of fluid but a smaller amount of urinary solids.

The relations of cardiac failure to dropsy in all forms and stages of Bright's disease, appear to me to have received too little attention.

Personally, I am inclined to regard cardiac failure even in the earlier stages of acute Bright's as among the important factors determining dropsy. Two forms of dropsy may be recognized. One in which anæmia and other hæmic as well as vascular changes are associated causes, but which are attended for only a brief period by high arterial tension and forcible cardiac action, that quickly give place to weakened and irregular cardiac impulse under the influence of the urinary poisons. The second is largely mechanical, and resembles that of primary cardiac dilatation and failure.

CARDIO-VASCULAR CHANGES.

Both cardiac hypertrophy and increased arterial tension have been recognized as part of the clinical history of nephritis from the earliest history of the disease, but the relations which they bear to the renal lesions, and the character and causes of the changes have never been definitely settled. A few points, however, seem fairly well determined. Until a comparatively recent period all the cardio-vascular changes were looked upon as secondary to the renal disease, and many theories were offered for their ætiology upon this basis, but later observers, with considerable unanimity, have come to regard them as part of a

general disease in which the renal lesions play almost a subsidiary part.

Cardiac hypertrophy is the most prominent of these changes. It is found in all forms of Bright's disease, though more especially associated with cirrhotic kidney and the later stages of parenchymatous nephritis.

Histologically it is not found to differ from the hypertrophy found with any form of arterial obstruction or valvular lesion. In its earlier stages, and indeed until degeneration or dilatation have induced cardiac failure, it is always associated with a marked increase of arterial tension. Early there may be no evidence in the pulse of change in the artery, but a microscopic examination, and later, even the finger will show a thickening and hardening of the arterial coats. Before stating our own opinion as to the causes of the cardiao-arterial changes it is desirable to consider the inter-dependencies which have been assumed to exist between cardiac, arterial, and renal disease. The fact that the cardiac hypertrophy was found in the left ventricle only, except so far as the right ventricle participates by reason of contiguity, or in the later stages when left cardiac failure commences, demanded some obstruction in the systemic circulation as an efficient cause.

The early supposition of Traube, that the obstruction in the renal circulation, from decrease in the elimination of water and lessened amount of blood

which passed to the venous system, was alone a sufficient explanation of the increased arterial tension and cardiac change, was quickly abandoned, and the recognition of a general arterial fibrosis led to a more comprehensive understanding and explanation of the associated processes.

Although the description of the pathological changes given by Gull and Sutton was shown to be incorrect, their comprehensive explanation of a general arterial disease, coincident with the renal changes, as the cause of the hypertrophy was fully accepted, and has been carried so far by Mahomed as the assumption that the kidney changes were either secondary or simply associated with the more important systemic condition. Gull and Sutton, however, recognize the fact that the cardio-vascular changes vary greatly as the kidney lesion affects the vascular or tubular structure, and ascribe the hypertrophy found in parenchymatous nephritis to retardation of the circulation through general œdema of the tissues and malnutrition from anæmia and uræmia, a point which I wish specially to emphasize. While high arterial tension throughout the body thus became the recognized cause of the cardiac change, the explanations of its cause and nature were both various and contradictory.

So long as the renal disease was looked upon as primary, the arterial thickening was considered inflammatory in character, and due simply to direct irritation, by the excrementitious products in the blood, of

the delicate capillary coats. When, however, the arterial disease was supposed to be primary and the kidney change secondary or concomitant, an irritant must be found elsewhere. An excessive production of uric acid and other waste products as readily explained their presence in the blood in irritating quantities as did defective elimination. The recognized ætiological relations of gout and the uric acid diathesis to granular kidney thus suggested deficient hepatic function, either inherited or acquired, as the starting point in the chain of pathological processes which eventuate in cardio-vascular disease and coincident granular kidney.

That such is the order of change from uric acid, scarlatinal, alcoholic and other systemic poisons, seems indisputable.

In 1868 Dr. George Johnston stated that the thickening of the walls of the vessels in the brain, muscles and tissues generally, which is found in connection with Bright's disease, is due to an hypertrophy of the muscular coat.

In this he is supported by Waller, who states that the change is a true hypertrophy. Ewald admits a muscular hypertrophy but not hyperplasia. Others, however, deny the presence of any muscular hypertrophy. Dr. Johnston's own explanation, that the hypertrophy is due to an attempt on the part of the system to shut off from the tissues blood which is deleterious by reason of being surcharged with excrementitious products, seems untenable.

The possibility of such a muscular hypertrophy, however, even when resting upon no further authority, becomes of extreme interest in connection with the recent theory of Conheim concerning the cause of the high arterial tension. The two theories together afford an explanation of the increased arterial tension and cardiac hypertrophy, developed in acute parenchymatous nephritis and whenever cardio-vascular changes are secondary to renal disease, which to our mind is more in accord with the well recognized principles of pathology than any which has yet been presented for our acceptance.

Briefly stated Conheim's affirmation is, that the circulation in the kidney varies with the demands for their functional activity, or in direct ratio to the amount of excrementitious matter contained in the blood, and conversely the functional activity of the renal epithelium depends upon the amount of blood passing through the organ. Any diminution in the activity of the glandular elements at once lowers the ratio between waste products in the blood and the functional power of the kidney.

In order, then, that the total excretion shall not be diminished, the flow must be increased. To accomplish this object without disturbance in the general circulation, requires that the increased heart's action be met by general arterial contraction. Moreover, that this contraction shall vary according to the needs of the various organs, necessitates the intervention of the

sympathetic system and a variable contractile element in the vessels. The muscular coat alone can supply this.

Upon the basis of this theory, the recognized fact that the arterial tension is high in some young and healthy persons, whose urine never gives evidence of any renal disease, and the occurrence of marked cardiac hypertrophy in some cases of acute parenchymatous nephritis, afford grounds for the belief that the functional activity of the renal epithelium may depend not only upon the amount of blood passing through the vessels, but also upon the tension under which the circulation takes place.

It is not our purpose to deny the importance of cardiac hypertrophy in connection with Bright's disease but to insist upon its being considered as either:

1st. A necessary consequence of the development of the arterial changes of the fibroid diathesis, beneficent in its purpose, and bearing no ætiological or secondary relation to the renal disease as such.

2d. A compensatory process, depending upon the obstruction to the circulation through the renal vessels; more especially in cirrhotic kidney, but possibly in any form of Bright's disease or other renal lesions causing obstructed circulation, and developed in direct ratio to the amount of arterial obstruction found in the entire systemic circulation.

3d. A physio-pathological condition connected with the renal disease solely through the sympathetic

system, and directed to the re-establishment of the renal secretion and augmentation of functional activity in the parenchymatous elements.

Recently, DaCosta claims to have established a connection between certain degenerative changes in the ganglionic centers and both the renal lesions and cardiac hypertrophy. Even admitting his claims as to the pathological changes found, we are unable to see that he has established any causal relations between such changes and the cardio-vascular conditions.

The generally accepted fact that renal cirrhosis, far more frequently than even chronic parenchymatous nephritis, is associated with cardiac hypertrophy, indicates beyond question that arterial obstruction due to permanent fibroid disease of the arteries, offers a far more serious obstacle to the circulation than can ever result from reflex and sympathetic contraction, however extensive may be the arterial muscular hypertrophy; and the more rapid development of cardiac degeneration and cardiac failure which is so characteristic of parenchymatous Bright's disease, must receive some other explanation than that of failing nutrition from excessive activity or obstructed coronary arteries. My own observations lead me to believe that cardiac hypertrophy is developed in every case of renal cirrhosis in direct ratio to the amount of mechanical obstruction to the circulation, save when from extreme malnutrition muscular growth

in any part is impossible, and that cardiac degeneration, dilatation and failure depend in similar direct ratio upon decrease in functional activity of the renal epithelium and consequent systemic poisoning, remembering always that the urinary poisons are multiple and developed in very different proportions in each case. With direct bearing upon this point is Senator's claim that the hypertrophy of parenchymatous nephritis is *eccentric* while that of renal cirrhosis is simple or even concentric, implying a concomitant degeneration in the parenchymatous disease.

When one considers that it is a failing and not an hypertrophied heart which is to be feared in Bright's as in other diseases, it is a cause for surprise, when comparing the opinions of various authors upon the relations of renal to cardiac disease, that almost without exception they make little reference to cardiac degeneration as one of the frequent and important complications of renal disease.

The importance of the conservative and protective growth has been magnified to the neglect of the degenerative and eventually destructive disease. Even so late an authority as Fagge makes slight mention of cardiac degeneration as one of the important changes in Bright's disease, but specifically states that "the great point to be insisted upon is that hypertrophy of the heart occurs in both parenchymatous nephritis and renal cirrhosis." Strümple also says: "We now know that cardiac hypertrophy is not confined to con-

tracted kidney, but that it is almost as constant in many other forms of nephritis." Yet he makes no mention of degeneration as a *primary* and important change.

Many cases, however, present themselves to the careful clinical observer, in which, although seen from the onset of the disease, a weak and diffuse apex beat, irregular pulse, dyspnœa and dropsy, give evidence of cardiac failure without there having been present at any time the heavy apex beat and high tension pulse so characteristic of cardiac hypertrophy; or if the evidences of hypertrophy have developed in moderate degree, all the signs of cardiac failure supervene with a rapidity and severity which cannot be accounted for upon the theory of excessive hypertrophy or obstructed cardiac circulation. I am forced to believe that the degenerative changes which lead to cardiac failure depend upon nutritive lesions of the myocardium, induced by failure upon the part of the kidney to eliminate from the blood the elements of the uræmic poison, and that cardiac degeneration, dilatation and failure, rather than hypertrophy, are the characteristic features of what should be known as the Bright's heart, when Bright's disease means renal disease, and not all the complex of complicating and associated conditions.

Personally, I have not found cardiac hypertrophy in so large a proportion of cases of chronic Bright's disease in this country as is reported by English and

Continental observers, and when it is associated with extensive changes in the glandular structure of the kidney, I am convinced that it is due to the primary arterial, rather than to the renal, disease. The most constant cardiac changes which I have met with in parenchymatous Bright's disease are degeneration of the heart walls and dilatation of the heart cavities. In most instances where I have found tubular and interstitial changes in the kidneys in addition to obliterating arteritis, cardiac hypertrophy, when present, was associated with degenerative changes in the heart walls and dilated cavities. When the principal changes were in the tubes, malpighian capsule and connective tissue stroma with little obliterating change in the vessels, I have found no true hypertrophy, but rather the degenerative changes which I consider characteristic of a Bright's heart. One who studies Bright's disease clinically soon realizes that the heaving impulse and increased arterial tension, which seem to be the essential features of the disease as described by many writers, are the exception rather than the rule, for in most of such cases it is difficult to determine the point of maximum cardiac impulse, it is so diffused and indistinct, and although the cardiac area of dullness may be increased the other signs of hypertrophy are wanting, and when at the autopsy a large flabby heart s found one looks for other cardiac changes in chronic Bright's disease than muscular hypertrophy.

It seems unnecessary to record the symptoms of

either form of cardiac change or the arterial thickening. The ringing cardiac sounds, forcible beat, and hard arteries of the one are as familiar as the weak indistinct signs of the other.

Casts.—The history of renal casts is like that of most medical facts, one of gradual discovery. They were described as early as 1837 by Vogla and later by Rayer, Nasse, and Simon. They are more frequently associated, however, with the name of Henle for it was not until as late as 1844-or-5 that they came to be recognized as among the valuable signs of renal disease. Accepting the fact that casts may be formed in any of the renal tubes from the glomeruli down it is necessary to consider their symptomatic value, and their formation so far as it bears upon this point. Pathologically the hyaline cast alone need be considered, as the granular and epithelial casts probably have the same hyaline basis. Practically there are two theories of their formation. 1st, the exudative. 2nd, the degenerative. According to the former they represent a coagulated albuminoid or fibroid material which is exuded from the glomeruli. Upon such a supposition casts become, in some instances at least, no more significant of organic disease of the kidney than is albuminuria, unless we suppose that a further degree of inflammation or degeneration of the glomerular epithelium is imperative for the passage of this hyaloid matter. Such a supposition is opposed by the fact that casts often appear in

the urine some days before albumen can be detected, and may even be present and disappear without the occurrence of albuminuria. It is difficult to believe that different forms of epithelial degeneration are ætiological to the excretion of albumen or the hyaline material, and unless such is the case, it is difficult to explain the occurrence of casts in non-albuminous urine. A second form of the exudative theory, which assigns the active part to the tubular epithelium and regards the casts as a secretion of this epithelium, avoids some of the former difficulties. It is true that masses of plasma may often be seen protruding from the cells of the tubular epithelium in diseased conditions, a condition, it must be stated, which Wagner claims may also be seen in healthy kidneys.

The degenerative theory regards the hyaline material as formed by a colloid degeneration and fusion of the epithelial lining of the renal tubes. Such is known to be quite certainly the case in the nephritis of animals induced by injection of certain poisons, and is quite probably the origin of casts in most cases of Bright's associated with the specific diseases. If it is admitted, however, that large hyaline casts are formed in tubes denuded of their epithelial lining, it is evident that the source of the hyaline matter must be epithelial elements nearer the glomerulus or the malpighian tuft itself. Neither theory thus seems to offer a satisfactory explanation in accord with known facts, for the formation of casts, and we are led to believe that, under

different influences, both degenerative and exudative processes furnish the albuminoid material. Under any circumstances, theoretrical conclusions would lead us to believe what clinical experience has clearly proven, that the presence of casts in the urine is far more significant of serious and organic disease than is albuminuria. The character of the elements found imbedded in the hyaline body is also of special value as indicating the character and extent of the degenerative changes in the kidney, especially in the parenchymatous forms of the disease. As a rule, except in cirrhotic kidney, hyaline casts are indicative of the lighter grades of inflammation and the earlier stages of the disease, while granular and epithelial elements become more abundant as the destructive processes progress. In the cirrhotic form, the casts more constantly maintain their hyaline character; the denudation of the tubules from epithelial degneration may be shown by increase in the size of the casts. On the contrary, the presence of the hyaline variety must not be accepted as conclusive evidence of Bright's disease. A desquamative process with the prodcuction of epithelial casts even may be the result of transient non-inflammatory conditions.

Retinal Changes.—Amaurosis of Bright's disease may develop as an acute manifestation of uræmia, or depend upon distinctly appreciable changes in the retina. In the acute form it is not an infrequent result of the uræmic convulsion. A patient whose eye-

sight has been perfect, or who at most has suffered only from muscæ volitantes, passes through an acute uræmic convulsion only to find himself totally blind. It is quite constantly bilateral, but may not always cause entire loss of perception of light. The pupils are usually dilated, and although they are often sluggish and possibly immovable, they more frequently show some reaction to light. The only change which has been recognized upon ophtalmoscopic examination is slight œdema of the discs. The rapid recovery of sight, which usually takes place in from 24 to 72 hours, gives support to the view that œdematous changes, either in the eye itself or more probably in the visual centres, are the cause of this rather alarming symptom.

The more serious results of the uræmic state are found in connection with the chronic forms of the disease, and are characterized by distinct inflammatory processes in the retina and optic nerve, which show rather a marked tendency to become degenerative in character. The inflammation is exudative in character, and affects the central rather than the peripheral portions of the retina. The primary stage of hyperæmia is very distinct when attention is directed to the eye sufficiently early. The optic nerve entrance and surrounding area appear deeply reddened, by abundant distended vessels. The veins in particular are distended and tortuous while the arteries are often even smaller than normal, although they may be seen to pulsate strongly.

Irregularities in the swelling due to congestion and œdema will be indicated by contrasting areas of light and shade. Capillary hæmorrhages occur early and may appear as delicate linear injections or more distinct blood clots which possibly obscure the vessels.

As the exudative stage advances, a diffuse veil-like cloud appears thrown over the retina. It is most distinct about the optic papilla, and in this region as it thickens unevenly, irregular gray or milk white spots are developed, which completely obscure all the structures beneath. Similar points and areas of white exudation appear about the macula lutea and gradually extend until they fuse in one or more large patches. As the areas of exudation increase in number and size they change color to a glistening yellow and gradually retreat to the posterior layer of the retina so that the vessels again become visible. Finally a circle of diffuse exudation is formed as these patches coalesce, which presents an opaque yellowish or glistening fatty appearance in which extravasations and distended vessels are dimly seen. The borders of the papilla are indistinct and the inner boundary of the exudation often presents a zig-zag or flame-like appearance, in which the prominent points correspond with the larger vessels.

Although the exact pathological relations of these retinal changes are not well understood, it is certain that they are not pathognomonic of Bright's disease. Jaeger, Graefe, and Bouchut report similar ophthal-

moscopic appearances in diabetes and descending neuritis from cerebral disease. That they are very characteristic of albuminuria must be accepted. They cannot depend solely upon albuminuria, however, since they are often present in advanced degrees when albuminuria is exceedingly slight and intermittent. That retinitis occurs more frequently and in severer form in such cases as are marked by severe cerebral symptoms, leads to the belief that direct action of the uræmic poison upon the delicate nervous tissues must be received as an important factor in its ætiology. The retinal hæmorrhages doubtless depend upon a similar change in the retinal vessels as affects the systemic circulation generally. The amblyopia due to extravasations may extend to complete amaurosis, but sight is seldom entirely lost through inflammatory changes alone, and in the minor grades they may continue for protracted periods without causing sufficient subjective symptoms to lead the patient to seek medical advice.

I now pass to a consideration of the clinical manifestations of Bright's disease.

From the earliest history of the disease, the classification of Bright's disease has been a controversial point. To our mind, the *casus belli* is a failure to remember that classifications made upon different bases cannot be made to harmonize in all respects. The divisions of a pathological classification do not correspond in all points with those of one made on

gross anatomy. Similarly theoretical and clinical classifications cannot be made identical.

Personally, I am in the habit of employing a slightly mixed classification based upon Virchow's original distinctions.

Clinically, we recognize an acute and chronic Bright's disease, and pathologically we distinguish in the chronic form a parenchymatous, cirrhotic, or amyloid process as predominating and giving more or less distinctive characters to both the anatomical appearances of the kidney and the clinical manifestations. Upon a strictly pathological basis, we believe every case of chronic Bright's disease shows both cirrhotic and parenchymatous changes in varying proportion, and that "diffuse nephritis" is, therefore, a strictly appropriate synonym for chronic Bright's disease. In such a statement, purely degenerative, non-inflammatory parenchymatous changes are, of course, excluded. The preponderance of one or the other process, however, results in such characteristic symptoms, and anatomical changes as seem to justify the further division. Nor does the fact, that in some cases the processes are so commingled as to render it impossible to say from the morbid appearances which was the primary change, render the distinction any the less real and obvious as regards the majority of cases. Varying lines of development are also but accidents due to irrelevant causes, and in no sense affect the character of the fundamental changes. Whether par-

enchymatous inflammation results in cloudy swelling, granular, or granulo-fatty changes with extensive hyaline exudation and obstruction of the tubes, causing enlargement of the kidney; or degenerative and liquefactive processes in the tubular epithelium and a larger ratio of fibroid formation, result in collapse of the tubes and atrophy of the organ, the essential change is parenchymatous inflammation. It is only for that class of cases in which neither change predominates, but all the tissues are so equally involved as to render distinctions invidious that the term diffuse nephritis seems at all necessary. Distinctive cases so largely predominate that I shall employ the following classification:

1. *Acute Bright's Disease.*

2. *Chronic Bright's Disease.* — Chronic — (1) Parenchymatous nephritis. (2) Cirrhotic Kidney. (3) Amyloid Kidney.

ACUTE BRIGHT'S DISEASE.

Pathology.—The pathological processes of acute Bright's disease are strictly inflammatory in character and affect almost solely the parenchymatous elements of the organ, that is, the epithelial structures of the tubes and glomerular capsule. Until quite recently the changes in the tubular epithelium have attracted special and almost exclusive attention, quite possibly

owing to the fact that they are usually more extensive and may be recognized even upon gross examination. Since, however, the epithelium of the glomerular capsule has come to be regarded as in a large degree part of the parenchymatous structure of the kidney, the changes to which it is subject in inflammations of the organ have been more carefully observed. Some pathologists have even gone so far as to consider these glomerular changes to be the primary and essential lesion, and to look upon the exfoliation and degeneration of the tubular epithelium not only as a secondary, but even as an unimportant part of the pathological history. Upon a basis of the glomerular changes it has been proposed to substitute the term glomerular for parenchymatous nephritis. It does not seem to be sufficiently well determined as yet, that those glomerular changes, which are unquestionably quite characteristic of scarlatinal nephritis, are equally characteristic of other forms of acute Bright's disease, to warrant the change of name, although Conheim has established the fact that the same changes are present in some other forms of acute Bright's disease.

The vascular changes of acute Bright's disease are not confined to any one part of the organ, and are not always sufficient even to attract attention. In some cases of scarlatinal nephritis there may be no appreciable change in color. Usually, however, all the vessels are distended by an active or passive hyperæmia. In any case, and with passive congestion

especially the stars of Verheyn stand out prominently in areas more or less anæmic.

In the earlier stages the hyperæmia of the malpighian tufts is extreme and active in character while the congestion is most marked about the bases of the pyramids, in the venous arcade between the medullary and cortical portions, and extends often in increasing degree to the medullary portion. A similar hyperæmia is present in the lining of the pelvis. When death has taken place in the uræmic attack the passive engorgement may be extreme and involve all of the renal tissue in an apparently equal amount. Even the lighter grades of hyperæmia are usually attended by rupture of capillaries and minute extravasations, and such hemorrhages may form quite appreciable extravasations throughout both the cortical and medullary portions; even the vessels of the pelvis may be similarly affected and the blood form ecchymoses upon the mucous surface or break through the membrane and pass off with the urine.

Similarly the capillary tufts may give way with extravasation into the capsule, passing into the tubes and pelvis.

The exudative processes are quite constant in character, but vary in amount, extent and proportions in the various forms of the disease.

Although a slight serous exudation is probably always present, it is not appreciable post mortem, nor can fibrinous exudate be recognized as such, for

although the tubes are filled in some cases with a hyaline material, which resembles the fibrinous exudation of inflammatory processes, we have already shown that it is more probably the result of hyaloid degeneration of the epithelium or the product of cellular action. It must be admitted, however, that in many cases the microscopic appearances uphold very strongly the supposition that it is strictly a fibrinous exudate. It is the cellular portion of the exudation which is most characteristic. Cellular infiltration of the inter-tubular tissue is present in all cases. In some it is only in moderate degree. In others the small cells and multiplying nuclei fill not only the interstitial tissue, but pass into the tubules and glomeruli. In the so-called glomerular nephritis, especially in connection with scarlatina, this cellular infiltration of the capsule and tufts in connection with the nuclear hyperplasia form the essential features of the disease.

It not only involves the capsule, but the capillary tuft and periglomerular tissue become crowded with cells and nuclei, which compress the vascular tuft by exudative and proliferating force in the early stages and as we shall see later, by formation of fibrous tissue, when the disease has become chronic.

It is not common for the white cell elements to pass on to form pus, but such a change is not impossible and is, indeed, rather common in connection with degenerative parenchymatous changes found in the nephritis of infectious disease.

The parenchymatous changes in acute nephritis are much more varied and have even given rise to a sub-classification of the disease.

In the simpler forms the changes are most marked in the convoluted tubes and correspond quite closely to catarrhal processes upon mucous surfaces. The epithelial lining of the tube is simply lifted from its basement membrane and is thrown into the calibre of the tube, not having undergone any very marked degenerative changes. It may be replaced by fresh epithelial growth to be lifted off in turn, or the tube remains denuded when the epithelial debris has been washed away. More commonly the epithelium of the convoluted tubes has undergone cloudy swelling, and further on, and in the loops of Heull the cells are granulo-fatty. It is in connection with this form of "catarrhal" nephritis that the cellular exudation within the tubes becomes purulent. In such cases the hyaline material found in the tubes is apparently exudative in character. When the parenchymatous elements are more deeply affected, the tubular epithelium rapidly passes from the stage of cloudy swelling and granular degeneration into granulo-fatty changes and necrosis, and in its desquamation fills the tubes with broken down cells and fatty matter. In glomerular nephritis nuclear proliferation both of the capillary and glomerular endothelial nuclei is the prominent process, which occurring both upon the surface and throughout the tuft, causes, in connection

with the cellular infiltration, a matting of the entire glomerulus in one mass of embryonic connective tissue.

It is seldom that the pathological processes are confined to any one of the forms described. More commonly catarrhal, desquamative and exudative changes will be found scattered throughout the kidney in varying proportions. Some of the gromeruli may be entirely normal, while others are compressed and rendered functionally inactive by the mass of embryonic tissue in which they are imbedded.

Morbid Anatomy.—On removing the kidneys in a case of acute nephritis, they will be found enlarged even to twice their normal weight, their surface is smooth and mottled by areas and lines of deep red-purple or chocolate and patches of unusual pallor; they appear thickened and as though the capsule were stretched and tense. On section the capsule is easily stripped off and the cut surface presents upon the thickened cortical layer, which may be darker or even paler than normal, bright red and darker purple or black spots which correspond to malpighian tufts and blood extravasations. The medullary portion is darker than normal, varying with the intensity of the congestion, and, like the cortical layer, presents light striæ corresponding with the pyramids. When the degenerative processes are marked pressure over the pyramids may extrude a dirty purulent fluid from their apices, which contains pus cells, granular and fatty

epithelium, hyaline matter and casts. Under the microscope may be seen the evidences of the pathological processes already described.

Ætiology.—In an enumeration of the causes assigned for acute nephritis in previously healthy subjects cold is generally placed first. Such a statement requires some modifying explanation. It is very doubtful if a low temperature *per se* has any marked tendency to induce nephritic disease. On the contrary, those persons who by occupation are often exposed to extreme low temperature for protracted periods, as car and hack drivers, do not especially suffer from acute nephritis, provided the reduction of surface temperature be gradual. On the contrary, acute Bright's disease is decidedly infrequent among farmers, lumbermen, and is less frequently induced even among men working immersed in cold water than many other diseases. Sudden variation of temperature, on the other hand, even when the absolute degree of cold is not extreme, is a most distinct and important cause of renal congestion and subsequent inflammation, as evidenced by its frequency among bakers, firemen, molders, blacksmiths, and men in mercantile pursuits who run out without an overcoat, and young people who sit or lie in a draft after violent exercise. While such sudden chills tend in general to react upon the weakest point in the system, the kidneys evince a special susceptibility to reflex vascular disturbances arising in contraction of the peripheral cir-

culation. Many less sudden or severe changes of temperature may at times induce an acute nephritis in susceptible individuals or those in whom from any cause the kidneys have become weakened. In persons of a gouty habit, whose kidneys are under continual strain functionally, or even when a prolonged course of dining out has induced persistent hyperæmia of the organs of excretion, a very light chill or draft of wind striking upon the loins or back for but a comparatively short time may excite an acute nephritis. The two early changing from heavy to light underwear, or the still worse habit of not wearing flannel in northern climates, are always attended with danger of renal inflammation.

That no satisfactory explanation of the action of such surface irritations in causing tubular nephritis has been found does not affect the clinical evidences of the causal relations.

The most frequent cause of acute renal inflammation is undoubtedly direct local irritation by some foreign element in the blood, or an excess of normal elements demanding removal by the kidneys. Irritation is but a step beyond stimulation, and degeneration is the direct consequence of excessive functional activity, so that all those elements which excite normal action of the kidney may in excess lead to inflammation and degeneration. The more common of these are the direct results of waste of nitrogenized tissue, as uric acid, kreatin, kreatinin, and allied ele-

ments. Even when not the sole cause of the renal changes, they induce such a condition of hyperæmia and hyper-irritability as renders the action of cold and other reflex causes more serious. It is under this head that pregnancy must be placed, since the older theory, of pressure upon the venal veins by the uterus has been almost entirely abandoned. The tissue changes in the growing fœtus are exceedingly rapid, so that the extra amount of excrementitious matters removed by the maternal organs is increased in far greater ratio than it would be if her own tissues were increased by an equal amount in weight. This excessive demand not only induces the hyperæmia of excessive activity, but the excrementitious elements are directly irritating to the kidney. Of the foreign elements in the blood, alcohol is often regarded as of prime importance. It is doubtful, however, if alcohol alone often excites acute nephritis. When taken in very excessive quantities within a short time, it may possibly cause a tubular inflammation, but usually its rôle in the causation of nephritis is to induce renal hyperæmia and lead the subject to carelessness in exposure to wet and cold. All the poisons of the acute infectious diseases must be included in this class, of which the scarlatinal poison is probably the most active.

This element, however, presents most decided variations in its activity. Some epidemics of scarlet fever will present renal complications in a very large

proportion of cases, while others will prevail in which such complications are very infrequent or entirely absent. Not every case of albuminuria, however, even when a few hyaline or epithelial casts are present, is to be regarded as a true nephritis, for the renal epithelium suffers more or less, as do all parenchymatous tissues in the course of prolonged febrile diseases, both from the direct action of the peculiar poison and the malnutrition arising from hæmic degeneration. In such cases the epithelial changes are simply atrophic and degenerative rather than strictly inflammatory. The present developments of pathological study do not enable one to say whether the nephritis of some acute inflammations, more especially pneumonia, should be classed under this head or stand by itself. Such a clinical connection exists and special watch should be held for its occurrence in lobar pneumonia.

A further class of renal irritants includes such drugs as copaiba, cantharides, turpentine, and the mineral poisons, arsenic, lead, phosphorus, etc. The degenerative changes of old age affect the epithelium of the kidneys in connection with that of other organs, but they can hardly be regarded as inflammatory.

Symptoms.—The onset of acute Bright's disease rarely presents symptoms to attract the patient's attention. When due to scarlet fever, exposure to cold, or some concentrated poison, it may possibly begin with a chill and distinct rise of temperature, which are quickly attended by the more characteristic evidences

of the disease. As a rule, however, the earliest symptom is dropsy, or, in anæmic patients, the peculiar white waxy appearance of the skin. Observant patients may possibly have noticed a diminution in the quantity of the urine and that it has been rather high colored, but even such patients seldom attach significance to the fact. Commencing dropsy will excite attention. This will appear first probably about the eyelids and upper part of the face, but rapidly attacks the feet and ankles, the lower part of the back and the loose connective tissues generally. The face and entire skin thus rapidly assume a characteristic appearance. If not present before, anæmia develops rapidly and increases the white, œdematous appearance of the skin.

For a time this dropsy may disappear at night, but in severe or distinctly acute cases it increases rapidly and soon becomes permanent. By the time the dropsy is distinct the urine will be found decreased in quantity, of high color and high specific gravity, ranging from 1020 to 1030 or more.

The desire to pass urine will be almost constant, but with each effort only a few drops of bloody fluid are passed, and that without relief.

Although the relative amount of urea is greatly increased, the absolute amount excreted in the 24 hours is diminished ⅓ or ½. On chemical and microscopical examination, the urine will be found to contain large amounts of albumen, with red and white blood globules and various forms of casts.

Early the small hyaline and epithelial varieties will predominate, later large hyaline, granular and fatty casts will be present in abundance.

Symptoms indicative of uræmic poisoning are somwhat irregular in their development.

In some cases restlessness, headache, nausea, and vomiting will be such prominent symptoms as to fix the attention upon the stomach alone, but sooner or later in unfavorable cases the uræmic state will be developed and convulsions or coma, with the attending symptoms already described, will close the scene. When recovery is to take place, improvement generally begins before the extreme symptoms of uræmia are developed. The urine increases in quantity, the dropsy subsides, the nervous and gastric symptoms disappear, and in a few weeks the patient finds himself quite recovered.

In a certain proportion of cases in which the disease becomes sub-acute, without much change in the urine and with few or none of the evidences of uræmia, the dropsy continues to increase until general anasarca is developed. This is attended, largely from mechanical causes, but in part on account of œdema of the lung, by marked dyspnœa, which can be differentiated frem uræmic dyspnœa by the physical signs of œdema and the absence of other indications of uræmic poisoning.

Another class of cases is distinguished by the violence of the symptoms and the rapidity of the

development of uræmia. The initiatory chill, which is severe, is accompanied by a rapid rise of temperature to 104°–106° or higher, intense pain in the back and loins, which passes down the ureter to the penis, with retraction of both testicles, and almost complete suppression of urine. The nervous symptoms are present from the onset. The extreme restlessness quickly becomes delirium and coma succeeds within from 12 to 24 hours, to end in death within two or three days. When such an acute inflammation invades kidneys already crippled by former or chronic diseases, death may occur before any œdema is developed, but in most instances some puffiness of the face will appear in connection with, or soon after the advent of coma. When such cases escape death the kidneys are permanently disabled.

Prognosis :—While the general tendency of acute Bright's disease is to recovery, there are no special conditions of which certain recovery may be predicated. In general young subjects furnish a larger proportion of recoveries than those past middle life, and individuals whose general vitality is good offer stronger resistance to the inflammatory processes and uræmic poisoning. General prognosis must therefore be based upon the intensity of the individual symptoms. Of these, suppression of the urine is of the utmost significance. Profound anæmia, extreme anasarca, persistent vomiting and headache, with convulsions or

coma, are symptoms which necessitate a guarded prognosis. Many cases will occur, however, more especially among children, in which recovery follows the severest forms of convulsions, or after coma has been partial for some days, so that such cases are not to be given over until death takes place. Among the complications of serious import acute meningitis stands first. It is always fatal but fortunately a rare complication. Inflammations of other serous membranes are less dangerous, although peri and endocarditis render the prognosis exceedingly grave. All the pulmonary complications are of comparatively frequent occurrence and serious import.

Pulmonary œdema, as a part of the general anasarca, is less to be feared than when pulmonary inflammation acts as an exciting cause of concomitant œdema. Simple bronchitis is exceedingly frequent, but does not materially increase the danger; when, however, it extends to the capillary tubes, it is soon accompanied by œdema and quickly becomes fatal. Localized œdema of the glottis develops with great rapidity in some cases, and unless the physician be near at hand and radical measures speedily employed, may cause asphyxia and death within a few hours.

Complications affecting the gastro-intestinal tract and liver, although less serious may nevertheless often render the prognosis unfavorable.

Treatment.—There is no condition in which a

rational treatment depends more upon a thorough comprehension of the pathology, the histological conditions in the kidney, and the mechanical as well as physiological effects of the inflammatory changes.

It is undoubtedly true of the kidney, as of other organs, that such inflammatory changes as depend upon a single irritation tend of themselves to recovery. The acute nephritis due to cold, or some transient poison in the blood, falls under this head, and in many ways their treatment differs from those cases which are due to persistent irritation carried to sudden excess, in which, even when the direct excitant is removed, more or less strain is thrown upon the organ.

The kidney stands in an almost unique position among the organs, for, however extensive the inflammation, its functional activity must go on in a measure at least. Assistance may be given by the stomach, bowels or skin, but such vicarious action can never entirely supplant the renal function, and it must be carefully borne in mind that when any organ assumes this vicarious action it is only under the most severe irritation, and that its continuance for any protracted period must not only react upon the organ so functioning, but at the same time be a most serious drain upon the general strength. We thus find several indications presented for consideration in the treatment of acute Bright's disease. The foremost of these is the relief of the kidney from both functional activity and the irritation of its normal products of excretion,

namely, acid urine and partially converted elements of retrograde change. The former has received much attention, the latter has attracted hardly any attention from clinical teachers or theoretical writers.

The two available channels for vicarious elimination of urea are the bowels and skin, and their activity has been called in play for both the elimination of urea and the reduction of dropsy, and consequent relief of the symptoms mechanically produced. Too often no differentiation has been made in the objects to be attained, and the same means employed for both.

The former object is perhaps the more important and for its successful accomplishment two things are required, an active condition of the bowels and some element which shall render the excrementitious matters as soluble as possible. The action of the one is greatly supplemented by the other. The cathartics best adapted to this purpose are such as induce decided hepatic activity with secondary increase of peristalsis and watery evacuations. Calomel and podophyllin are to be preferred. Their action may be called triple, for undoubtedly the increased hepatic activity results in a more complete metabolism of the waste materials in the blood and their partial excretion in the bile. The total quantity remaining in the blood for further removal is thus not only lessened but the metabolic processes are more complete and the elements of excretion are rendered more soluble and less irritating to both the kidney and the bowels and

skin; urea is much more readily eliminated than uric acid or still lower products of waste.

And thirdly, the cathartic action of bile is entirely sufficient for the rapid removal of all the intestinal excretions at the same time that its antiseptic action prevents any tendency to ammoniacal decomposition in the intestine. While we do not accept the extreme views of those who hold uræmia to be an intestinal absorptive disease, we endorse the use of chologogue cathartics when the catharsis is directed against uræmia rather than dropsy. Disappointment often attends the cathartic treatment, however, when employed alone. Without supplemental treatment it is soon inefficient. The waste of both water and albuminous elements necessitated by the profuse catharsis must be fully compensated. Elimination of urea is not only favored by high dilution, but it becomes far less irritating to the excreting organ, whether that organ be kidney, bowel or skin. The watery evacuations should then be fully compensated by free ingestion of pure water, or, perhaps better, some natural mineral water, offering such elements as in combination with uric acid form a more soluble compound. Of these the Lithia waters are of great service. Nor should the practice of some physicians of adding more lithia to these waters be sustained. It were far better to secure the requisite amount of the salt by an increase in the fluid consumed. It is undoubtedly to their qualities as solvents, and the fact that

they are used in unlimited quantities, that such waters as the Poland, Bethesda, etc., owe their reputation as curative agents in Bright's disease.

It must not be omitted to replace, so far as possible, the albuminous elements lost in the intestinal discharges. This is best accomplished by the free use of milk, either pure or skimmed.

No one should allow the value of any one of these remedies to expand itself to the obscuring of all others, as has been done in the development of the "skim-milk," "grape," and other cures.

Of the three objects to be attained as above stated, the increase of hepatic action appears to us to merit special consideration.

Turning now to the use of the bowel as a means for reducing dropsy, we find entirely different conditions prevailing. When thus employed, the excretory function becomes subsidiary. Water is simply to be drained from the blood and its restoration induced by absorption from the cellular tissue. Therefore those highly irritating cathartics whose action is followed by watery transudation from the bowel are to be preferred.

The objections we have mentioned to the persistent use of the bowel for vicarious elimination do not apply of course, to the use of cathartics for more natural purposes. Whether we accept Bouchard's statement or not, as to the proportion of the uræmic poison derived from the intestinal contents, it is well

established that absorption of deleterious elements may take place through the intestinal mucous membrane whenever there is marked constipation. It is therefore desirable in all cases of acute, or indeed chronic, Bright's disease to maintain a full, healthy activity of the bowels at all times.

We have discussed thus fully the indication for the use of cathartics without mention of the skin as an eliminating organ, since the general principles are the same and reliance is never to be placed upon one alone.

It remains, then, simply to enumerate the measures employed for exciting cutaneous activity. The most common method of producing diaphoresis is by means of the hot-air bath. The patient is placed in bed, or on a chair, and small air space made about his body by blankets, rubber cloth, or any convenient material. Into this space heated air from a specially prepared apparatus, alcohol lamp, gas jet, or oil stove, is conducted, either with or without steam. A profuse action of the sudoriparous glands is thus induced, which can be continued for half or three-quarters of an hour. Reduction of the temperature is gradually attained, or sufficient clothing may remain to maintain a light diaphoretic action. These baths may be repeated two or three times in the twenty-four hours. For a time the patient may be greatly relieved by the baths and cathartics; their use should never be continued after the renal activity is restored, for after

a short time, while the catharsis and diaphoresis continue, they appear to lose their eliminative action, and they not only rapidly weaken the patient, but the uræmic symptoms continue to increase. I have frequently seen patients pass into convulsions while in the bath. The use of pilocarpine in place of the hot bath is hardly to be advised Its action is uncertain; it frequently produces unpleasant or even alarming symptoms, and when a case has reached the condition where hot-air baths will not induce diaphoresis, little is to be hoped from pilocarpine. If used at all, the indication would be an urgent case of uræmia or pulmonary œdema developed suddenly, in which relief was imperative before a hot bath could be arranged or become effective. Small doses are also allowable in obstinate cases to start a diaphoresis, which is to be continued by heat.

It is to be especially noted that both these measures, for which ever purpose employed, are purely palliative or adjuvant to more direct treatment of the renal condition. In the kidney itself we find three indications: 1st, to remove so far as possible the inflammatory products, degenerated epithelium and cellular infiltration of the tubules. While the tendency of the epithelial elements is to soften and extrude themselves, their incorporation with hyaline and exudative material results in a more compact mass whose removal is less rapidly accomplished.

We possess no drug which can soften these tube

casts and compressed debris, so that our efforts are confined to attempts at removal by mechanical means, by increasing the amount of watery elements in the urine and so augmenting both the direct pressure upon the obstructing matter, and the lateral pressure which tends to dilate the tubes. Such increase of renal function, should be gained with as little irritation of the kidney as possible. Success in removal of the tubular obstruction, however, must be obtained at almost any cost. Digitalis in the form of infusion (U. S. P.), combined with copious draughts of an alkaline water is always to be first employed. It may be given in one-half ounce doses as often as every two hours until a more copious flow of urine results.

When the digitalis alone is sufficient the result desired will be accomplished with the least possible irritation of the kidney.

But in the more severe cases when the urinary suppression is extreme it is often desirable to combine some of the simpler diuretics, as the bitartrate, or citrate of potash, with the digitalis.

These milder remedies should always be tried first, but the more stimulating preparations, as spirits of nitrous ether, acetate of potash, tincture of the perchloride of iron, or squills, may sometimes be employed with advantage. In carrying out the measures indicated for the increase of the watery parts of the urine it will be found that the second indication has

been fulfilled. The renal function will also have been increased as regards the solid portions, and the total amount of urea excreted will be very materially increased. The amount of excrementitious matter removed from the system, by even a very moderate increase in the urinary flow, will be found largely in excess of what can be eliminated vicariously through the skin and bowels by an amount of catharsis and diaphoresis calculated to react most deleteriously upon the patient's general strength. In considering the use of mercury in cases of acute Bright's disease, it were useless to repeat the arguments already worn threadbare, *pro* and *con*, its action upon glandular activity and degenerative changes.

The one clinical fact remains that from the time of the fathers mercury has been used to stimulate nutritive activity and parenchymatous action.

Clinically I am in the habit of employing small repeated doses of calomel or some other mild preparation in connection with digitalis and other remedies.

Both the parenchymatous activity of the kidney, and the mechanical removal of tubular debris are retarded by the congestion of the kidney and therefore measures directed to an equalization of the circulation favor and assist the action of the remedies already advised.

Dry cupping, when properly executed, is the most rapid in its action and the most powerful of the

measures. Special care, however, should be taken not to induce rupture of the cutaneous vessels or even permanent congestion. Filling of the cutaneous capillaries alone is desirable, but the application of cups may be continued from twenty minutes to half an hour. Following this the loins should be covered with hot poultices, preferably of digitalis leaves, turpentine stupes or capsicum cloths. The cupping may be repeated from two to three times in the twenty-four hours.

The third indication concerns the effects of the retained excrementitious products upon the nervous system, and the same measures are to be employed as in the treatment of acute uræmia, either convulsions or coma. Special reliance is to be placed upon hypodermics of morphine, and only in extreme cases are anæsthetics required.

Aside from these specific indications, the general treatment includes careful protection of the surface from cold or sudden changes of temperature; a uniform temperature above 70° should be maintained in the apartment; the patient's body clothed in wool throughout, and ventilation secured through adjacent rooms and not directly upon the patient.

The safest, and at the same time most nourishing, diet is milk. When employed in varied forms, it can comprise the only article of diet, as it should, without becoming especially distasteful to the patient. Removal of the cream does not materially detract

from its value in this condition, and when the stomach is especially sensitive, milk predigested by pancreatine or rennet whey will be retained when nothing else is.

As previously stated, the use of hydrogogue cathartics and diaphoretics should be reserved for the more serious conditions, after other measures have failed to restore the urinary flow, and they should be discontinued as soon as the secretion is re-established.

CHRONIC NEPHRITIS.—Chronic Bright's disease will be described under the following heads:

1. Chronic Parenchymatous Nephritis.
2. Interstitial Nephritis, or Cirrhotic Kidney.
3. Amyloid Degeneration, or Waxy Kidney.

CHRONIC PARENCHYMATOUS NEPHRITIS.

Pathology.—The pathological processes of chronic parenchymatous nephritis differ from those of acute Bright's disease in both degree and character. When developed as a continuation of the acute process the glomerular changes heretofore described may sometimes be recognized in their later stages in which the connective tissue developments have gone on to organization, causing more or less atrophy of the glomerulus and agglutination with its capsule. The characteristic change of the chronic disease is one of degeneration, affecting the cellular elements of the organ more particularly, but not entirely. It thus happens that the glomerular exudation undergoes the same granular or fatty change as the rest of the organic and exudative elements. This degeneration

affects more especially the cells of the convoluted tubes which are exfoliated in all stages of the process from the earlier condition of cloudy swelling to the final development of granulo-fatty metamorphosis.

In many instances the cells do not disintegrate but are exfoliated and closely packed into the tubes distending and compressing them.

The same change also invades the inter-tubular tissue and both the cellular elements and the interstitial spaces become filled with granulo-fatty matter. Nor do the blood-vessels escape. Here the change is most marked in the cells of the external coats of the smaller vessels, which contain more or less abundant deposits of granular or granulo-fatty matter.

The extent of the fibroid changes will vary very decidedly in different cases. When the process has been markedly chronic and the character of the changes has been inflammatory rather than degenerative, the fibrous element may be sufficient to cause some slight adhesion of the capsule, but the lighter grades of change are manifest in the glomerular capsule, the walls of the tubules and blood vessels. In the majority of cases, however (as we shall note later), the changes are more degenerative than inflammatory from the start, and in such conditions the fibrous changes are slight or even unappreciable. Hyaline exudation also plays a prominent part in the process. These changes result in large white or pale kidneys, which are from twice to three times the normal size,

with a smooth, mottled, yellowish-white surface and non-adherent capsule. The kidney appears swollen and the capsule distended and tense, the mucous membrane of the pelvis and calices is thickened and shows an opaque, anæmic appearance, and is marked by distended veins such as cover the surface and traverse the body of the organ.

On section the change is seen to occupy the cortical portion almost entirely.

The malpighian tufts are not prominent on account of the atrophy and the surrounding granular matter. The pyramids appear streaked with degenerative products.

In certain cases the epithelial changes are confined to cloudy swelling, with more prominence of the hyaline exudation. Although the epithelium is partially exfoliated the increase in size is due principally to the epithelial swelling. The exudation and distended tubes compress the capillaries and such large kidneys may present an almost ivory white surface upon which there are but few vessels to be seen.

Some authors describe a large pale kidney of parenchymatous nephritis in which interstitial changes predominate, and a large white kidney of obstructive cardiac disease.

In the latter form unusual thickening of the blood-vessel may often be noticed.

It is a disputed point whether the small granular kidney is ever a result of the large kidneys of paren-

chymatous nephritis. We believe there is sufficient clinical and post mortem evidence to prove that this may be their origin in exceptional cases.

Theoretically they are the legitimate result of the combined fibroid and parenchymatous processes. When the fibroid element is prominent it seems possible that they may develop from the large kidney in a comparatively short time.

It must be admitted, however, that many cases occur in which from post mortem examinations it is impossible to say whether the kidney comes under the parenchymatous or cirrhotic form of the disease.

Such kidneys, are more commonly atropic from the outset, although the parenchymatous element of the inflammatory process is the more prominent, and gives character to the clinical manifestations.

They are developed as a rule only when the disease has been chronic for several years, and the pathological processes have been distinctly inflammatory and not purely degenerative. The fibroid growth is marked and allies them to the true cirrhotic kidney. This development affects not only the interstitial, or inter-tubular portions of the organ, but the glomerular capsule is thickened and adherent it may be to the atrophied tuft; the convoluted tubes are thickened and stiffened, and the changes extend to the capsule of the organ also.

On removal from the body the kidneys present a

granular surface of a more or less yellow color, on which the venous congestion is marked by spots of simple mottling or extravasation. The organ itself may be but slightly reduced in size or may be only one half its normal size. Its granular surface, on which the granulations mark the pyramids may possibly be distinguished from that of cirrhotic kidney by the fineness of the granules, the absence of cysts, the distinct yellow color and patches of yellow granulo-fatty deposit. The kidney never reaches this stage, without sufficient connective tissue formation to cause decided thickening of the capsule and such adhesion as to cause considerable laceration of the renal cortex when it is stripped off. On section it is seen that the preponderance of changes is in the cortex as in other forms of disease. Indeed the medullary portion may show no diminution in size. The granular appearance of the organ is as marked in section as on the surface, but the areas in which the epithelial debris is retained become more apparent, and present both streaks and masses of yellow or gray matter scattered throughout the cortex. Under the microscope it will be seen that the atrophic changes in the tubular epithelium have been somewhat irregular and the removal of the degenerated elements still more so. Most of the tubes will be denuded and emptied of epithelium, but many will still be filled partially or completely with granular matter. The former will be collapsed, shrunken, and almost obliterated, the others distended unevenly; at

points forming sacs of granular matter, while a little further on they contain only a few granules and fatty cells. The fibrous changes will be seen to involve not only the inter-tubular tissue but to have caused thickening of the tubular walls and the vascular coats.

The changes described form what is known as the small granular fatty kidney.

It is true that these changes correspond in many points with those of cirrhotic kidney, but the larger size of the organ, its softer consistence, the absence of cysts, and the presence of more or less numerous masses of granular epithelium in the distended tubes usually suffice for a differentiation.

Ætiology:—In a small proportion of cases chronic parenchymatous nephritis may have its starting point in the acute disease. The more acute and characteristic manifestations of the inflammatory process gradually subside, the exudative processes largely cease and there remains only that deterioration of parenchymatous action which is characterized by epithelial proliferation and rapid degeneration. In short, it becomes a condition of perverted nutrition, a strict degeneration rather than an inflammatory process. Most cases of chronic parenchymatous nephritis assume this type from the start, and never have an acute stage, indeed may almost be said never to have been inflammatory so far as the parenchymatous changes are concerned, although the fibroid processes are clearly inflammatory in character.

Such cases may have their origin in any of the causes of perverted nutrition. Moderate but persistent alcoholism, especially from the use of malt liquors; the gouty diathesis in moderate degree; many of the infectious diseases; the chronic states of malnutrition, as phthisis and emphysema; chronic rheumatic poison; diabetes and even bad hygiene in general. An obstructed venous circulation, as is developed most commonly from cardiac disease but may attend abdominal tumors, peritoneal adhesions, etc., may also result in that perverted nutrition characteristic of chronic parenchymatous nephritis. In short, it occurs in all those conditions which cause perverted nutrition of the tubes and their epithelial lining whether the cause mechanically obstructs the circulation, induces disintegration of the blood, or acts directly upon the tissue elements to interfere with their vitality.

Symptoms.—In those cases which follow acute Bright's disease the history of the chronic process begins when the scanty high-colored urine of the acute condition gives place to free urination, an increased amount of water, even above normal, and a gradual subsidence of the acute symptoms, with decrease of the dropsy and albuminuria.

The patient may be in an apparently hopeless condition from the acute disease, when gradually the urine is increased in quantity, the proportion of albumen is diminished, the dropsy, or quite as possibly, general anasarca, which had mechanically threatened

life, slowly disappears until a little puffiness under the eye, a slight line of fulness at the top of the shoe at night, or a little unusual rotundity of the leg, which, on pressure, one learns is due to œdema, are the only remaining suggestions of the previous state. And it may be said just here that so long as the patient has any of the chronic changes taking place in the kidney these light œdemas will not desert him, but will oscillate up and down as a very exact indicator of the amount of disease present and the success with which the kidneys are performing their function. If the disease is held in check years may pass in which the œdema remains unnoticed. Sooner or later, however, and generally sooner, the previous anasarca is redeveloped, and if developed while the patient is under proper treatment it will quite certainly be persistent until the end. In those cases which are chronic from the start, the dropsical history begins with the slight recurrent œdemas about the ankles and eyelids, and follows the same course as when secondary to the acute condition. In these cases this œdema of the ankles is often the first symptom which attracts the attention of the patient. The extent to which œdema may extend before uræmic symptoms are developed is often a source of surprise. Unless the case is suddenly terminated by the invasion of acute inflammatory processes, most cases reach a state of almost disguising deformity. The legs become almost as large as the body normally. The penis is distended

and curled up until its anatomical relations afford the only means of identification, even the passage of urine being less significant when from all the tissues serum is constantly oozing through cracks in the skin. The scrotum appears like a large bladder of fluid, and can not rest between the thighs; the abdomen is enormous, and even the face may be distressingly distorted.

Whether the disease comes on as the result of acute Bright's or is chronic from the start, the urinary changes are marked by an increase in the quantity passed. The patient's attention is usually attracted to the fact by an increased frequency of micturition. While seldom equalling the amount secreted by cirrhotic kidneys, it may reach twice the normal amount. It is pale in color, of low specific gravity (1010 to 1004), and always contains more or less albumen, and in most cases granular, fatty or hyaline casts. The casts may vary greatly in number or be entirely absent, while the albumen is never entirely absent, although increasing and decreasing with the changes in the kidney. Many, if not all, cases of chronic parenchymatous nephritis will give a history of a sufficiently acute irritation at some time in the disease to have been marked by a temporary decrease in the quantity of urine, with high color and specific gravity. Symptoms due to vicarious elimination of urea, or its action upon the nervous system, are not prominent; accumulation of urea goes on so gradually that the system becomes

habituated to its presence, and diarrhœa, nausea and vomiting, headache, etc., are often entirely absent until near the close of the case. The evidences of malnutrition, however, are very prominent. Loss of muscular and mental vigor, gradual ennervation and lack of energy are the early indications of a rapidly advancing degeneration. The skin becomes dry and harsh, the nails are brittle and furrowed, and the surface of the body assumes a peculiar dirty white, sallow or waxy appearance. The beginning of the end is distinctly indicated when the malnutrition begins to affect the heart walls. In many patients this occurs early and from comparatively slight amounts of renal disease. In others, and especially when the fibroid changes markedly predominate over the parenchymatous, hypertrophy of the heart is developed in extreme degree before the degenerative changes end in cardiac dilatation and failure.

The retinal changes already described are often developed to an extreme degree, not only when the disease runs a chronic course, but often, also, when it is more acute and the general symptoms are less indicative of uræmic poisoning.

Irregularity in course is one of the special characteristics of the disease. Periods will occur in which, to the patient's eye, all signs of the disease have vanished and he is confident of eventually regaining complete health. Albumen, possibly but a trace, in the urine, the light œdema of the ankles and the per-

sistent lassitude, however, all show that the disease is not eradicated, and suddenly a rapid development of urgent symptoms, such as possibly the patient has successfully passed through before, passes on to acute uræmia, with convulsions, coma, and death.

Complications. — Both acute inflammations and chronic degenerations are associated with parenchymatous nephritis. Pleurisy, pericarditis, and meningitis are the more frequent. While usually subacute or possibly chronic in their development, they render the prognosis exceedingly unfavorable. Chronic pericarditis is more frequent with those cases of nephritis which depend upon some hæmic cause, that also has a selective action on the heart and vessels, and is thus more common with the nephritis of gout than that of alcohol, or when it follows acute inflammation.

The gastric mucous membrane is liable also to subacute inflammation, which not only causes permanent changes of structure but also materially affects its function, thus contributing to the general malnutrition and consequent degenerative changes. The mucous membrane of the respiratory tract is similarly affected. Chronic bronchitis is an almost invariable accompaniment of parenchymatous nephritis, and pneumonia is not infrequent. The more important complications, however, are those in the heart and arteries. In both they are the direct result of malnutrition, assisted, it may be, in some cases by the

primary cause of the renal disturbance. As we have already pointed out, the amount of cardiac hypertrophy will depend upon the obstruction to the circulation both in the kidney and general circulation. It is usually a late development, though it may be associated with the earlier stages of the disease. While seldom an immediate cause of danger, it becomes so when associated with degenerative changes in the arteries, when it may induce rupture, apoplexy and sudden death. As soon, however, as the malnutrition affects the cardiac muscle, degeneration with dilatation or failure are speedily developed.

Neuro-retinitis, often accompanied by retinal hemorrhages, is an exceedingly distressing though less serious complication. In a few instances amaurosis may be developed suddenly without evident changes in the retina.

The structural changes of the advanced forms of the disease are such as do not admit of repair, and it is rare for complete recovery to be attained after parenchymatous degeneration has been fully established. Under favoring conditions, the extension of the disease may be delayed, and as comparatively large numbers of tubes are unaffected in the earlier stages, a fatal termination may often be delayed for years. Such kidneys are especially subject to invasion of acute processes, and slight exposure, over-exertion, or indulgence in alcoholic liquors may rapidly induce acute uræmia with all its attendant manifestations and consequences.

Treatment: The indications for treatment are in some points identical with those of acute Bright's. The epithelial accumulations in the convoluted tubes require elimination the same as when the exfoliation is more rapid. Owing to the degenerative tendencies this is accomplished the more easily, and the diuretic treatment while it is continued, need not be so constantly employed. The amount of digitalis given in the twenty-four hours may be materially less or its use may be intermittent. The quantity of water passed, the amount of albumen and the character of the casts will determine the extent to which it should be employed. Any diminution in the quantity of urine or other indications of concomitant acute inflammation will point to an increase of the amount given. The alkaline mineral waters are even more useful here than in acute Bright's, and are to be employed for the same purposes and upon the same rules of treatment. The two most important objects to be attained are the arrest if possible of the degenerative changes with restoration of healthy nutrition to the kidney and tissues generally and stimulation of the functional activity of those portions of the kidney which are still healthy or in which the degenerative process have not rendered activity impossible.

For this purpose it is necessary that the general nutritive processes be crowded to their utmost. In such cases I believe that milk is without exception the best article of diet, and may often be employed to the

exclusion of all other articles offered. It not only furnishes all the elements required by the tissues, but also contains sufficient water to act as a diuretic. When subacute gastritis coexists, the milk may often be predigested with advantage. In such a condition, three, four or more quarts may often be consumed in the twenty-four hours when a much smaller amount raw could not be borne.

When patients are able to take a mixed diet its character becomes a matter for serious consideration. Generally it may be stated that large amounts of albuminous food are not desirable.

A vegetable and farinacious diet is more desirable, and in most cases sufficient albuminous elements will be obtained from the milk taken in connection with the mixed diet. With patients who suffer from dyspepsia a moderate amount of stimulants, of which the light wines are to be preferred, will be found of advantage.

While general tonics may be of use in stimulating the appetite and hastening absorption, the hæmic foods are by far the most valuable. Iron should be given from the start in chronic cases, as soon as decreasing specific gravity indicates functional failure. The tincture of the chloride is the preparation most frequently employed, doubtless on account of an old established belief that it has a selective action upon the kidney. But in many cases the milder forms are more useful. Cod-liver oil is also of value.

Our knowledge of the remedies which may stimulate the functional activity of the kidney is largely empirical. Most of the diuretics have a much stronger action in promoting flow of the watery elements than in stimulating excretion of the solid portions of the urine.

Mercurials have been extensively employed in times past with a view of keeping up a persistent constitutional effect for long periods. This method has been abandoned, though I shall have occasion to refer to the use of the bichloride in cirrhotic disease. When, however, the specific gravity is decreasing and œdema and dropsy advancing, and even in conditions of extreme anasarca from parenchymatous nephritis, I have found no remedy so valuable in reducing the dropsy and increasing the solid elements of the urine as the so-called Fothergill's pill, containing a grain each of squill, digitalis and calomel. The proportions may be varied as tenderness of the gums or cardiac weakness shall indicate.

Attention to the general habits and hygienic conditions is of the utmost importance. The functions of the skin should be maintained by frequent baths and frictions, the surface of the body should be protected by pure wool garments from all sudden changes of temperature, and removal to an uniformly warm, dry climate will always be found of great benefit.

The urinary secretion should be watched with the greatest care, and marked diminution in quantity

should be followed by a few doses of digitalis, dry cups over the kidney, and the other measures employed in acute Bright's disease. All depleting measures should be reserved for an emergency. Even when dropsy is severe it is better removed by improved action of the kidneys than by hot-air baths or cathartics. Both these measures, however, as well as aspiration of the serous cavities and puncturing the skin of the legs and scrotum, may be employed when danger is imminent.

Pilocarpine should be used in such cases with the greatest caution.

CIRRHOTIC BRIGHT'S DISEASE.

Pathology.—The pathological processes involved in cirrhotic kidney present no peculiarities, but are identical with cirrhotic change in other organs and tissues. Owing to the chronic manner in which they are developed they present no distinction of stages, indeed the primary enlargement of the organ which is usually found in the liver is seldom present. The earlier products become organized and pass to the contractile stage before sufficient new connective tissue elements are present to cause enlargement.

The cellular hyperplasia and infiltration begin in the malpighian tufts and their capsules and gradually extend to the inter-tubular tissue of the cortex. As the disease advances the walls of the capillaries and smaller arterioles become involved as well as the urin-

iferous tubules themselves. When, however, the cirrhotic process develops in connection with the fibroid diathesis, or from the gouty poison the vessels are implicated early and the first change may be found in the capillary walls and nuclei of the tufts. This cellular infiltration, which is very gradual, slowly develops into a fibrillated structure that soon begins to contract. As a result the tuft is atrophied and shrunken. Under the microscope it appears filled with small round or flat cells and retracted from its capsule which is thickened by concentric layers of connective tissue in which is the same cellular infiltration.

In the earlier stages the tubes and parenchymatous element are little affected and the epithelium may appear quite normal even when the tufts are atrophied and shrunken. But as the disease continues and the contracting tissue compresses the tubes and the nutrient vessels the epithelial elements undergo simple atrophy and dissolution, or become granular and fatty and are thrown off into the lumen of the tube. This atrophy is so gradual that the degenerative products are not retained in the tubes but are washed away in the free urinary flow. At some points, however, where either contracting connective tissue has caused partial or complete obstruction in the tube, or the degenerative processes and exfoliation have been rapid, the tubes may become partially filled with granular matter.

As the fibroid changes become more extensive

the inter-tubular tissue, the capsule, and even the medullary portions are involved, and the contracting tissue in connection with atrophy of the parenchymatous elements draws the tufts into closer apposition, until the affected areas present only masses of connective tissue in which are imbedded atrophied tufts, thickened, denuded and collapsed tubes and tortuous indurated vessels. Here and there throughout the cortical portion may be seen imprisoned granulo-fatty matter, and still more characteristically, both in the cortex and upon the surface, cysts of all sizes, some filled with a clear fluid and others distended by colloid matter.

Such a kidney on removal from the body appears shrunken, it may be to one-fourth its normal size, unless it be in the earliest stages of the disease, when the stroma of the cortex may be slightly increased. The kidney is firm and knobby, its surface lobulated and dotted with cysts of varying size, the capsule is thick, opaque and tough, and when torn from the organ brings with it shreds and masses of the cortex, which then presents a granular appearance or is traversed by larger and firmer bands and masses of connective tissue. On section the loss of substance is seen to be mainly in the cortex, which may be only one-fifth or one-sixth its usual thickness. Often, also, the atrophy extends among the pyramids of the medullary portion. The blood vessels, especially the veins, are often prominent, but the capillary tufts are

less so. The thickening of the arterial coats causes them to protrude with open mouths from the cut surface like small quills. The cystic development which is so prominent upon the surface is more marked throughout the cortex. Not only are large numbers developed to a size which is appreciable to the naked eye, but under the microscope innumerable others are often seen scattered along the course of the tubes, forming rows of minute glistening objects which resemble strings of beads. It seems evident that these, as well as the larger ones, are dilatations in the uriniferous tubules, which are filled by fatty matter, serum or colloid material.

Among the more infrequent changes found in connection with cirrhotic kidney is a deposit of lithic acid salts scattered throughout the cortex and along the tubes. They may be either amorphous or composed of masses of crystals, and appear to be located in the inter-tubular tissue, and within the calibre of the tubes. If sufficient to be seen by the naked eye they present a light yellowish appearance, with points of sharp reflection, which glisten with reflected light. While such deposits may occur without other evidences of gout, they may form simply a part of general gouty deposits and be one ætiological factor in the cirrhotic changes.

It is not to be understood that the foregoing changes either affect both kidneys in the same proportion or are distributed evenly throughout one

organ. On the contrary, it is only in the most advanced cases that either kidney is devoid of comparatively healthy tissue, and in many cases it may be quite abundant. In still other cases, while the cirrhotic process is well developed in some portions of the kidney, other areas will present the characteristic changes of parenchymatous nephritis, and without the clinical history it may be difficult to differentiate such cases, in which an acute or chronic parenchymatous inflammation has become engrafted upon the fibroid condition, from cases in the later or atropic stage of parenchymatous nephritis. Fortunately such a differential diagnosis is of more value at the time the clinical history is afforded than at the post-mortem table. The special point of value, however, is that parenchymatous nephritis may develop in a case of cirrhotic kidney with all its attendant phenomena, and that, although fibroid changes are characteristic of the later stages of tubular nephritis, yet cirrhotic processes may and do constitute the only pathological change in a large proportion of cases.

Ætiology.—The later developments of pathology appear to me to require an unquestioning admission of a fibroid diathesis as an exceedingly important ætiological factor in the development of cirrhotic processes throughout the body. Whether we regard this diathesis as a part of the gouty constitution or not its force in tending toward fibroid change is undoubted, and whether we regard it as a developmental defect in

the nutritive processes or as simply an hepatic functional weakness, it appears equally as an inherited condition which may be developed and increased by negligence, or restrained and checked by careful attention to those habits which tend to allay vascular irritation, with increased arterial tension, and hasten the retrograde tissue changes with free excretion of waste products.

Among the exciting causes of renal cirrhosis gout and rheumatism stand prominent. It is not only an attendant upon acute gout but is almost as frequent in those who live all their lives just upon the border of an acute attack, but succeed in avoiding it. Indeed the acute attack with its clearing out of lithic acid salts seems at times to relieve the kidney from its condition of over work and chronic irritation.

The rheumatic poison is less active in inducing fibroid changes throughout the body; indeed it is often questioned whether in those cases which are called rheumatic the offending element is not the same as in gout. The name "gouty kidney," so long associated with this condition, indicates the accepted ætiological relations.

The prolonged use of alcohol may also induce cirrhotic kidney. Occasional indulgence to excess is less liable to result in gouty kidney than is the persistent use daily of only moderate quantities of stimulants. Generally speaking, the use of the stronger liquors is more apt to cause cirrhosis, while beer and

ale drinkers are more liable to develop chronic parenchymatous nephritis, a general rule, which of course has many exceptions.

Chronic lead poisoning is regarded as one of the more prominent causes of renal cirrhosis, and the disease is certainly found with exceptional frequency among painters, typefounders, printers, and those engaged in the manufacture of lead. The relations existing between chronic valvular disease of the heart, such as produce passive renal hyperæmia, and renal cirrhosis have not been clearly determined. That such hyperæmia may cause fibroid change is certainly in accord with pathological facts regarding the effect of a similar hyperæmia upon other organs. The changes induced, however, although fibroid in character are associated with less atrophy and shriveling of the kidney than are characteristic of a pure cirrhosis.

The ætiological relations of nervous irritation to cirrhotic changes are best expressed in the clinical fact that active brain workers are more liable to cirrhotic kidney, "ceteris paribus," than are those of a phlegmatic temperament and who use their brain but little. It is clearly recognized that alcohol and hard mental labor can not go together without injury to the kidneys. Some authors have attempted to demonstrate a causative relation between ganglionic degeneration of the sympathetic nerves and renal disease. Without questioning the histological facts presented and admitting the ætiological relations of

mental strain, we are inclined to regard its action as being exerted through some interference with the general nutritive processes. Males as being more subject to its exciting causes, suffer, as compared with females, in the ratio of 2 to 1, and persons in middle and active life for similar reasons furnish the larger number of cases.

Symptoms.—The earlier stages of cirrhotic kidney as well as the lighter forms of the disease often pass without presenting any appreciable symptoms. Indeed many cases are recognized only at the post mortem table. So long as a sufficient amount of active renal tissue remains for the removal of the waste elements, and even after the normal amount of urea is no longer excreted, the only symptom may be an increase in the amount of water passed. Since this increase is more marked in the water excreted at night, the patient usually first has his attention drawn to the urine by being obliged to rise at night to urinate. Chemical examination will show little change except low specific gravity, varying from 1010 to 1004, with possibly a trace ol albumen. With his attention thus fixed upon the kidney he will doubtless notice that he is also passing water more frequently during the day. If this warning is unheeded the results of defective elimination will manifest themselves in various ways. Most commonly a general muscular weakness and unaccountable lassitude gradually develop until the

patient begins to count his years and wonder if old age has been stealing a march upon him. Such a condition has been rarely developed until the accumulation of waste products in the system has begun. An examination of the blood, however, at this time, may give almost negative results, and we are forced to believe that the primary metabolic changes in the tissues themselves are at fault. Gradually there is developed some slight œdema about the ankles which is most marked at night and may be entirely removed after a night's rest in bed. This œdema is very variable or may be wanting entirely. A week or ten days in which it is present every night, or after long standing or walking, may be followed by a still longer period during which it will be entirely absent. Sooner or later other more marked symptoms of deficient excretion will be developed. Gradual loss of appetite becomes a distinct dyspepsia which is often characterized by persistent acidity and anorexia, most marked in the morning. These dyspeptic symptoms are often the earliest to attract the patient's attention, and he consults a physician for their relief, who very possibly fails to learn that unappreciated urinary symptoms have been present for a long time, but treats the gastric condition alone, and promises a speedy recovery. In connection with the gastric symptoms or soon after, occasionally before, there will be developed various evidences of the action of the poison upon the nervous centres. Irritability of temper, fretfulness

and an unusual moody morose feeling, with an unreliable, treacherous memory, become matters of surprise even to the patient himself, who is unable to account for a change which even he recognizes. Sleeplessness, which appears quite early, is attributed possibly to the headache which has become severe and persistent, or both, are ascribed to overwork, worry, and anxiety. The headache of cirrhotic Bright's is one of its most distressing symptoms. In nervous subjects it begins early, is not easily relieved and is both severe and persistent, attacking not only the frontal region, but quite as often extending to the occiput and vertex. In connection with these more marked symptoms the skin assumes a dingy though anæmic appearance, and the weary listless expression of the face, is increased by the peculiar expression of the eyes, due to œdema of the conjunctivæ. In the later stages, the urinary symptoms become more urgent, the quantity being so largely increased as to lead to the suspicion of diabetes, but the ratio between the daily and nocturnal secretions still remains unchanged. The amount of albumen present, which has always been small, seldom amounting to over 0.5 per cent., is but slightly increased, unless parenchymatous changes have supervened, the specific gravity is still low and the clear limpid appearance is unaffected by mucous or sediment. Casts are never present in large numbers, and when found are usually small hayaline

with now and then a granular and possibly fatty form. Although the specific gravity is so low the amount of urea excreted in the 24 hours, is not far below normal and may even reach 500 grains until the latest stages of the disease. One of the most characteristic evidences of cirrhotic kidney is found in the condition of the heart's actions. The hypertrophy and arterial changes already described are constant in this form of Bright's disease, and in patients who are constantly under observation by a family physician, the increasing arterial tension with its firm pulse, loud ringing second cardiac sound, and forcible apex beat, may give warning to the trained observer years in advance of the development of the more patent, but no more characteristic symptoms.

Even when fully developed the disease may run a comparatively mild course for years, until finally under the strain of some complication or accidental disease, or from gradual exhaustion, the patient passes into a state of extreme restlessness, persistent insomnia or partial delirium that finally merges into coma and death.

Perhaps with equal frequency, some sudden exposure, over-work or unusual strain, leads to the accession of acute inflammatory changes in the still healthy renal tissue and a fatal termination is reached with all the manifestations of acute uræmia. In such cases, the urine is often suddenly decreased in quantity, though seldom much below normal, the albumen

is increased, œdema develops and convulsions or coma close the scene. In studying cases of cirrhotic kidney it is necessary to remember that very many cases occur in which the symptoms are confined to those affecting a single organ.

We thus have several classes clinically. Perhaps the most important class is that in which the symptoms are mainly cardiac. Such cases are especially apt to be developed in gouty subjects, and those of a fibroid diathesis. They comprise the class already mentioned, when considering the cardiac changes of Bright's disease in which the renal cirrhosis as well as the arterial degeneration are both secondary to the constitutional diathesis, depend upon some blood irritant for an exciting cause.

The main symptoms are forcible heart's action, pulsating vessels, hard pulse attended by dyspnœa, and œdema of the dependent parts. Such patients have usually suffered from urinary disturbances attended by scanty, high-colored urine, with brick dust sediment and they are inclined to regard the more abundant urination and clearer appearance of the urine as favorable symptoms, or if struck by the amount of water passed, may believe themselves afflicted with diabetes. Errors in diagnosis may easily follow an examination for sugar alone. Various authorities have placed the proportion of these cases as from 15 to 20 per cent. of all cases of renal cirrhosis.

Frequently a systolic murmur usually heard most

clearly at the apex may still further divert the attention from the kidneys. Such a murmur is rarely anæmic, but may depend upon coincident endocarditis, or upon dilatation of the ventricle, in the later stages of the disease. If death occurs from accidental complications in the earlier stage of the disease, cardiac hypertrophy will be the predominant change, but later on degenerative changes will be quite constantly present. It is frequently stated that the cardiac dilatation and failure are due to excessive strain. We are of the opinion, however, that degenerative changes will be found in all cases where dilatation is present unless it has been exceedingly acute in its development. We have already referred to a similar cardiac hypertrophy which is due directly to the renal disease, and we must admit that endocardial changes, especially of the mitral valve, may also develop when there is no other apparent cause than the traumatic irritation incident to the high arterial tension and the direct action of retained excrementitious matters in the blood. We are not inclined to the belief, however, that endocarditis is a frequent result of cirrhotic kidney.

The group of cases in which patients seek relief from dropsy or general anasarca, can no longer be classed as forms of cirrhotic kidney. Although the kidneys may be found markedly atrophied on autopsy the dropsical symptoms must be regarded as due to a secondary parenchymatous inflammation.

Another set of patients will suffer almost solely

from symptoms pertaining to the gastro-intestinal tract. Nausea and vomiting, with profuse diarrhœa, may be utterly uncontrollable by any of the remedies directed to the stomach or intestine. The dangers in diagnosis in such cases have already been noticed.

An important class of cases present symptoms mainly referable to the nervous system. These patients suffer from a constant, intense headache, with dizziness and vertigo, often accompanied by numbness and formication, muscular spasms, temporary paresis or even paralysis of a single limb or possibly one-half of the body. Coincidently there may be transient aphasia, diplopia or amaurosis, and often loss of hearing.

Diminution of the mental powers is often prominent; the memory suffers early; confusion of thoughts may slowly develop into a semi-idiotic state or the more acute manifestations of mania; vomiting and persistent dyspepsia are frequent results of the central nervous irritation, and "Cheyne-Stokes," respiration may have a similar cause. A sudden explosion of extreme nervous symptoms is especially apt to occur in such patients, and under slight provocation they pass at once into coma or reach it through a brief stage of delirium and convulsions.

Finally, we must mention those cases in which gradually advancing weakness and exhaustion are the only evident results of the renal change; patients whose malady passes under the various names of

anæmia, nervous exhaustion, senile decay, etc. Such cases may even pass through their entire course without the true nature of the trouble being recognized.

It is to be noted in all these forms of the disease, in marked contradistinction to what occurs in parenchymatous nephritis, that the dropsy is never a permanent symptom. Many cases run their entire course with so little dropsy as to escape attention, unless especially sought for. In all, it is a variable state, and rarely passes beyond a slight thickening about the ankles, with possibly some puffiness of the eyes and face. When dropsy becomes a prominent symptom, it is almost indisputable evidence of a secondary parenchymatous process.

Complications.—So many of the attendant conditions in cirrhotic Bright's disease are looked upon as parts of the disease that few remain which can be put under this head. Cerebral apoplexy is perhaps the most frequent. The cerebral vessles are early affected by the fibroid changes in the vascular system and capillary aneurisms form throughout the brain. Some unusual strain induces a cerebral hyperæmia and rupture, or the weakening may have reached the point where the walls give way, it may be during sleep without unusual strain.

Inflammatory affections of the peri- and endocardium are very common attendants upon renal cirrhosis, often, however, as we have explained elsewhere, as the result of a common cause rather than

secondary to the renal lesion. Similarly, the bronchial mucous membrane shows chronic inflammation, which is often aggravated by acute exacerbations. Extension of the bronchial irritation may result in catarrhal pneumonia, or an acute lobar pneumonia may be developed at any time. Pleuritic inflammations are more frequently adhesive or sero-fibrinous in character, but acute plastic processes are common.

Neuro-retinitis and retinal hæmorrhages are quite certainly developed, unless the case is terminated by some complication before the contractile stage is reached. The hæmorrhagic tendency is not confined to the brain and retina, but extravasations are frequent on the mucous and serous surfaces and in the substance of organs.

Treatment. — When the pathological processes which characterize this form of Bright's disease are once established, their tendency is to progress and extend to other parts of the organ. Fibrous tissue, once developed, is never removed, but continues to contract and cause increasing atrophy of the organ and obliteration of its anatomical elements. Thus, although a long period may intervene before the fatal termination, there can be but one ending; during all the duration of the disease the patient is in constant danger from an increase in the renal disease, the development of parenchmatous changes, or the advent of complications.

The indications for treatment thus become evi-

dent. When the disease is recognized early something may be accomplished by removal so far as possible of the exciting cause. While the new connective tissue already formed will not be affected, and although further fibroid development will doubtless take place, still relief afforded the organ by freeing the blood so far as possible from irritating substances will render the extension of the disease somewhat less rapid. As gout is its most frequent cause, we may employ all those measures recommended when discussing parenchymatous nephritis and acute Bright's, for the decrease of uric acid, and to assist in its elimination. It is in this class of cases that the alkaline waters so highly recommended by French and German authors are especially useful.

The use of mercury when advised does not imply its employment in long-continued doses, as formerly has been done, with a view of causing absorption of the new tissue. The only cases in which such a use of mercury is admissable are those associated with cirrhosis of the liver. In such conditions the bichloride may be given in small doses for protracted periods at times with evident benefit.

Persistent use of mercury is not to be allowed in rheumatic cases or those due to lead poisoning. A strict diet in all cases is one of our most powerful means both for relieving the kidney from sources of irritation and for counteracting the strong tendency to malnutrition and exhaustion. As in other forms of

Bright's disease, the milk diet is exceedingly valuable. It is not possible, however, to confine a patient for months and years to milk diet alone, and such other articles should be added as will throw the least strain upon the kidneys—what may be called an anti-gout diet, containing only a modicum of albuminoid food. The simple milk, the skim-milk and buttermilk cures have all had their advocates, but one will seldom find it desirable to confine a patient to any single article of diet for so long a period as would be necessary.

It is of the utmost importance that the patient should be warmly clad with wool next the skin, since the kidney is unusually susceptible to the reflex effects of chill, and any sudden and acute inflammation of the organ is a matter of most serious importance.

As a rule, although such patients are typically anæmic, they are not so markedly benefitted by iron as are those suffering from parenchymatous nephritis. Indeed, in many instances the nervous symptoms are decidedly aggravated by the use of iron. Cod-liver oil, on the other hand, is beneficial in a large proportion of cases, and especially so when combined with the hypophosphite of soda. General tonics are also of value in relieving the gastric symptoms, and as adjuvants to other more distinctive measures. The action of the heart often calls for special attention, and it should be remembered from the first that heart failure is one of the most dreaded complications.

To maintain the nutrition of the hypertrophied

organ and so postpone the stage of dilatation is of the utmost importance. The general tonic treatment employed will be of value, but the use of iron, preferably Blaud's pills, should be persisted in so long as there are no untoward symptoms developed that can be traced to its action on the nervous system. It is our most valuable and powerful heart tonic. Those remedies which lower arterial tension, or stimulate the heart's action without increase in arterial tension will be useful. Nitroglycerin, strophanthus and digitalis may be employed singly or in combination for this object. The diuretic action of the digitalis will not be required except upon the advent of some parenchymatous complication. When used in combination, however, with stropanthus and nitroglycerin, its cardiac tonic effect may be obtained without material increase in arterial tension.

Cod-liver oil is an especially valuable tonic in these cases, and the rule which holds good in most other cases, that oil is less valuable in old people may be more freely disregarded. Perhaps the most valuable means for delaying the cirrhotic processes, for relieving the kidneys and avoiding the dangers of those sudden changes of temperature which predispose to renal congestion, or acute inflammation, is a permanent residence in a warm climate, which need not imply continuous residence at the south. On the contrary, a migratory existence in which the colder winter months are passed on the Gulf coast, the spring

in the Carolinas, and the summer in the north, may not only afford all the desired benefits of warm temperature, but add also the advantages of change of air and food and the desirable mental stimulant of variety.

Personal habits, and the use of flannel next the skin should be insisted on with the same urgency as in parenchymatous nephritis and the general hygienic directions given will apply equally to this form of nephritis. Throughout the disease for those symptoms or complications demanding an anodyne opium is always to be preferred. Although dropsy is less frequent in this than any other form of Bright's disease general anasarca may develop in the later stages. Its treatment requires no special consideration beyond what has already been stated. When renal cirrhosis, however, is complicated by similar disease of the liver, the ascites then often present may be reduced by aspiration, not only with relief of the general symptoms but often with marked benefit to the kidneys. Incisions and punctures of the skin and even the insertion of drainage tubes have been resorted to. Such measures afford a temporary relief and may prevent the development of gangrene or bed-sores, but can be of no permanent assistance. Acute uræmia occurring in cases of cirrhosis will call for the treatment already described.

AMYLOID NEPHRITIS. WAXY KIDNEY:

Pathology.—Although waxy degeneration bears no

special relation to renal disease but affects other organs with equal frequency, the waxy kidney has always received a place under the head of Bright's disease. It seems probable that some of the cases described by Bright himself under the head of large white kidney were of this variety. Aside from this however, it is so invariably associated with characteristic pathological changes of parenchymatous nephritis, that whether the amyloid process is regarded as ætiological to the inflammatory process or not, the complex of changes represent a non-suppurative nephritis. Cornil and Ranvier have stated that not only is the amyloid process invariably associated with parenchymatous changes, but that the latter condition is always precedent to the degenerative change. It seems useless to discuss the pathology of the amyloid change per se, since it is unknown whether it is derived from the blood or the albuminous elements of the parts themselves. It is thus impossible to state if it be a local degeneration or a deposit of new material. We are simply acquainted with its anatomical situation and reaction under certain chemical reagents.

The primary waxy changes occur in the walls of the capillaries and minute arteries.

The glomeruli are most affected and the change may be entirely limited to them, and when present in slighter degrees may even be confined to a few of the capillary loops in each tuft; in a more advanced stage the entire tuft may be involved, while the change has

extended to the vasa recta and middle coats of the smaller arteries. Under a still further development the walls of the urinferous tubes and possibly the lining epithelium are similarly affected. Contrary to what holds in other forms of Bright's disease the cortex and medullary portion are often simultaneously involved, but the change is always more extensive in the cortical portion.

Advanced stages of the disease are invariably associated with changes in the tubes and interstitial tissue. The tubular changes are those of a parenchymatous nephritis, with exfoliation, and granular or fatty degeneration of the epithelium and an exudation of hyaline material which does not give the characteristic reaction with iodine. In these changes degenerative processes predominate. The new connective tissue formation in the interstitial spaces in part undergoes fatty degeneration, while other elements pass on to organization and the stage of contraction.

Under the combined influences of pressure from deposited amyloid matter, fatty degeneration and contracting fibrous elements, the nutritive processes of the organ are retarded, and atrophy follows as a legitimate result. Under a rough anatomical division we have an hypertrophic and an atrophic stage of the disease.

In the first, the kidneys will be found enlarged, with a smooth glistening surface, which varies in color according to the amount of amyloid material and the

extent of the fatty changes, from a pale gray or yellow color to the deeper yellow which has given them the name of butter kidneys. This tinting may be diffuse or the surface may be mottled by the gray translucent swollen glomeruli or with patches and masses of yellowish, fatty material. The dilated veins show with marked prominence in deeper blue stellate markings over the light ground work of the renal tissue.

The section of such kidneys shows still more distiuctly the amyloid changes. The outlines between the cortical and medullary portions are indistinct. The entire surface, though more especially the outer portions, presents a distinct glistening appearance, in which the gray translucent glomeruli may be seen beneath the surface or standing out more prominently like grains of boiled sago. The tubes and often the inter-tubular spaces are outlined and dotted with creamy striæ and points of fatty matter. Under iodine the characteristic change of color is manifest by the development of brown and black points and lines where the waxy material is most abundant, or by the darkening of the entire surface in extreme cases.

Under the microscope, areas of amyloid degeneration will be developed which were unappreciable in the coarser test. The entire section may present a shining yellow appearance, as if all the tissues were infiltrated with the amyloid material.

The impediments to the circulation will here be

apparent at points where the amyloid deposit has caused protrusion of the inner arterial wall and diminution in the calibre of the vessel.

In the atrophic stage, the kidneys may be reduced to one-half their normal size, and their surface be rough and granular, and the capsule more or less adherent. Evidences of waxy material remain, however, on section. The tufts are more prominent, but atrophy is seen to have affected both the cortical and medullary portions. Under the microscope, the atrophy is seen in the tubes and their epithelial lining, and in the inter-tubular tissue. Many of the tubes will be collapsed, others obstructed and distended by granulo-fatty matter. The vessels are thickened and irregular in outline, and at points entirely obliterated. It is not necessary to suppose that the atrophic form of amyloid kidney has been preceded by the hypertrophic. It is quite as unreasonable to believe that in every case the amyloid change has been engrafted upon a cirrhotic or parenchymatous inflammation. To whatever extent the atrophic processes may have extended, the nature of the amyloid change can always be recognized upon applying the iodine test and examining microscopically with a low power.

Ætiology:—The two important if not the sole causes of amyloid degeneration, not only in the kidney but other organs as well, are syphilis and chronic suppuration, especially when the latter is associated with diseases of the bone. It is not essential, however,

that the suppurative process be in bone, since it is not infrequently met with in those who die of pulmonary phthisis, or intestinal ulcerations, or who are suffering from cold abscesses, caseous degeneration of the lymphatic glands, etc. When developed in connection with cancer it is probable that chronic ulcerative changes with suppuration have been present. It is less easy to appreciate the suppurative element in cases following chronic rheumatic affection, but the possibility of an unrecognized syphilitic element being present must be considered in all cases which appear to depend on other causes than specific infection or suppuration.

Statistics of lardaceous disease show such an exceedingly small per cent. of cases in which one of these two causes cannot be recognized that it seems fair to assume that hidden specific infection may be allowed to account for these few. The scrofulous cachexia has been suggested as a possible cause of amyloid change and there is some reason for the belief that it occurs in connection with Hodgkin's disease without suppuration. There seems to be no sufficient ground for the statement that the malarial poison can induce this form of degeneration.

Symptoms:—The early symptoms of waxy kidney which are referable to the renal change are such as mark the development of cirrhotic Bright's. The gradual loss of strength and enfeeblement of both the mental and physical powers are prominent develop-

ments. Anæmia is even more marked than in renal cirrhosis, and the skin assumes a peculiar waxy appearance with spots of pigmentation about the face and eyes. Anorexia becomes annoying and fatty articles of food not only are distasteful but cause severe dyspeptic symptoms. Vomiting may occur but is not a prominent symptom. Dyspnœa upon exertion appears early and soon the patient is unable to assume the recumbent posture without great distress in breathing.

The urinary symptoms appear early in the disease. The patient notices the increase in the urine and that he is compelled to rise at night to pass water. This increase in quantity of the urine is one of the most characteristic symptoms. The amount passed in 24 hours may reach one hundred or more ounces when the renal changes are well established. It is very light color, often being like pure water, or at most having only a faint amber tint. The specific gravity is often as low as 1005 or even 1003, but may be as high as 1020.

Authorities differ materially in their statements regarding albumen, some claiming that the amyloid change *per se* does not produce albuminuria, but that its occurrence is proof of the advent of parenchymatous changes. On the other hand others claim that albumen is always present in greater or less amount. Conheim claims to have made autopsies on cases of amyloid kidney in which albuminuria was said never

to have been present. In the earlier stages the amount of albumen may be small and doubtless depends in large degree in all cases upon the extent of secondary changes. Later as a rule the amount is relatively large, and may possibly reach one or two per cent. Casts are quite invariably present, though seldom in large numbers and several examinations may be required before they will be found. Large and small hyaline casts predominate, but as the disease progresses and parenchymatous processes become degenerative in character fine granular and possibly fatty casts will be added.

The amount of urea excreted in the 24 hours is seldom materally decreased, although it is relatively small in any given specimen. As a direct consequence all that class of symptoms which depend upon uræmia are seldom well marked and may be entirely absent. It seems hardly necessary to say that when a distinct acute nephritis supervenes in an amyloid kidney the symptoms will be correspondingly changed. It must be stated, however, that, occasionally in the last stages of the disease, without apparent cause, the urine is decreased in amount, of high color and specific gravity, and that the change is associated with distinct uræmic developments. Similarly in typical amyloid cases dropsy is never a prominent symptom. Slight œdema of the feet and a little puffiness of the lids are transient rather than permanent symptoms.

The ascites, moreover, which is quite common, as

well as the abdominal enlargement is due to a corresponding amyloid change in the liver and spleen. This localized dropsy becomes an important aid in diagnosis since the recognition of amyloid degeneration of other organs than the kidney is often the decisive point in establishing the existence of the renal disease. The cardio-vascular changes are also important points in diagnosis.

The cardiac hypertrophy which is so constant in both chronic parenchymatous, nephritis and cirrhotic kidney is seldom present in amyloid disease. This can not be accounted for entirely upon the ground that the interstitial changes do not cause obstruction to the circulation in this as in other forms of renal disease.

When it is remembered, however, that malnutrition and general wasting of all the tissues is the especial characteristic of waxy degeneration, we may find a ready explanation of the absence of cardiac hypertrophy and the more frequent degeneration and dilatation of the heart muscles, with its consequent and typical œdema.

Finally, it must be observed that many cases of amyloid kidney pass entirely unnoticed until some other disease calls for a close examination of the patient. Even the exhaustion and muscular atrophy may be absent and the patient continue severe manual labor after the amyloid change has involved the liver spleen and kidneys to an extent generally productive of marked symptoms.

Prognosis.—A few cases of recovery from what had been diagnosticated as lardaceous disease are on record, and the ability of the observers forbids doubt as to correctness of the diagnosis. Such cases can almost be enumerated upon the fingers, however, and have been invariably due to specific infection. It cannot then be said that it is always an incurable disease. In nearly every instance the amyloid degeneration, when once established, is surely though slowly progressive, and sooner or later reaches a fatal termination. Its duration is exceedingly variable. Patients may live for years in comparative comfort, in whom the change is unquestionably well advanced. It is difficult to make any exact estimate of its average duration, owing to the uncertainty always attending the exact time of its invasion. Many patients have been under observation for eight, ten, or more years, and known to enjoy reasonable health and comfort during that time.

The direct cause of death is quite as frequently some complication arising from the implication of the of the liver, from the general degenerative changes, or from cardiac failure. A chronic diarrhœa, dependent upon amyloid disease of the intestine, not infrequently induces fatal exhaustion. Acute inflammatory complications are infrequent. When general dropsy sets in, the downward course is more rapid than in other forms of renal disease, but this is due to the fact that anasarca is quite certainly due to cardiac

failure and not to the renal lesion itself. Lardaceous disease, due to syphilis, is more frequent in middle life, from 30 to 40, while those cases dependent upon protracted suppuration are found most commonly in still younger persons.

Treatment.—Prophylactic treatment is evidently of the utmost importance in preventing the development of amyloid changes. The frequency with which it is found to depend upon syphilis, and the fact that it is a tertiary manifestation indicate at once that many cases of syphilis give up treatment before the disease is fully eradicated, and make evident the necessity of protracted courses of mercury and potash after all manifestations of the specific action are obliterated. With the developments of modern surgery there is less necessity for insisting upon the treatment of suppurating foci and the removal of necrotic and carious bone. Such sources of danger are no longer allowed to remain as centres of infection. Even in cases where upon other grounds surgical interference is less desirable, the dangers which always attend chronic suppuration become strong arguments in favor of radical operative measures. When waxy changes are once developed there can no longer be any question as to the necessity of at once removing the offending disease when it is at a point where the necessary surgical procedure is not certain to be attended with fatal results, for amyloid change with its exciting focus of suppuration still present becomes absolutely fatal.

When developed as a result of specific infection, the same measures must be employed as are used for prophylaxis, only remembering that, as it is a tertiary manifestation,all debilitating treatment must be avoided, while tonic measures are especially indicated. Phosphorous, nux vomica and iron are all of service. Personally, I have found the pil. ferri iodidi the most serviceable to this class of patients. Diuretics, digitalis and cathartics will be of service only when the secondary renal changes are developed, or when cardiac dilatation is threatened.

INDEX.