ACUTE AND SUB-ACUTE NEPHRITIS.

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Acute nephritis may be so mild a disease that it passes unnoticed by the patient and is only recognized by the examination of the urine ; or it may be so severe as to cause death within a few days of its onset. It may heal rapidly and completely, or may lead slowly to a condition of chronic invalidism terminated by uræmia.

It is therefore desirable that some clinical distinction should be made between varieties of the disease, so that when confronted with a case, an opinion may be given as to the course it is likely to run.

Of the various types which have been described the two which seem to be most distinct, and which some consider to be separate diseases, are *acute focal (or hæmorrhagic focal) nephritis*, and *acute diffuse nephritis*.

Acute Focal Nephritis.

Acute focal nephritis is a disease of children and young adults which occurs during the course of a febrile illness. Most commonly this illness is a streptococcal infection, but focal nephritis may occur also in typhoid fever or pneumonia. Usually the only symptom is hæmaturia which is sudden in onset and may be intense, but the passage of the blood may give rise to some pain referable to the urinary tract. The blood-pressure is normal throughout the illness, and oedema does not occur. The hæmaturia is usually recognizable by the naked eye, and the accompanying albuminuria is slight in degree. Estimation of the albumin by Esbach's tube shows amounts of $\frac{1}{2}$ to 1 gram per litre, and the urinary deposit consists of blood cells with a few granular casts or blood casts.

Pathologically the renal lesion is in the glomerulus but only a few of the glomeruli are affected. Some observers have shown the presence of bacteria in the glomeruli and this is said to be a point of distinction between the focal and diffuse forms of acute nephritis.

The diagnosis of focal nephritis in a typical case is easy. Hæmaturia with casts, occurring during the height of a febrile illness is unlikely to be due to any other cause. Diffuse nephritis is excluded by the absence of hypertension or oedema. Other conditions causing occasional difficulty in diagnosis are pyelonephritis (*Bacillus coli* infection) accompanied by hæmaturia, Henoch's purpura, renal tuberculosis, and the embolic nephritis of malignant endocarditis which will be mentioned later. Less commonly renal or vesical calculus, papilloma of the bladder or other surgical causes of hæmaturia may need consideration.

Treatment. The disease rapidly subsides as the patient recovers from the initial infection, and no treatment directed to the kidney is usually required. The diagnosis between focal nephritis and a mild attack of acute diffuse nephritis is not, however, always easy, and it is therefore necessary to be on the look out for any sign of oedema, or any rise in blood-pressure. In cases of doubt the treatment appropriate to the diffuse form should be adopted. The existence of

focal nephritis should, moreover, be looked upon as an indication for the thorough treatment of the causative infection, and any septic focus should be properly eliminated. For example suppurating glands may require incision, or mastoiditis a radical operation. The renal lesion does not contraindicate the use of ordinary general anæsthetics.

When the disease has subsided, any residual infection should be dealt with as there is otherwise a strong tendency for focal nephritis to recur. For instance, a history of recurring hæmaturia coinciding with attacks of tonsillitis is not infrequent, and both will usually cease after a satisfactory tonsillectomy.

Acute Diffuse Nephritis.

Acute nephritis, which without any further adjective indicates the diffuse form, is again prone to occur as a complication of infective illnesses, especially streptococcal. Most commonly, however, it is seen not at the height of the illness, but some 10 days to 3 weeks after the pyrexial period has subsided. By far the commonest antecedent illness is streptococcal tonsillitis, including of course the scarlatinal variety. Nephritis may occur, however, during the course of other infective diseases, even those of a relatively chronic nature such as impetigo or chronic otitis media. In some cases no relation to an infection can be established.

Opinions differ as to the nature of the process which actually causes acute nephritis. Bacteria are not found in the kidney and the current practice is to assume that the disease is either due to their toxins or to some type of anaphylactic phenomenon. The pathology will be dealt with elsewhere but one may summarize the matter by saying that the vessels of the glomerular tuft show signs of congestion and inflammation, the tubules undergo varying degrees of degeneration, and the vessels throughout the body tend to be in a state of contraction, which accounts for the characteristic pallor and rise of blood-pressure.

Clinical Appearances. Acute nephritis is not common in infants though it does occasionally occur. It is largely a disease of children and young adults, and is rarely seen over the age of 35.

The three outstanding features of the disease are oedema, rise of blood-pressure (hypertension), and the presence of albumin and blood in the urine. These vary very much in degree from case to case and only the albuminuria is practically a constant finding. The oedema is sudden in onset, diffuse in distribution but never extreme in degree. It exhibits the well-known tendency to be at its worst in the morning and to be most noticeable in the eyelids and ankles. Sometimes there is ascites of moderate degree and oedema of the back and abdominal wall. Even when there is no demonstrable oedema, the skin is usually pale, pasty and inelastic, and easily marked by the bed clothes, showing that excess of fluid is being retained in the body.

The hypertension again is rarely extreme and may be transient. In estimating the blood-pressure age must be taken into account. Pressures of say 140/90 in young patients are of considerable significance.

The hæmaturia and albuminuria also vary considerably but the latter usually amounts to some 5 grams per litre and is out of proportion to the quantity of blood in the urine.

Other symptoms and signs of course occur. At the onset, headache and abdominal pain with vomiting are common, though pain in the back is unusual. The temperature may be raised in the early stages and the pulse is usually full but not very rapid. The optic discs may show oedema but retinal hæmorrhages and exudates rarely occur. Examination of the urine shows its volume to be decreased. Its appearance may be obviously bloody, characteristically 'smoky' or merely concentrated. Its specific gravity is most commonly about 1020. The deposit after centrifuging or standing contains much cellular debris, many red cells and leucocytes, with granular, cellular and hyaline casts, the most typical of which are the brown or reddish granular variety. The blood may show a moderate leucocytosis, but in cases of ordinary severity there is no significant retention of urea or other waste-products and the blood-urea and non-protein nitrogen do not rise to more than 40 or 50 mgs. per 100 c.c.

Some other symptoms of acute nephritis require separate mention, as they occur only in certain cases, and when present modify the clinical picture so as to constitute almost a separate variety of the disease. These are convulsions, anuria, uræmia and heart failure.

Convulsions may occur at any time during the early stages of acute nephritis, and may be the first symptom. They are prone to develop when the rise in blood-pressure has been pronounced (160-180 mm. in young adults). Such cases are often not the most oedematous ones, and the cause of the convulsions is probably cerebral anæmia rather than oedema. The convulsions are epileptiform in type and may follow each other so frequently that no period of consciousness occurs between them. They are indistinguishable from the convulsions of eclampsia, and are not constantly or even usually associated with any increase in the blood urea or non-protein nitrogen. It is thus wrong to speak of them as being uræmic in origin.

Anuria may be an alarming and dangerous complication of acute nephritis though as a rule this does not last more than 2 or 3 days.

True uræmia as indicated by a significant retention of nitrogenous substances in the blood, for instance a non-protein nitrogen of 100 mgs. or more per 100 c.c., rarely occurs. It is likely to be present in the anuric cases and may be associated with severe headache, drowsiness and vomiting.

A certain small percentage of cases of acute nephritis suffer from **cardiac symptoms** brought on by the rapid increase of blood-pressure. These are shortness of breath, in some cases amounting to cardiac asthma, congestion of the liver and lungs, and oedema of the dependent parts. Occasionally acute pulmonary oedema occurs. Such symptoms are more likely to develop in adults than in children, and occasionally the cardiac symptoms are so much in evidence that the true nature of the disease is not at first suspected.

All these complications of acute nephritis occur in the early stages and, although they add something to the immediate gravity of the prognosis, they may disappear completely as the acute phase of the illness subsides.

Diagnosis, Course and Prognosis. The acute onset of oedema and albuminuria in a child following closely on the recovery from tonsillitis, makes the diagnosis obvious in the majority of cases. The chief difficulties are encountered when the

œdema is absent or minimal and it is not known how long the albuminuria or hypertension have existed. In such cases chronic renal disease may have to be considered and other renal abnormalities such as polycystic kidney. The so-called functional or orthostatic albuminuria occurs in persons of the same age (adolescents and young adults). In this condition the history of infection is not usually present and there is neither hypertension nor œdema. Specimens of urine obtained in the morning or while the patient is in bed usually contain no albumin, or at most only traces, but the albumin returns when the patient is allowed to walk about. In these functional albuminurias the protein excreted is not the same as in nephritis, and the addition of acetic acid to the urine without heating will usually give rise to a definite cloud.

Cases of acute nephritis in which hæmaturia is the presenting symptom may also cause difficulty in diagnosis, and physicians who have had a large experience of kidney disease will have seen young patients with advanced chronic nephritis in whom the only symptom of an acute attack was hæmaturia some years previously. Several such patients have told me that they were at that time sent to a surgical department to be cystoscoped and investigated and that no cause for the hæmaturia was found. Presumably the urine had not been examined for casts and the possibility of acute nephritis had not been considered. This is a serious omission, since it means that correct treatment is not applied until the disease has reached an incurable stage.

In acute nephritis seen in an early stage the prognosis should never be unconditionally good, as even apparently mild cases may suffer from exacerbations or recurrences and eventually develop chronic nephritis. Nevertheless, certain rules of prognosis can be laid down. Cases starting suddenly, perhaps with anuria and convulsions, following closely on an infection and running a stormy course in the first few days, are grave at the outset but usually make a complete recovery if they can be steered through their initial dangers. The opposite type, starting insidiously with no definite relation to infection, and with pronounced pallor and œdema, are most likely to run a slow but unfavourable course. In them the hæmaturia is usually slight but the albuminuria profuse. The blood-pressure, though never very high, is notable by its persistence. Nevertheless, I have seen a number of cases of this type make a complete recovery after very prolonged treatment and strict confinement to bed for a period of several months. Some of these cases may practically be labelled subacute nephritis from the start, and in the worst of them the blood-pressure gradually rises and the œdema increases and the final stage of renal failure develops within a year or less of the onset.

The reader with experience of obstetrical cases will see in this a resemblance to eclampsia and pregnancy albuminuria, as it is often the case that the more sudden the onset of eclampsia the more rapid and complete is the recovery after delivery.

In the most favourable cases of acute nephritis, after a few days or perhaps a week or two of oliguria and slight œdema, there is a sudden diuresis which lasts for 2 or 3 days and is followed by a rapid disappearance of all the signs and symptoms of the disease.

One cannot stress too firmly the importance of residual albuminuria following acute nephritis. Many text books give the impression that if the other symptoms clear up a certain amount of albumin may remain in the urine for months or years, and does not represent a sign of activity of the renal disease. This is, in my experience, only true of residual albuminuria when it amounts to nothing

more than a trace, i.e., less than $\frac{1}{2}$ gram per litre. But, if one follows up patients who are left with 2 or 3 grams of albumin or more, one finds that the great majority of them slowly develop chronic nephritis in the course of the next few years. In other words they are not cured but have passed into the latent stage. Treatment should therefore not be given up until either the patient is for practical purposes free from albuminuria, or until all hopes of a permanent cure have been abandoned.

Treatment. Before considering the treatment of acute nephritis it is as well to have in mind some conception of the functional pathology of the disease.

The essential lesion in the glomerulus causes slowing of the glomerular circulation. This in turn leads to a slow secretion of urine and excessive re-absorption of saline fluid in the tubules. In the author's opinion this accounts for the oedema and the oliguria of acute nephritis. The renal changes are accompanied by a general constriction of the arterioles of the body, though whether this is occasioned by the same cause as the nephritis, or whether it is a compensatory mechanism to raise the blood-pressure and thereby aid the secretion of the kidney, is not decided.

The first and by far the most important item of treatment is adequate rest for a sufficiently long time. I have often observed that patients who have been allowed to get up while still showing much albumin and perhaps even blood in the urine, or with still a trace of oedema, have run a particularly unfavourable course. Strict confinement to bed should be continued until all oedema and hypertension have disappeared, until the urine no longer shows a positive reaction for blood, and until albumin has been reduced to a mere trace. This period of complete rest may be little over a week in the mild cases but must if necessary extend to several months in the more severe. To allow the patient to go about with a pronounced albuminuria or other symptoms is equivalent to giving up any further attempt to cure the disease.

Second in importance to rest is warmth. Experiments have shown that chilling of the body surface leads to constriction of the renal vessels, and there is no doubt that in practice exposure to cold increases the intensity of an existing nephritis. The temperature of the room should therefore be kept at 60 to 65 degrees F., the patient should be nursed between blankets, and superficial cleanliness should not be procured at the expense of warmth and comfort. In severe cases with oedema, hypertension, and pronounced oliguria or anuria, it is traditional to apply heat in some form either as hot packs, hot air baths, or in more recent times radiant heat or an electric blanket, and the benefit which was thought to accrue from the removal of poisons by the production of sweating was probably due to the general effect of heat in relieving vascular spasm. In the author's opinion these intensive methods of applying heat are not desirable as a routine method. It has been asserted that the application of diathermy to the renal area produces an increased secretion of urine, but the results of this treatment have not been such as to give it an important place in the therapy of acute nephritis.

Dietetic therapy is not to be looked upon as in any way curative, but only as a means of guarding the patient as far as possible against the worst effects of the disease and saving the kidney from excessive work. The aim is therefore to restrict the intake of salt and water so as to counteract the tendency to oedema, and to give a diet low in calorie value and containing a minimum of protein.

A diet consisting purely of milk is not at all suitable as it contains too much fluid, too much salt, and too much protein. In the severe case especially if pyrexia, hypertension, and oedema co-exist, the diet for the first few days may consist merely of a pint of orange juice, sweetened if preferred. If the patient is hungry, a few biscuits or sweets may be given in addition. In the average case the following diet is suitable in the early stages and represents quite a severe restriction of fluid:—

Breakfast	...	4 ozs. coffee or tea with milk. 1 slice bread and jam.
Mid-morning		Half an orange.
Lunch	...	6 ozs. potatoes and vegetables (<i>not</i> peas or beans). 3 ozs. fruit.
Tea	...	4 ozs. tea with milk. Biscuits.
Supper	...	4 ozs. fruit. No salt. No extra fluid.

After the first few days, if progress is satisfactory, the following diet may be substituted:—

Breakfast	...	5 ozs. milk. Oatmeal, toast, marmalade. 2 ozs. tomatoes.
Mid-morning		Half an orange.
Lunch	...	6 ozs. potatoes and greens (<i>not</i> peas or beans). Yorkshire pudding. Milk pudding. 4 ozs. fluid (water or lemonade, &c.).
Tea	...	Toast, butter, jam. Cake. 3 ozs. fruit. 4 ozs. tea with milk.
Supper	...	Biscuits, bread, butter. 4 ozs. salad. 4 ozs. fluid (water or lemonade, &c.). No salt to be eaten or cooked with the food. No extra fluid.

When the patient is convalescent, and his renal function appears to be normal but for the presence of a little albumin in the urine, there is probably no need for specific dietetic therapy of any kind and an ordinary convalescent diet can be given. This will help to counteract the tendency to anæmia which develops if restricted diets are given for too long a time.

Drugs have little or no place in the treatment of acute nephritis. The mild diuretics have no effect and the efficient ones are dangerous. Drastic purgatives which used to be given as a routine only increase any tendency to toxæmia and

most of them are capable of producing nephritis experimentally if given in large doses. Medicinal treatment is therefore usually reduced to the giving of a saline aperient when necessary (which should consist of magnesium rather than sodium sulphate) and the administration of iron during convalescence. Drugs may have to be ordered, however, for the treatment of certain complications.

In cases of complete anuria the administration of large quantities of fluid usually tends to produce vomiting or oedema instead of the desired secretion of urine and it is probably better to treat them on restricted fluids and allow the congestion in the glomeruli to pass off. Most cases respond to such treatment within 2 or 3 days. If they do not do so, rapid administration of a litre of fluid by mouth or of a pint of 5% glucose solution intravenously may be tried. The operation of decapsulation of the kidney has been recommended if anuria persists for more than three days but it is of considerable danger and uncertain in its effects. Where uræmia co-exists with acute nephritis fluid restriction may have to be temporarily relaxed and intravenous glucose administered in the hopes of combating the toxæmia.

Convulsions are best treated by venesection, at least a pint of blood being taken from an adult. This may be followed by lumbar puncture. If the convulsions still continue—which is unusual—morphia or chloral may have to be given. 30 grs. of chloral can be administered by the rectum to an adult patient if he is unable to swallow. Heart failure in acute nephritis may also be treated by venesection, digitalis having little or no effect on this type of case. Severe abdominal pain and vomiting may be treated by morphia or luminal provided that independent disease of the stomach or intestines can be reasonably excluded.

The treatment of nephritis as so far described represents an attempt to protect the kidney and the body as a whole against the major effects of the disease in its active stage and to give the natural process of healing the best chance of taking place. The only treatment which can in any way be considered specific or curative is an attack on the causative infection. As acute diffuse nephritis tends to follow rather than to coincide with acute streptococcal infections, there is usually no septic focus requiring urgent treatment and it is wrong to disturb the more chronic foci of infection during the early or active stages of the disease for fear of precipitating a temporary exacerbation. When the patient has passed out of the early acute stage, whether albumin is present or not, a search should be made for foci of infection and any necessary operation for their removal should be performed. This is usually a few weeks or a month or two after the onset of the illness. The most common source of sepsis to be found is in the tonsils, and a tonsillectomy is advisable in the majority of cases. There is now considerable evidence to show that cases treated in this way are less liable to become chronic or develop subsequent attacks of nephritis. Some increase in the amount of albuminuria or a temporary recurrence of hæmaturia for a few days may occur after the operation but this is to be looked upon merely as a sign that the causative infection has been found.

Embolic Focal Nephritis.

Subacute bacterial endocarditis, which is in the majority of cases due to a streptococcus viridans septicæmia, is a disease in which multiple emboli occur. The kidneys may be considerably damaged by this process, minute infarcts occurring in the glomeruli or larger macroscopic infarcts due to occlusion of interlobar

or interlobular arteries. As a rule the only clinical symptom is the presence of red blood cells in the urine, but in some cases with large infarcts there may be pain in the back and gross hæmaturia. Very occasionally the kidneys become so disorganized that renal œdema or uræmia occur, but these complications are much more frequent when a true diffuse nephritis develops in the course of the same disease as is sometimes the case.

Acute Interstitial Nephritis.

This condition, referred to in practically all the literature on kidney disease is never seen as a clinical entity. It occurs in the course of a serious septic illness and is characterized pathologically by cellular and fluid exudations in the interstitial tissues of the kidney. It does not produce any clinical manifestations except occasional hæmaturia, or rarely anuria, and its treatment is that of the causative disease.

Sub-acute Nephritis.

It has already been said that acute nephritis, if it remains unhealed, may progress directly into a stage of prolonged œdema generally known as sub-acute nephritis, or may, after a latent period varying from about 1 to 10 years or more, develop into chronic nephritis.

In sub-acute nephritis, as in the acute form, the outstanding symptoms are albuminuria, œdema, and hypertension. Frank hæmaturia is rare but there is nearly always blood to be found in the urine from time to time. In some cases the onset is so insidious that it may be said that the case has been sub-acute from the start. The presence of hypertension and hæmaturia distinguish the disease from nephrosis, with which, in its early stages, it is otherwise identical. A great deal of what is described under nephrosis therefore applies to sub-acute nephritis.

Pathology. Sub-acute nephritis is one of the varieties of the large white kidney. The changes in the glomeruli which are seen in acute diffuse nephritis are now present in a more chronic stage, represented by a proliferation of the epithelium of the capsule forming the characteristic crescentic mass which partially obliterates the capsular space. The tubules however show profound degenerative changes and the vessels are beginning to show thickening. In advanced cases there may be sufficient fibrosis to have caused the kidney to contract.

Clinical Course. In the early stages of sub-acute nephritis the patient commonly complains of nothing except the œdema. This is usually most marked in the legs though in bad cases it may spread to the abdomen, back, arms and pleural cavities. The face also is pale and puffy and the eyelids swollen in the mornings. If the œdema is extreme there may be interference with respiration. The blood-pressure is only moderately increased in the early stages but tends to rise as the disease advances. The urine during the œdematous phase is reduced in amount ; its specific gravity is from 1015 to 1020. It contains a very large amount of protein, commonly 10 grams and sometimes as much as 30 or 40 grams per litre. The deposit contains numerous granular and cellular casts, much cellular debris and often many leucocytes and red cells. The blood shows an increasing degree of anæmia, the sedimentation rate is always very rapid, the cholesterol content is increased as it is in nephrosis, but the nitrogenous constituents are not much altered until late in the disease. The proteins of the blood plasma are much reduced in cases with severe œdema.

Cases of sub-acute nephritis are apt to run a particularly rapid and unfavourable course. Some cases are prematurely cut short by the development of complications such as peritonitis, pericarditis, or œdema of the glottis, but even if these accidents are avoided the hypertension increases and signs of renal failure develop. With the rise of blood-pressure, headache, vomiting, convulsions and retinitis may appear, the retinal changes leading sometimes to attacks of blindness. At this stage the amount of urine usually increases and its specific gravity becomes fixed at about 1010. The increase in the urinary volume often leads to a reduction or even complete disappearance of the œdema and the case then takes on the aspect of a rapidly developing chronic nephritis. Nitrogenous products may then accumulate in the blood and the symptoms of true chemical uræmia are added to the clinical picture. The prognosis depends on the rate at which the disease is progressing, but many cases run their full course within 6 to 12 months.

Treatment. In the early stages and in those cases which show little or no rise in blood-pressure and practically no hæmaturia, the treatment may be on the lines indicated under nephrosis, but in the rapidly advancing, malignant cases nothing can be done except to relieve the more distressing symptoms. Œdema may have to be treated by mechanical methods (paracentesis, Southey's tubes, etc.) as the kidney does not respond to diuretic drugs. The diet should be as in chronic nephritis except that salt and water must be restricted in the presence of œdema.

Latent Nephritis.

In latent nephritis there are no symptoms. This stage of kidney disease is only indicated by the presence of a persistent albuminuria and a gradually rising blood-pressure. As a rule there is a history of a recent attack of acute nephritis, but some cases are discovered accidentally, the urine being examined for some other purpose such as a life insurance examination. The condition has to be distinguished from functional albuminuria, and here the presence of albumin in the night urine as well as the day, and the presence of numerous casts usually makes the diagnosis clear. The amount of albumin varies but is commonly from 2 to 5 grams per litre. The patient may show some pallor but otherwise appears to be in normal health. The blood-pressure is at first only slightly increased but later becomes very high. Tests of renal function may show no abnormality in the early stages, but a series of tests taken at intervals show a progressive deterioration in the concentration power of the kidney. Sooner or later the patient complains of symptoms either due to the deficient excretory power of the kidney or to the development of hypertension, and this marks the transition between the latent and chronic stages of the disease. Latent nephritis may last for many years before these symptoms develop. The discovery of the disease in the latent stage should lead to a search for any septic focus which may be acting unfavourably on the kidney. Any such focus should be treated as radically as possible.