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Renal system disease, any of the diseases or disorders that affect the human urinary system. They include benign and malignant tumours, infections and inflammations, and obstruction by calculi.

Diseases can have an impact on the elimination of wastes and on the conservation of an appropriate amount and quality of body fluid. Many of the manifestations of renal disease can be accounted for in terms of disturbance of these two functions, and the alleviation of symptoms in those renal diseases that cannot be cured depends on knowledge of how these two functions are affected.

The eliminatory process does not, of course, end with the formation of urine; the urine has to pass down the ureters to the bladder, be stored there, and voided, usually under voluntary control. The whole mechanism can be deranged by structural changes in the lower urinary tract, by infection, or by neurological disorders that lead to abnormal emptying of the bladder. Disturbance of the lower urinary tract is an important cause of pain and distress, notably during pregnancy and in the elderly; and it can lead to serious and progressive damage to the kidneys, either by interfering with the drainage of urine or by allowing bacterial infection to have access to the kidney.

Acute renal failure

Acute renal failure occurs when renal function suddenly declines to very low levels, so that little or no urine is formed, and the substances, including even water, that the kidney normally eliminates are retained in the body. There are two main mechanisms that can produce acute renal failure. When the cardiac output—the amount of blood pumped into the general circulation by the heart—is lowered by hemorrhage or by medical or surgical shock, the renal circulation is depressed to an even greater extent. This leads directly to inefficient excretion, but, more importantly still, the kidney tissue cannot withstand prolonged impairment of its blood supply and undergoes either patchy or massive necrosis (tissue death). Given time, the kidney tissue may regenerate, and it is on this hope that the treatment of acute renal failure is based. The form of acute renal failure that is due to a poor supply of blood (ischemia) has many causes, the most common and most important being multiple injuries, septicemia (infections invading the bloodstream), abortion with abnormal or excessive bleeding from the female genital tract, internal or external hemorrhage, loss of fluid from the body as in severe diarrhea or burns, transfusion reactions, and severe heart attacks; a special case is the transplanted kidney, which commonly goes through a phase of acute renal failure that is independent of possible rejection.

The second common mechanism of acute renal failure is toxic. Many poisons are excreted by the kidney, and in the process, like other urinary constituents, they become concentrated and thus reach levels in the tubular fluid that damage the lining cells of the tubules. Though the tubular cells die and are shed in the urine, regeneration can take place and the patient survive, if he can be maintained during the period of depressed renal function and is not killed by other effects of the poison. Poisons that can affect the kidney in this way are numerous, but the main groups are heavy metals (mercury, arsenic, uranium); organic solvents (carbon tetrachloride, propylene glycol, methanol); other organic substances (aniline, phenindione, insecticides); and antibacterial agents (sulfonamides, aminoglycosides, amphotericin), and some fungi (e.g., Amanita phalloides). In addition to the ischemic and toxic causes of acute renal failure, mention must be made of fulminating varieties of acute renal illnesses that are generally mild (e.g., acute glomerulonephritis—see below) and of the acute form of immunologic rejection that can destroy a kidney irrevocably within minutes of transplantation. Another mechanism of acute renal failure is characterized by acute obstruction of the flow of urine from the kidneys; this condition is easily treated by restoring adequate urinary drainage from at least one kidney.

The course of acute renal failure can usefully be divided into three phases: an onset phase, a phase of established acute renal failure, and a recovery phase. In general, but not invariably, the second of these phases is characterized by a low output of urine (oliguria) and the third by an increasing urine output (polyuria). The onset phase is dominated by general illness, in which the episode of acute renal failure arises; at this stage there may be evidence of threatened renal damage such as blood in the urine or pain in the loins. At this early stage, renal damage may be reversible by prompt treatment of circulatory failure (e.g., by the transfusion of adequate amounts of plasma, whole blood, or electrolyte replacement fluids) and by maintaining adequate blood oxygen levels. Infection or any underlying causative disorder also must be treated quickly.

In the second phase, small amounts of urine, often containing red blood cells, or hemoglobin, are passed; complete absence of urine is not common and suggests that an obstruction is preventing urine from being passed. In quantitative terms, a urine volume of less than 500 millilitres per day constitutes significant oliguria; this is the least amount in which the excretory demand imposed by an ordinary diet can be met. In the actual situation of acute renal failure, the excretory demands may in fact be much greater, since many of the causes of acute renal failure also are causes of increased breakdown of the tissues in general. The blood urea increases, the rate of increase being conditioned both by the degree of renal failure and by the amount of tissue breakdown. Besides nitrogen, the kidney can no longer excrete adequate amounts of water, sodium, and potassium.

These various inadequacies point the way to the necessary management of acute renal failure—

the elimination from intake of any dangerous substance that the kidney can no longer handle. The diet must either be free of protein or contain small amounts of high-quality protein to lessen tissue breakdown. It must also be free from sodium and potassium: many persons with renal failure have died from pulmonary edema, a correlate of sodium retention, and others from the acute toxic effects on the heart of a raised level of potassium in the blood. Water cannot be excluded from the intake but must be limited to an amount estimated to equal the unavoidable loss of water from the skin and in breathing. The weight of the patient and the concentration of sodium in the blood are good guides to the adequacy of water restriction. In the absence of continuing losses of sodium from the body, as might occur from vomiting or diarrhea, a progressive fall in serum sodium implies that too much water is being taken in. Kidney function may recover, often in seven to 10 days. The use of dialysis, the removal of waste products by straining the blood through semipermeable membranes, gives further time for renal recovery. Potassium can be removed from the body by resins, but this is less often required if dialysis is available.

Although by comparison with the oliguric phase the recovery phase presents fewer problems, the convalescent kidney takes time to recover its full regulatory function, and electrolytes and water may be lost at an unusual rate during this stage, requiring replacement. Most individuals who survive completely recover from acute renal failure, but residual renal damage persists in some persons. In a few, this is so severe as to bring them effectively into the category of chronic renal failure. The artificial kidney has transformed the outlook for many patients with acute renal failure, and this, together with developments in the control of infection with more powerful antibiotics, constitutes one of the miracles of medicine in the last few decades.

Chronic renal failure

The term uremia, though it is sometimes used as if it were interchangeable with chronic renal failure, really means an increase in the concentration of urea in the blood. This can arise in many acute illnesses in which the kidney is not primarily affected and also in the condition of acute renal failure described above. Uremia ought to represent a purely chemical statement, but it is sometimes used to denote a clinical picture, that of severe renal insufficiency.

Infections of the urinary tract are more frequent during pregnancy, and women who have acute infections of the bladder and kidneys while…

As with acute renal failure, there are many conditions that can lead to chronic renal failure. The two most common causes are pyelonephritis and glomerulonephritis (kidney inflammation

involving the structures around the renal pelvis or the glomeruli), and other common causes are renal damage from the effects of high blood pressure and renal damage from obstructive conditions of the lower urinary tract. These primary disorders are described below. They have in common a progressive destruction of nephrons, which may be reduced to less than a 20th of their normal number. The quantitative loss of nephrons can account for the majority of the changes observed in chronic renal failure; the failure in excretion is due directly to loss of glomerular filters, and other features such as the large quantities of dilute urine represent a change in tubular function that could be accounted for by the increased load that each remaining nephron has to carry. There are many other causes of chronic renal failure aside from the four common ones. They include congenital anomalies and hereditary disorders; diseases of connective tissue; tuberculosis; the effects of diabetes and other metabolic disorders; and a number of primary disorders of the kidney tubules. Of the many causes, there are some that have importance out of proportion to their frequency, by virtue of their reversibility; these include renal amyloidosis (abnormal deposits in the kidney of a complex protein substance called amyloid), whose causes may be treatable; damage to the kidney from excessive calcium or deficiency of potassium; uric acid deposition in gout; the effects of analgesic agents (substances taken to alleviate pain) and other toxic substances, including drugs.

The person suffering from renal failure, especially in the early stages, may have no symptoms other than a feeling of thirst and a tendency (shared with many normal people) to pass urine at frequent intervals and through the night; or he may be in a coma, with occasional convulsions. The general appearance of the sufferer may be sallow because of a combination of anemia and the retention of urinary pigment. Even if not in actual coma, the affected person may be withdrawn; muscle twitchings and more general convulsions may occur. The coma is thought to represent poisoning, and convulsions are often related to the severity of the high blood pressure that commonly complicates advanced renal failure. Blurred vision is also a manifestation associated with high blood pressure. Bruising and hemorrhages may be noticeable.

Although the toxin (or toxins) of uremia has yet to be identified, the rapid improvement that follows dialysis points strongly to a toxic component. Urea itself is not notably toxic. Not all the chemical alterations in uremia are simple retentions. There is acidosis—a fall in the alkalinity of the blood and tissue fluids—reflected clinically in deep respiration as the lungs strive to eliminate carbon dioxide. The capacity of the kidney to adjust to variation in intake of salt, potassium, and water becomes progressively impaired, so that electrolyte disturbances are common. Poor appetite, nausea, vomiting, and diarrhea are common in uremic patients, and these in turn add another component to the chemical disturbance. Phosphate is retained in the blood and is thus associated with low blood levels of calcium; the parathyroids are overactive in

renal failure, and vitamin D is less than normally effective because the kidneys manufacture less of its active form (1,25-dihydroxycholecalciferol). (Parathyroid hormone causes release of calcium from the bones, and vitamin D promotes absorption of calcium from the intestines.) These changes can lead to severe bone disease in persons suffering from renal failure, because bone calcium is depleted and the calcium stores are not adequately replenished.

In chronic renal failure, excessive production of renin by the kidney can lead to severe high blood pressure (hypertension), and the effects of this may even dominate the clinical picture. In addition to damage to the brain and the retina, the high blood pressure may lead directly to heart failure. Hypertension can also accelerate the progress of renal damage by its impact on the renal blood vessels themselves, setting up a cycle that can be hard to break. Anemia is also often severe due in part to a failure to produce erythropoietin.

The patient in advanced renal failure is vulnerable to infection and other complications, such as vomiting or diarrhea, which need special care. When symptoms of advanced renal failure appear, deterioration can be delayed by a strict low-protein diet, 18–20 grams of high-quality protein each day. In terminal renal failure, the affected person can be rescued only by some form of dialysis and then maintained by dialysis or transplantation.

Glomerulonephritis

Glomerulonephritis is the disorder commonly known as nephritis, or Bright’s disease. The primary impact of the disease is on the vessels of the glomerular tuft. The suffix “-itis” suggests an inflammatory lesion, and glomerulonephritis is indeed associated with infection, in the limited sense that it may begin soon after a streptococcal infection and may be aggravated in its later course by infections of various kinds. Nevertheless, there is convincing evidence that glomerulonephritis does not represent a direct attack on the kidney by an infective agent; it appears to be, rather, an immunologic disorder, in the sense of the formation of antibodies in response to the presence of a foreign protein (antigen) elsewhere in the body; these form antigen–antibody complexes that lodge in the glomerular tuft or, in a small number of cases, themselves become deposited on the capillary glomerular walls. In each case the antibody or the antigen–antibody complex reaches the kidney via the circulation, and the mechanism is usually referred to as circulating complex disease. Glomerular damage is a consequence of the reaction that follows within the glomeruli. These deposits of foreign protein and complexes react with other protein components of blood (see the article complement) and attract to the site white blood cells and platelets, which also are circulating in the blood; these in turn release protease enzymes and other chemical mediators of tissue injury.

This view of glomerulonephritis is based partly on analogy with the renal damage that can be induced in animals by allergic mechanisms and partly on finding that a protein component of the allergic reaction is deposited in the diseased glomerulus. Within the general concept of an immunologic disorder, there is ample room for a variety of primary stimuli and of later immunologic disease-causing mechanisms. These include the possibility of primary glomerular damage, causing the glomerulus itself to become antigenic and so to provide a secondary antibody response, and also the participation of (or lack of participation of) T lymphocytes. Such a diversity is strongly suggested not only by the variations in the glomerular tissues observed both with the ordinary and with the electron microscope but also by the varying manifestations of the disease observed in the affected person.

Typically, glomerulonephritis appears as an acute illness one to two weeks after a sore throat, or—less commonly—after a persistent streptococcal infection of the skin. Other infective agents may be responsible, however, including some viruses and protozoans. A small number of drugs that act as foreign macromolecules can also do so.

The affected person has puffiness of the face and ankles and at the same time scanty and noticeably blood-stained urine. On examination, loose tissues show edema, and the fluid is easily displaced by light pressure; both the blood pressure and the blood levels of urea are slightly or moderately increased. The illness is an alarming one, but the fact is that the acute attack of glomerulonephritis needs no particular treatment other than the eradication of the infection or withdrawal of the offending drug, with some restriction of fluid and protein. Nine out of 10 affected persons recover completely. Exceptional outbreaks, with a higher mortality, have sometimes been observed. A very few patients may die in the acute attack, however, or in a few months' time, when the impact of the disease has been unusually severe. Another possibility is that the affected person may appear to have recovered completely, having lost all symptoms; but the disease process remains active, and there is progressive loss of nephrons, leading ultimately to chronic renal failure. This process may take many years, for most of which the person has no definite symptoms of latent nephritis except that the urine contains protein and small numbers of red blood cells. It need not be assumed, however, that the finding of protein in the urine (proteinuria) in the absence of symptoms means automatically that the patient has kidney disease; symptomless proteinuria has many causes and may indeed be found in young people who never develop any later evidence of renal disease.

In summary, glomerulonephritis can lead to renal failure within a few weeks or months, after many years of symptom-free proteinuria, or after a period of massive proteinuria, which causes

the nephrotic syndrome. All of these manifestations may sometimes be seen in individuals who have never had, or cannot recall, an acute attack. Renal biopsies in many patients with glomerulonephritis show a range of glomerular reactions that include increased cellularity and basement membrane damage and thickening and varying degrees of progressive destruction of glomeruli. In those who recover, complete resolution of glomerular disease occurs.

A curious form of glomerulonephritis especially common in children is associated with little structural glomerular damage, at least as seen by the ordinary light microscope. Characteristic abnormalities affecting podocytes are revealed by electron microscopy. The condition is usually attended by heavy proteinuria and the nephrotic syndrome. Although the evidence for an immunologic cause of this form of glomerulonephritis is less certain than in other types, and the provoking antigen is unknown, paradoxically the disorder usually promptly resolves when the patient is treated with corticosteroids or other immunosuppressive drugs, and renal failure never occurs.

Vascular disease

In the discussion of chronic renal failure, attention was drawn to the cycle in which high blood pressure secondary to renal disease can produce further damage to the kidneys. Clearly, primary vascular disease—disease affecting the blood vessels—could equally well be a cause of renal damage.

The most dramatic instance of this is the condition known as malignant hypertension, or accelerated hypertension, which arises when the blood pressure attains extremely high levels, the diastolic figure (the blood pressure between heart contractions) being 140 millimetres of mercury or higher (the normal being around 80). Sustained levels of this magnitude cause serious damage to the arterioles, the smallest of the arteries; this damage is widespread, but as it affects the kidneys it produces rapid destruction of renal substance, with a scarred kidney. Unless the blood pressure is controlled, malignant hypertension can cause death in a few months; since treatment at an early stage is notably effective, the condition represents an important medical emergency. Since the retinas are damaged as rapidly as the kidneys, the affected person may first notice blurring or loss of vision and will typically have a severe headache. Prompt treatment is necessary to avoid stroke, as well as damage to other organs.

More modest, but still elevated, levels of blood pressure can cause more gradual renal damage in elderly people or in those made prematurely aged by widespread arteriosclerosis (“hardening of the arteries”). In this condition the damage is in the larger arteries rather than in the

arterioles, and the condition is one of slowly progressive scarring. Renal damage can also arise, by various mechanisms, in a large number of diseases that impair the proper functioning of the blood vessels, such as diabetes mellitus, the collagen disorders, bacterial inflammation of the heart lining, and many more.

A specific renovascular cause of high blood pressure that, although uncommon, is important from the point of view of the control of blood pressure in healthy individuals involves the juxtaglomerular apparatus (JGA) and the secretion of renin. Occasionally, following trauma or arising spontaneously as a result of vascular disease, one or the other of the main renal arteries becomes constricted (renal artery stenosis). The fall in blood pressure beyond the constriction leads to increased secretion of renin from the JGA with the formation of the vasoactive angiotensin II. As a result, the blood pressure rises. Removal of the affected kidney, surgical repair of the constriction, or percutaneous transluminal angioplasty (a balloon catheter inserted through the skin and inflated in the artery to flatten plaque build-up) usually restores the blood pressure and the blood renin level to normal.