TitleEtiology of Renal FailureAuthored ByMelissa Slate RNCourse NoERF072108Contact Hour1

Purpose

The goal of this course is to ...

Objectives

- 1. State three common causes for both acute and chronic renal failure.
- 2. Identify various pathological causes for the development of renal disease.
- 3. Differentiate between acute and chronic renal failure.

The discussion of the causes of renal failure is a vast subject covering many common and obscure processes and diseases. While we cannot possibly attempt to cover all of them in this study, we will present the clinician with an overview of some of the most common causes encountered in healthcare practice. It is strongly encouraged that the clinician further explores this fascinating subject in more depth.

ANATOMY

The kidneys are two bean shaped organs lying in the posterior abdominal cavity requiring a vast blood supply to function properly, the kidneys receive 20-25% of the total cardiac output or about 1200cc per minute. The renal arteries branch off the aorta and enter the kidney at the concave curved surface called the hilum. The kidneys are highly sensitive to changes in blood supply; a 1% change in circulating blood volume causes distinct changes in urine concentration and serum electrolytes (Wilkens, pp.835).

The renal arteries further subdivide, and become increasingly smaller until they reach the afferent arterioles, located deep in the renal cortex. Each afferent arteriole divides into a tuft of about 12 capillaries called the glomerulus. The glomerulus is contained within the nephron, which is the functional unit of the kidney. Each kidney contains approximately one million nephrons, which are present at birth. The body does not make new nephrons during its lifetime, in fact, there is a natural, slow and gradual loss of nephrons beginning about the age of 40 and continuing for life. When the kidneys begin to suffer damage and nephron loss occurs, the kidneys may compensate for a time by enlarging the remaining nephrons, but once the loss becomes great enough, the kidneys can no longer compensate and renal failure occurs (Lancaster). The nephron consists of a vascular component that includes the afferent arteriole, the glomerulus, and the efferent arteriole; and a tubular component that includes Bowman's capsule, the proximal and distal convoluted tubules and the loop of Henle (where water and electrolyte regulation occur), and the urine collecting tubules and ducts. The glomerulus projects into the Bowman's capsule. Water and solutes under pressure gradients filter from the glomerulus across capillary membranes to the Bowman's capsule. This mixture proceeds to the proximal tubule, through the loop of Henle, to the distal convoluted tubule. Along the way, this solution is concentrated and refined reabsorbing some substances and leaving others until the

final concentrate known as urine is obtained. The urine travels into collecting tubules and ducts finally passing from the kidney to the ureter and then the bladder. At least 500cc of urine is needed per day to effectively eliminate metabolic waste. Urine is made at approximately 1 cc per minute so output of less than 30 cc per hour is an important symptom and always warrants further investigation.

The kidney serves multiple vital metabolic processes and influences the entire biological system. The kidney removes nitrogenous wastes, regulates the electrolyte balance of the blood, controls acid/base balance by the production of hydrogen ions, produces the hormone erythropoietin which stimulates the bone marrow to produce red blood cells controlling anemia, and regulates blood pressure by controlling the production of rennin. The kidney also converts vitamin D to its active form and secretes hormones to regulate renal blood flow.

Alterations in renal function cause disturbances in every major body system. The skeletal system is affected due to the changes in the way calcium, phosphorus, and Vitamin D are utilized by the body. Calcium is pulled from the bone in the body's attempt to control rising phosphorus levels leading to osteoporosis and osteodystrophy. The muscular system and neurological systems are affected by altered levels of sodium, calcium, and potassium as well as the buildup of nitrogenous wastes. The heart, which is a muscle, does not escape. Sudden cardiac arrest due to hyperkalemia is an important cause of mortality in patients with renal failure. The circulatory system is afflicted with hypercholesterolemia, and mechanical stressors due to high blood pressure and fluid retention. Appetite and gastrointestinal function are disturbed leading to GI bleeding, nausea, and anorexia. The skin suffers from intense itching due to uremic toxins and high phosphorus levels.

Classifications of Kidney Failure

Acute

Acute renal failure (ARF) is defined as the sudden loss of renal function over a short period of time. ARF classified into three types: prerenal, intrinsic, and post renal. Acute renal failure carries up to a 50% mortality rate, prompt recognition can prevent further complications, potentially reverse renal damage, and prevent death. ARF most commonly occurs in the hospital setting. The elderly are particularly susceptible to ARF due to the natural, age-related nephron loss and decline in renal function. ARF may be asymptomatic and urine output may or may not be affected. Since creatinine is totally regulated by the kidneys, it is used as a measure of renal function. BUN elevations may be caused by other factors such as dehydration, GI bleeding or fever. Careful tracking of serum creatinine levels is essential to detecting ARF. Small increases in creatinine can be a signal that the kidneys have lost approximately one-half of their nephron function. The resultant rise in creatinine can be as little as 0.7 to 1.4mg/dl (Nally). The patient may also experience hyperkalemia and metabolic acidosis.

Prerenal failure results when a disturbance in the body's system results in decreased circulatory volume to the kidney, in other words filtration of wastes is not occurring due to inadequate blood supply to the kidney. CHF, hypovolemia due to shock, dehydration, or blood loss and hypotension are some of the causes of prerenal failure. Pre-renal failure accounts for approximately 70% of the cases of acute renal failure (Kallenbach, et al.). Medical management focuses on correction of the underlying cause to optimize renal perfusion. Vasopressors (opinions differ as to their usefulness), volume expansion, and possibly dialysis may be used as supportive therapy. Acute RF due to prerenal causes has an excellent prognosis if it is quickly recognized and appropriate therapy is instituted (Nally).

Intrinsic or intrarenal failure results when insult or injury occurs to the functional unit of the kidney itself. Approximately 25% of all acute renal failure cases are due to intrinsic renal failure

(Kallenbach, et. al.). The most common form of intrinsic renal failure is Acute Tubular Necrosis, which is the number one cause of all intrinsic acute renal failure (Nally). ATN usually occurs after an acute ischemic or toxic event and damage to the kidney tubules occurs. Tubular cells are quite sensitive to low perfusion, after 2 hours of ischemia renal tissue injury occurs. If the ischemia is serious enough, tissue injury can occur after 30 minutes with a Mean Arterial Pressure below 60mm HG (Kellenbach, et. Al.). Gram - negative sepsis may cause systemic vasodilatation leading to hypotension and decreased renal perfusion. Tubular cells die and slough off occluding the tubular lumen. The glomular basement membrane may also be damaged (Kelly).

There are usually three distinct phases to ATN. In the initial phase, glomular filtration rate decreases and creatinine rises. If nephron injury is excessive, urine output begins to decline. The maintenance phase is characterized by continued severe decrease in glomular filtration rate and further decline in urine output lasting 1-2 weeks. Be alert to sign and symptoms of fluid overload. Complications such as hyperkalemia, cardiac arrest, G.I. bleeding (elevating potassium levels further), and infection may occur. The resolution phase is hallmarked by large amounts of urine output and a decrease in BUN and creatinine levels.

Nephrotoxic ATN

The high blood flow that the kidney receives makes it a prime target for toxins. External nephrotoxins, the aminoglycosides (vancomycin, gentamycin, tobramycin for instance), amphotericinB, and radiological contrast media (i.e. IVP dye), cause renal vasoconstriction and are directly toxic to tubular cells. Tubular cell necrosis and obstruction follow. Dehydration further enhances this toxicity. Risks to the kidney are minimized if the patient is well hydrated before and during medication therapy or radiological procedures. Patients with nephrotoxic ATN more commonly exhibit urine output than patients with other forms of ATN.

Ironically, drugs commonly used in the renal transplant setting can cause ATN. Cyclosporine, acyclovir, sulfa drugs, and cephalosporins all can be nephrotoxic under the right circumstances. Monitor the patient carefully when these drugs are being used. NSAIDs such as ibuprophen can cause renal injury, particularly in elderly patients who consume these medications for relief of arthritis pain and are at risk due to age related nephron loss.

Injury to muscle tissue (rhabdomyolysis) causes myoglobinuria. The cause may be drug induced (cholesterol lowering statins), or as a result of crush injury, alcoholism, viral infection and cocaine addiction. The exact pathophysiology is not completely understood but may include DIC, tubular obstruction, and ischemia.

ATN may also be caused by transfusion reaction, crystal formation (gout, ethylene glycol poisoning) or multiple myeloma (Thatte & Vaamonde).

Post renal Failure

Postrenal failure is caused by obstruction of the urinary tract at any point past the kidney itself. The cause may be urinary stones, an enlarged prostate, or strictures. Urine backs up into the renal pelvis causing the tissues to dilate and internal kidney pressures to rise. Filtering of renal toxins does not occur because the blood cannot overcome the pressure gradient of the urine. The focus of treatment should be upon relieving the obstruction, with the method chosen being dependent upon the type of obstruction (Nally).

Chronic Renal Failure

Chronic renal failure is the slow, progressive, irreversible loss of nephron function, causing scarring and loss of kidney size. CRF may be silent until around 70% of nephrons are lost and symptoms appear. CRF that progresses to the need for dialysis is called End Stage Renal Disease (ESRD). Acute renal failure, regardless of cause, may progress to CRF and ESRD.

Chronic renal failure incidence more than doubled in the 1990's and obesity has been identified as a risk factor due to the role it plays in diabetes and hypertension. Chronic renal disease has five stages defined by the amount of kidney damage present.

Stages

- 1. Kidney damage but glomerular filtration rate remains normal >90ml/min.
- 2. Mild kidney damage- GFR 60-89ml/min.
- 3. Moderate kidney damage- GFR 30-59ml/min.
- 4. Severe kidney damage- GFR 15-29ml/min.
- 5. Kidney Failure (ESRD) GFR< 15ml/min. Dialysis is becoming necessary at this point (Kallenbach).

Diabetic Nephropathy

Diabetes is the leading cause of CRF in the US and European countries. Around 30% of patients with type 1 or type 2 diabetes will develop nephropathy. Diabetic nephropathy is silent in the beginning. Elevated blood glucose levels cause glucose molecules to attach themselves to blood and renal proteins. This causes chemical rearrangement of renal protein bonds and changes in tissues of basement membranes. The basement membrane begins to thicken. Blood pressure within the glomerulus rises and hyperfiltration develops. Blood proteins called albumins are squeezed through the damaged basement membrane and begin to appear in the urine. As diabetes advances, more glomeruli are damaged and urinary protein losses increase. Smokers, persons with poor glucose control, and patients with hypertension are at greatest risk. Patient education is vital to the treatment of the disease. Patients should be tested yearly for the presence of urinary microalbumins. For patients with hypertension, ACE inhibitors may be of some benefit in decreasing disease progression (Daugirdas, et. al.).

Hypertensive Nephrosclerosis- The Chicken or the Egg?

Hypertensive Nephrosclerosis is the second leading cause of ESRD in the United States. The opinions differ on whether hypertension causes primary renal disease or aggravates it. Some theorists state that other disease processes or factors disrupt sodium and water balance within the kidneys leading to hypertension. Hypertension then further damages the kidney and exacerbates the disease process.

The most common pathologic change in the kidney is sclerosis along with thickening and narrowing of the walls of the preglomerular blood vessels leading to decreased renal blood flow and increased vascular resistance. The glomeruli become ischemic and damage to the basement membrane develops with subsequent leakage of protein particles into the urine. Once this process is established, feedback systems are activated and a vicious cycle begins with worsening hypertension and advancing renal impairment (Fervenza).

Glomerulonephritis - Third most common cause of chronic renal failure.

A collection of disorders affecting the glomerulus and causing defective filtration processes. Most are inflammatory. The glomerulus responds to insults by cell proliferation or by thickening of the basement membrane. GN may be acute or chronic and is classified as primary or secondary.

Primary disease is focused within the kidney;

secondary GN is part of a systemic disease process. There are two main clinical manifestations of GN: nephritic syndrome and nephrotic syndrome. Both cause the retention of unwanted waste substance and the loss of needed substances.

Nephrotic Syndrome is characterized by protein loss via the urine from glomerular damage. The patient may experience water retention, which leads to edema. Changes in hepatic synthesis of lipids leads to hyperlipidemia. The cause may be related to several different disease process; amyloid disease, Lupus, and Goodpasture's syndrome are examples of immune system alterations that can lead to renal damage and nephrotic

Nephritic syndrome is hallmarked by hematuria, HTN, and edema, most often caused by inflammatory processes which lead to impairment of filtration causing uremia and water retention. The inflammatory processes are often due to immune mediated mechanisms. Post streptococcal GN is a childhood acute nephritic syndrome that occurs after strep throat. PSGN is also an immune mediated disease (Merck).

Polycystic Kidney Disease

Polycystic kidney disease is a disorder in which kidney tissue is replaced by non-functioning fluid filled cysts. There are three types of PKD, two inherited forms and one acquired form. Polycystic kidney disease is the fourth leading cause of renal failure and the most frequently inherited disease. PKD is the most common genetic disorder of the kidney.

Autosomal Dominant Polycystic Disease is caused by genetic mutations on three different genes. 1 in 1,000 people carry the gene for PKD. If one parent has ADPKD there is a 50% chance the child will inherit the disease. This disease is usually present at birth but symptoms do not appear until after the third decade of life. Hypertension is usually the first symptom seen and then renal cysts appear which are filled with a fluid closely resembling urine. The kidneys enlarge, sometimes weighing over 20 pounds, but functional tissue decreases. Cysts may appear on other organs, especially the liver. Abnormalities of the heart and major blood vessels are also seen.

Autosomal Recessive Polycystic Kidney Disease is a rare disorder that consists of two main components, a hepatic component with predominant hepatic symptoms and a renal component with largely renal symptoms, however the liver is involved in all cases. It is the most common inherited cystic renal disease appearing in childhood. Both parents must carry the cystic kidney gene for the child to become afflicted with the disease. Outcome and severity of the disease are largely dependent on which form predominates and the age of onset.

Acquired Polcycstic kidney Disease is usually seen in persons on dialysis greater than five years. People with acquired cystic disease can have any initial cause of renal failure. Sometimes these cysts cause hematuria and this is often the first sign that someone has acquired the disease (Torra).

With kidney disease and renal failure increasing at alarming rates, they eyes of medicine must turn toward preventative and offensive measures to combat the spread of this disease. Renal failure and ESRD treatment costs have escalated to millions upon millions of dollars. These facts are astounding considering during the late 1960" and early 1970's renal disease treatment was still in its' infancy. Health care professionals must answer the call and accept the challenge to educate themselves regarding the disease processes, for in knowledge the tools of battle are found.

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Course Exam

- 1. Nephrotic syndrome causes urinary protein loss
 - ○True ○False
- 2. Urine output of more than 30cc per hour needs investigated.
 - True False
- 3. Diabetic nephropathy is the leading cause of chronic renal failure in the US.
 - ○True ○False
- 4. Dehydration can cause prerenal failure.
 - ○True False
- 5. Creatinine is the most effective measure of renal function.
 - ○True False
- 6. Chronic renal failure is defined as the loss of nephron function over a short period of time.

○ True ○ False

- 7. Postrenal failure is caused by an autoimmune reaction to a virus.
 - ○True False

8. Autosomal dominant polycystic kidney disease is caused by a genetic mutation.

○True ○False

9. Nephritic syndrome is often due to an inflammatory process.

○True ○ False

10. Intrinsic renal failure means damage has occurred to the kidney tissue itself.

○ True ○ False