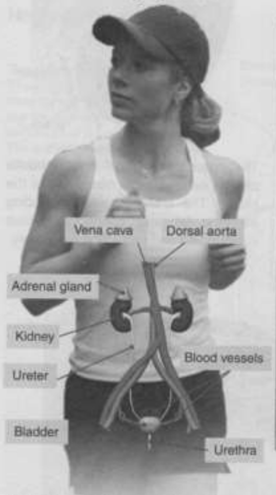
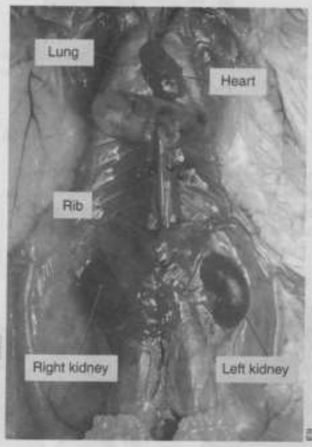
The Urinary System

The urinary system consists of the kidneys and bladder, and their associated blood vessels and ducts. The **kidneys** have a plentiful blood supply from the renal artery. The blood plasma is filtered by the **kidney nephrons** to form urine. Urine is produced continuously, passing along the **ureters** to the **bladder**, a hollow muscular organ lined with smooth muscle and stretchable epithelium. Each day the kidneys filter about 180 L of plasma. Most of this is reabsorbed, leaving a daily urine output of about 1 L. By adjusting the composition of the fluid excreted, the kidneys help to maintain the body's internal chemical balance. Human kidneys are very efficient, producing a urine that is concentrated to varying degrees depending on requirements.

Urinary System



Kidneys *in-situ* (Rat)

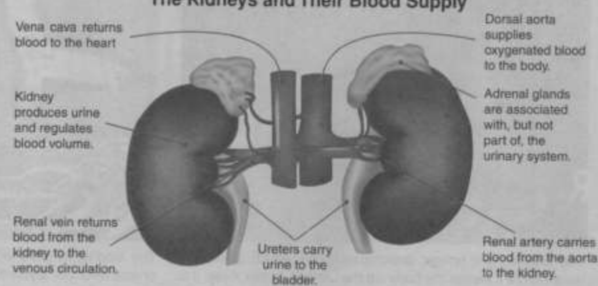


Sagittal Section of Kidney (Pig)

The kidneys of humans (above), rats (dissection, above center), and many other mammals (e.g. pig above right) are distinctive, bean shaped organs that lie at the back of the abdominal cavity to either side of the spine. The kidneys lie outside the peritoneum of the abdominal cavity (**retoperitoneal**) and are partly protected by the lower ribs (see kidneys *in-situ* above center).

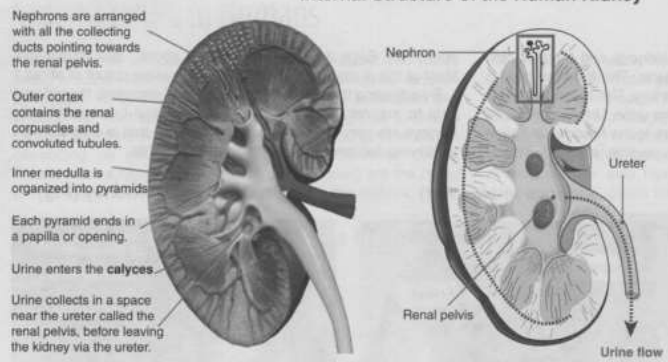
Human kidneys are ~100-120 mm long and 25 mm thick. A cut through in a sagittal plane (see photo above right), reveals numerous tough connective tissue calyces. These collect the urine from the papillae where it is discharged and drain it into the ureter.

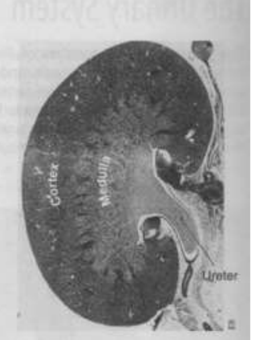
The Kidneys and Their Blood Supply



1. State the function of each of the following components of the urinary system:
   (a) Kidney: ____
   (b) Ureters: ____
   (c) Bladder: ____
   (d) Urethra: ____
   (e) Renal artery: ____
   (f) Renal vein: ____
   (g) Renal capsule: ____
2. Calculate the percentage of the plasma reabsorbed by the kidneys: ____

Internal Structure of the Human Kidney

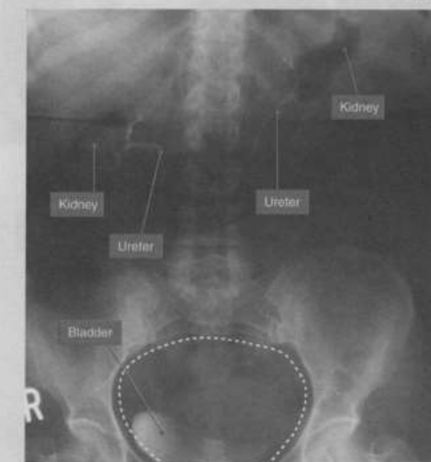




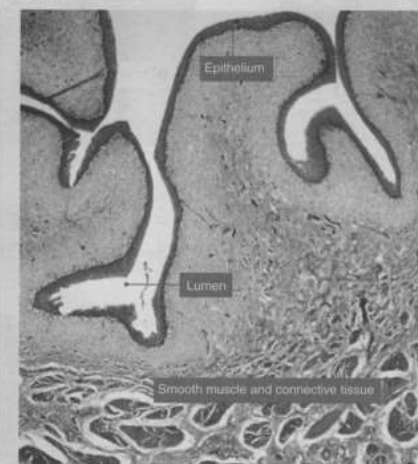
The functional units of the kidney are selective filter elements called **nephrons**. Each kidney contains more than 1 million nephrons and they are precisely aligned so that urine is concentrated as it flows towards the ureter (model and diagram above). The alignment gives the kidney tissue a striated (striped) appearance and makes it possible to accommodate all the filtering units needed.

The outer cortex and inner medulla can be seen in a low power LM of the kidney. The ureter is seen extending into the fat and connective tissue surrounding and protecting the kidney.

The Bladder



The bladder is a hollow stretchable organ, which stores the urine before it leaves the body via the urethra. In this X-ray, it is empty and resembles a deflated balloon. The dotted line shows where it would sit if full.



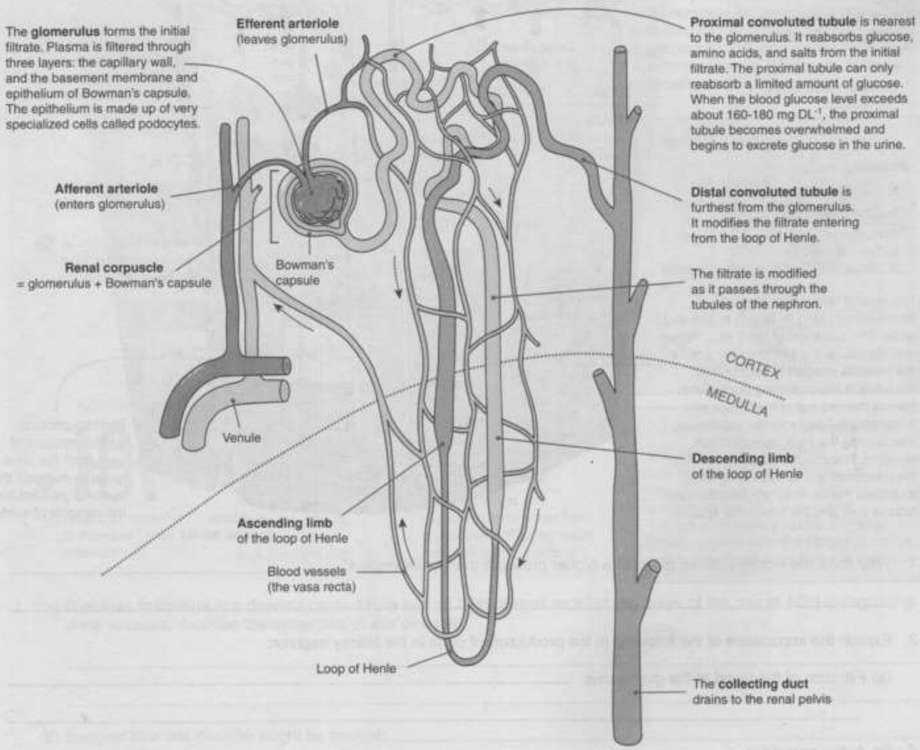
The bladder is lined with **transitional epithelium**. This type of epithelium is layered, or **stratified**, so it can be stretched without the outer cells breaking apart from each other. This image shows the bladder in a deflated state.

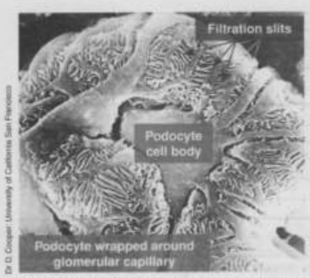
3. (a) What is a nephron? ____
   (b) What is its role in excretion? ____
4. (a) Where would you find transitional epithelium in the urinary system: ____
   (b) Why do you find this type of epithelium here? ____
5. In adults, the opening of the urethra is regulated by a voluntary sphincter muscle. What is the purpose of this sphincter?
   ____

The Physiology of the Kidney

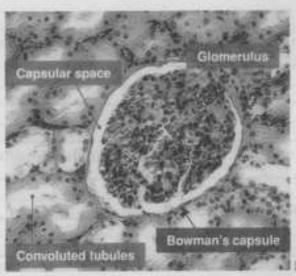
The kidney **nephron**, is a selective filter element, comprising a **renal corpuscle** and its associated tubules and ducts. **Ultrafiltration**, i.e. forcing fluid and dissolved substances through a membrane by pressure, occurs in the first part of the nephron, across the membranes of the capillaries and the glomerular capsule. The passage of water and solutes into the nephron and the formation of the glomerular filtrate depends on the pressure of the blood entering the afferent arteriole (below). If it increases, filtration rate increases. When it falls, glomerular filtration rate also falls. This process is so precisely regulated that, in spite of fluctuations in arteriolar pressure, glomerular filtration rate per day stays constant. After formation of the initial filtrate, the **urine** is modified through secretion and tubular reabsorption according to physiological needs at the time.

Nephron Structure





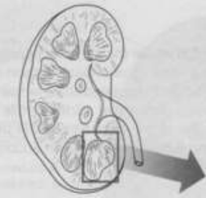
The epithelium of Bowman's capsule is made up of specialized cells called **podocytes**. The finger-like cellular processes of the podocytes wrap around the capillaries of the glomerulus, and the plasma filtrate passes through the filtration slits between them.



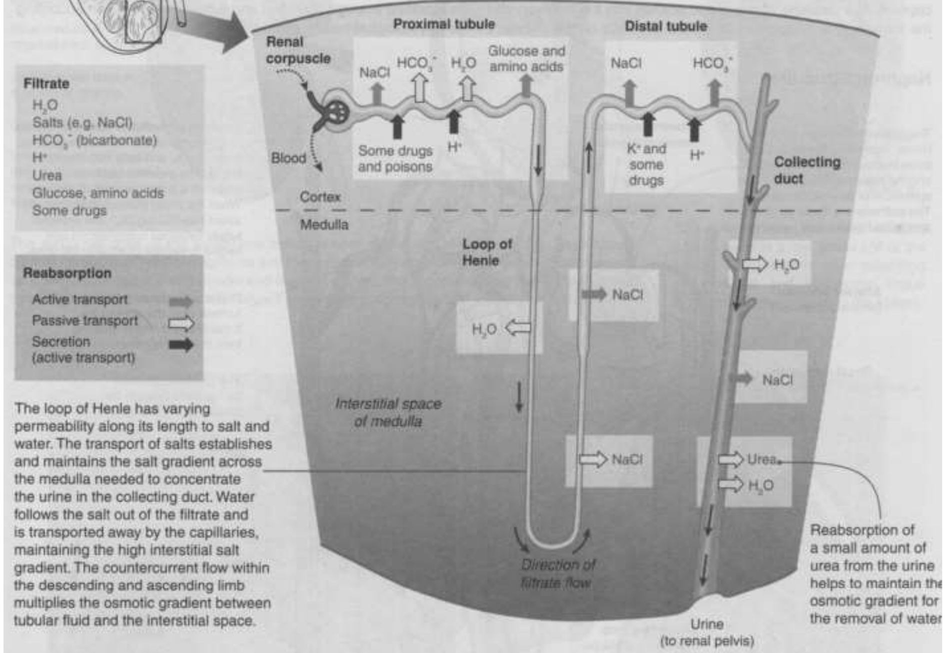
Bowman's capsule is a double walled cup, lying in the cortex of the kidney. It encloses a dense capillary network called the **glomerulus**. The capsule and its enclosed glomerulus form a **renal corpuscle**. In this section, the convoluted tubules can be seen surrounding the renal corpuscle.

Dipstick urinalysis is commonly used to detect metabolic errors. Less than 0.1% of glucose filtered by the glomerulus normally appears in urine. The presence of glucose in the urine is usually due to untreated diabetes mellitus, which is characterized by high blood glucose levels.

Summary of Activities in the Kidney Nephron



Urine formation begins by **ultrafiltration** of the blood, as fluid is forced through the capillaries of the glomerulus, forming a filtrate similar to blood but lacking cells and proteins. The filtrate is then modified by **secretion** and **reabsorption** to add or remove substances (e.g. ions). The processes involved in urine formation are summarized below. The loop of Henle acts as a **countercurrent multiplier**, establishing and increasing the salt gradient through the medullary region. This is possible because the descending loop is freely permeable to water but the ascending loop is not.



1. Why does the kidney receive blood at a higher pressure than other organs? ______________________

____

2. Explain the importance of the following in the production of urine in the kidney nephron:

(a) Filtration of the blood at the glomerulus: ______________________

____

(b) Active secretion: ______________________

____

(c) Reabsorption: ______________________

____

(d) Osmosis: ______________________

____

3. (a) What is the purpose of the salt gradient in the kidney? ______________________

____

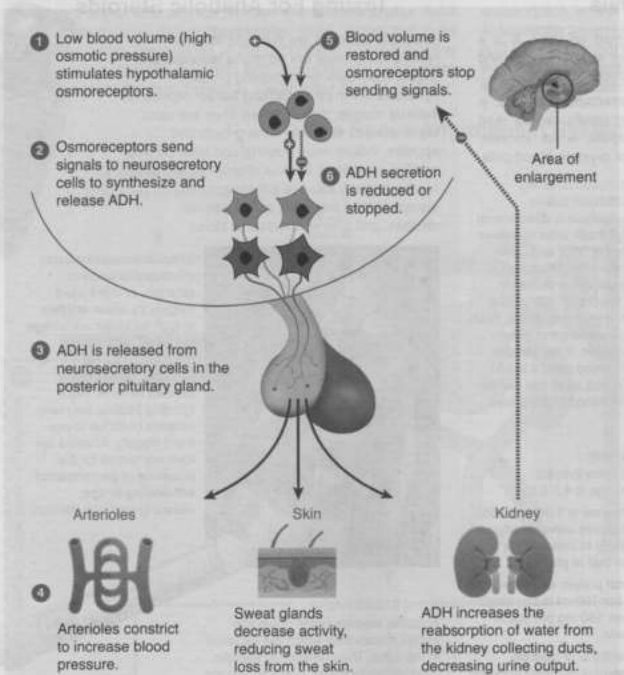
(b) How is this salt gradient produced? ______________________

____

____

Control of Urine Output

Variations in salt and water intake, and in the environmental conditions to which we are exposed, contribute to fluctuations in blood volume and composition. The primary role of the kidneys is to regulate blood volume and composition (including the removal of nitrogenous wastes), so that homeostasis is maintained. This is achieved through varying the volume and composition of the urine. Two hormones, **antidiuretic hormone** (ADH) and **aldosterone**, are involved in the process.



Osmoreceptors in the **hypothalamus** of the brain respond to changes in blood volume. A blood volume stimulates the synthesis and secretion of the hormone ADH (antidiuretic hormone), which is released from the posterior pituitary into the blood. ADH increases the permeability of the kidney collecting duct to water so that more water is reabsorbed and urine volume decreases. A second hormone, aldosterone, helps by increasing sodium reabsorption.

Factors causing ADH release

- Low blood volume
  - = More negative water potential
  - = High blood sodium levels
  - = Low fluid intake
- Nicotine and morphine

Factors inhibiting ADH release

- High blood volume
  - = Less negative water potential
  - = Low blood sodium levels
- High fluid intake
- Alcohol consumption

Factors causing the release of aldosterone

Low blood volumes also stimulate secretion of aldosterone from the adrenal cortex. This is mediated through a complex pathway involving osmoreceptors near the kidney glomeruli and the hormone renin from the kidney.

1. (a) **Diabetes insipidus** is a disease caused by a lack of ADH. Based on what you know of the role of ADH in regulating urine volumes, describe the symptoms of this disease:

   (b) Suggest how this disorder might be treated: ______

2. Explain why alcohol consumption (especially to excess) causes dehydration and thirst: ______

3. Explain how negative feedback mechanisms operate to regulate blood volume and urine output: ______

4. **Diuretics** are drugs that increase urine volume. Many work by inhibiting the active transport of sodium and chloride in the nephron. Explain how this would lead to an increase in urine volume:

Urine Analysis

Urine is the liquid waste product of the body. It contains water, electrolytes, and other waste metabolites which are filtered out of the blood by the kidneys. **Urine analysis** (urinalysis) is used as a medical diagnostic tool for a wide range of metabolic disorders. In addition, urine analysis can be used to detect the presence of illicit (non-prescription) drugs and for diagnosing pregnancy.

Diagnostic Urinalysis

A urinalysis (UA) is an array of tests performed on urine. It is a common method of medical diagnosis, as most tests are quick and easy to perform, non-invasive, and well understood diagnostically.

A typical urinalysis usually includes a **macroscopic analysis**, a **dipstick chemical analysis**, in which the test results can be read as color changes, and a **microscopic analysis**, which involves centrifugation of the sample and examination for crystals, blood cells, or microbial contamination.

MACROSCOPIC URINALYSIS
The first part of a urinalysis is direct visual observation. Normal, fresh urine is pale to dark yellow or amber in color and clear. Turbidity or cloudiness may be caused by excessive cellular material or protein in the urine. A red or red-brown (abnormal) color could be from a food dye, eating fresh beets, a drug, or the presence of either hemoglobin or myoglobin. If the sample contained many red blood cells, it would be cloudy as well as red, as in this sample indicating hematuria (blood in the urine).

DIPSTICK URINALYSIS
Commonly dipstick tests indicate:
Urine pH: normal range is 4.5-8.0.

Specific gravity: Normal is 1.002 - 1.035 Specific gravity measures urine density, or the ability of the kidney to concentrate or dilute the urine over that of plasma.

Protein: Normal total protein excretion does not exceed 10 mg per 100 ml in any single specimen. More than 150 mg per day is defined as proteinuria.

Glucose: Less than 0.1% of glucose filtered by the glomerulus normally appears in urine. Excess sugar in urine generally indicates diabetes mellitus.

Ketones: Ketones in the urine result from diabetic ketosis or some other form of calorie deprivation (starvation).

Nitrite: Nitrites indicate that bacteria may be present in significant numbers.

Leukocyte esterase: A positive leukocyte esterase test results from the presence of whole or lysed white blood cells (indicating infection).

Testing For Anabolic Steroids

Anabolic steroids are synthetic steroids related to the male sex hormone **testosterone** (right). They work by increasing protein synthesis within cells, causing tissue, especially skeletal muscle, to build mass. They are used legitimately to stimulate bone growth and appetite, induce male puberty, and treat chronic wasting conditions. Misuse of anabolic steroids can have many adverse effects including elevated blood pressure, cardiovascular disease, and altered cholesterol ratios.

Steroids increase muscle mass and physical strength, and are used illegally by some athletes to gain an unfair advantage over their competitors.

Anabolic steroid use is banned by most major sporting bodies, but many athletes continue to use them illegally. Athletes are routinely tested for the presence of **performance enhancing drugs**, including anabolic steroids.

Anabolic steroids break down into known metabolites which are excreted in the urine. The presence of specific metabolites indicates which substance has been used by the athlete.

Some steroid metabolites stay in the urine for weeks or months after being taken, while others are eliminated quite rapidly. Athletes using anabolic steroids can escape detection by stopping use of the drugs prior to competition. This allows the body time to break down and eliminate the components, and the drug use goes undetected.

1. Explain why urinalysis is a frequently used diagnostic technique for many common disorders: ______

2. Explain why the pH of normal urine (4.5-8.0) is much more variable than the pH of the blood (pH 7.35-7.45):

3. Identify what each of the following might indicate in a urine sample:

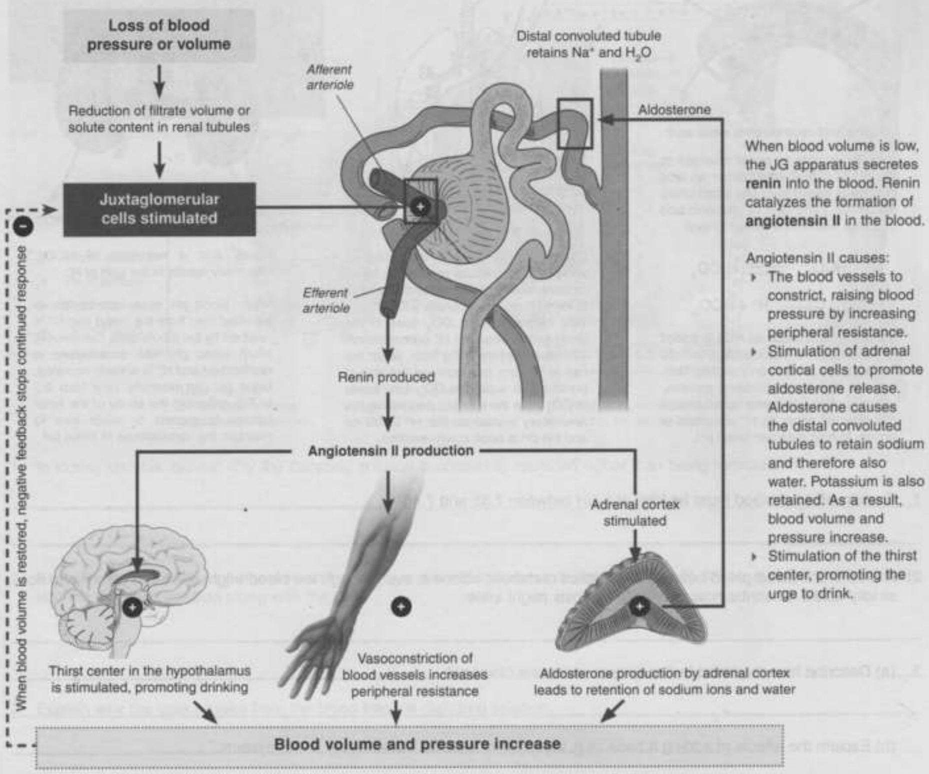
   (a) Cloudy, red color: ______ (b) Positive leukocyte esterase test: ______

4. Explain why athletes exploiting illegal drugs might withhold them for a period before competition: ______

Fluid and Electrolyte Balance

The body's fluid and electrolyte balance is critical to metabolic function. Water makes up around 60% of the body and is found within two main fluid compartments. The **intracellular fluid** makes up 60-65% of the water in the body and is found within the body's cells. The **extracellular fluid** makes up the rest of the body's water and can be divided into **intravascular fluid** (mostly blood) and the **extravascular fluid** (interstitial fluid around the cells). Electrolytes in the body fluids are responsible for maintaining osmotic gradients and permitting ion exchanges. For example, in the blood plasma, electrolytes help to maintain the blood volume by keeping water moving into the capillaries. When electrolyte (mostly Na^+) levels fall, water moves out of the capillaries and into the tissues. This causes blood volume and pressure to fall and plasma to thicken. Two hormones are involved in regulating blood volume: **ADH**, which promotes water reabsorption in the kidney collecting ducts, and **aldosterone**. Aldosterone promotes sodium reabsorption in the kidney tubules and the most important mechanism for regulating its release is the **renin-angiotensin system (RAS)**. The RAS is mediated by the **juxtaglomerular (JG) apparatus** in the renal tubules.

The Renin-Angiotensin System



1. Explain the difference between the intracellular and extracellular fluid compartments and their roles in the body: ______________________________

2. (a) Describe two situations that could cause a fall in blood volume: ______________________________

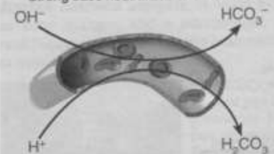
(b) Explain how the renin-angiotensin system responds to this loss of blood volume: ______________________________

Acid-Base Balance

The pH of the body's fluids must be maintained within a very narrow range (pH 7.35-7.45). The products of metabolic activity are generally acidic and could alter pH considerably without a buffer system to counteract pH changes. The carbonic acid-bicarbonate buffer works throughout the body to maintain the pH of blood plasma close to 7.40. The body maintains the buffer by eliminating either the acid (carbonic acid) or the base (bicarbonate ions). The blood buffers, the lungs, and the kidneys represent the three defense systems against disturbances of pH homeostasis. Changes in carbonic acid concentration can be effected within seconds through increased or decreased respiration. The renal system, although acting more slowly, can permanently eliminate metabolic acids and regulate the levels of alkaline substances, controlling pH by either excreting or retaining bicarbonate ions.

The Blood Buffer System

Strong base neutralized to weak base



Strong acid neutralized to weak acid

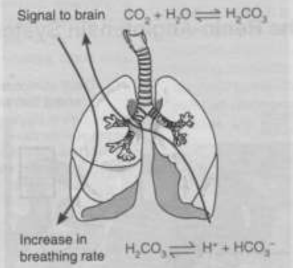
A buffer is able to resist changes to the pH of a fluid when either an acid or base is added to it. The bicarbonate ion (HCO_3^-) and its acid, carbonic acid (H_2CO_3), work in the following way:

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3$$

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

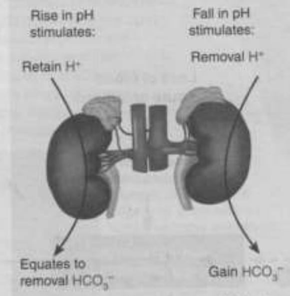
If a strong acid (such as HCl) is added to the system a weak acid is formed and thus the pH falls only slightly. Note that the blood also contains proteins, which contain basic and acidic groups that may act either as H^+ acceptors or donors to help maintain blood pH.

The Respiratory System



Carbon dioxide (CO_2) in the blood, an end-product of cellular respiration, forms carbonic acid (H_2CO_3) which dissociates to form H^+ and bicarbonate (HCO_3^-). This means that as CO_2 rises in the blood so too does the H^+ concentration. **Chemoreceptors** in the brain detect the rise in H^+ ions and increase the rate of breathing to expel the CO_2. Low levels of CO_2 have the effect of depressing the respiratory system so that H^+ builds up and the pH is once again restored.

The Renal System



Recall that a net loss of HCO_3^- effectively results in the gain of H^+.

When blood pH rises, bicarbonate is excreted (lost from the body) and H^+ is retained by the tubule cells. Conversely, when blood pH falls, bicarbonate is reabsorbed and H^+ is actively secreted. Urine pH can normally vary from 4.5 to 8.0, reflecting the ability of the renal tubules to excrete or retain ions to maintain the homeostasis of blood pH.

1. Explain why the blood must be kept at a pH between 7.35 and 7.45: ______________________________

2. A drop in the blood pH to below 7.35 is called metabolic acidosis, even though the blood might still be at pH >7 and not strictly acidic. Describe how metabolic acidosis might arise: ______________________________

3. (a) Describe how the blood buffer system maintains blood pH: ______________________________

(b) Explain the effects of adding a base (e.g. ingestion of alkaline substances) to the system: ______________________________

4. (a) Describe the respiratory response to excess H^+ in the blood: ______________________________

(b) Explain where these H^+ ions come from: ______________________________

(c) Describe how **respiratory acidosis** might arise: ______________________________

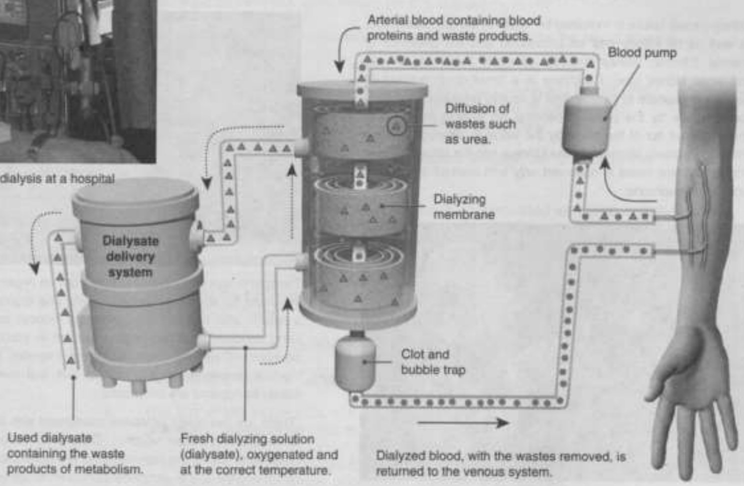
5. Explain the role of the renal system in maintaining the pH of the blood: ______________________________

Kidney Dialysis

A dialysis machine is a machine designed to remove wastes from the blood. It is used when the kidneys fail, or when blood acidity, urea, or potassium levels increase much above normal. In kidney dialysis, blood flows through a system of tubes composed of partially permeable membranes. Dialysis fluid (dialysate) has a composition similar to blood except that the concentration of wastes is low. It flows in the opposite direction to the blood on the outside of the dialysis tubes. Consequently, waste products like urea diffuse from the blood into the dialysis fluid, which is constantly replaced. The dialysis fluid flows at a rate of several 100 cm^3 per minute over a large surface area. For some people dialysis is an ongoing procedure, but for others dialysis just allows the kidneys to rest and recover from injury or the effects of drugs or other metabolic disturbance.

A patient undergoing kidney dialysis at a hospital

Principles of Kidney Dialysis



1. In kidney dialysis, explain why the dialyzing solution is constantly replaced rather than being recirculated:

2. Explain why ions such as potassium and sodium, and small molecules like glucose do not diffuse rapidly from the blood into the dialyzing solution along with the urea:

3. Explain why the urea passes from the blood into the dialyzing solution:

4. Describe the general transport process involved in dialysis:

5. Give a reason why the dialyzing solution flows in the opposite direction to the blood:

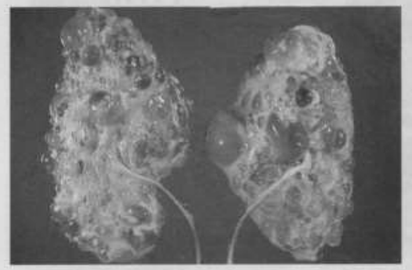
6. Explain why a clot and bubble trap is needed after the blood has been dialyzed but before it re-enters the body:

Kidney Transplants

Kidney failure (also called renal failure) arises when the kidneys fail to function adequately and filtrate formation decreases or stops. In cases of renal failure, normal blood volume levels and electrolyte balances are not maintained, and waste products build up in the body. Kidney failure is classified as **acute** (rapid onset) or **chronic** (developing over a period of months or years). There are many causes of kidney failure including decreased blood supply, drug overdose, chemotherapy, infection, and poorly controlled diabetic or hypertensive conditions. Recovery from acute renal failure is possible, but chronic renal damage can not be reversed. If kidney deterioration is ignored, the kidneys will fail completely. In some cases diet and medication can be used to treat kidney failure, but when the damage is extensive, **kidney dialysis** or a **kidney transplant** are required to keep the patient alive.

Renal Failure

Kidney (renal) failure is indicated by levels of **serum creatinine**, as well as by kidney size on ultrasound and the presence of anemia (chronic kidney disease generally leads to anemia and small kidney size). Creatinine is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass). It is chiefly filtered out of the blood by the kidneys, although a small amount is actively secreted by the kidneys into the urine. A rise in blood creatinine levels is observed only with marked damage to functioning nephrons.

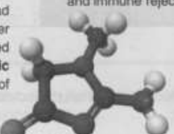


Acute renal failure (ARF) is characterized by decreased urine production (<400mL per day), and commonly arises because of low blood volume (blood loss), dehydration, or widespread infection. In contrast, chronic renal failure, which develops over months or years, is commonly the result of poorly controlled diabetes, poorly controlled high blood pressure, or **polycystic kidney disease**, a genetic disorder characterized by the growth of numerous cysts in the kidneys (above).

Kidney Transplants

Transplantation of a healthy kidney from an organ donor is the preferred treatment for end-stage kidney failure. The organ is usually taken from a person who has just died, although kidneys can also be taken from living donors. The failed organs are left in place and the new kidney transplanted into the lower abdomen. Provided recipients comply with medical requirements (e.g. correct diet and medication) over 85% of kidney transplants are successful.

There are two major problems associated with kidney transplants: lack of donors and tissue rejection. Cells from donor tissue have different antigens to that of the recipient, and are not immunocompatible. Tissue-typing and the use of immunosuppressant drugs helps to decrease organ rejection rates. In the future, xenotransplants of genetically modified organs from other species may help to solve both the problems of supply and immune rejection.



Creatinine

Creatinine levels in both blood and urine is used to calculate the creatinine clearance (CrCl), which reflects the glomerular filtration rate (GFR). The GFR is a clinically important measurement of renal function and more accurate than serum creatinine alone, since serum creatinine only rises when nephron function is very impaired.

1. Distinguish between acute and chronic renal failure and contrast their causes:

2. (a) Explain why a rise in blood (serum) levels of creatinine would indicate a failure of nephron function:

   (b) Explain why a creatinine clearance is a more accurate indicator of renal function than a serum creatinine test alone:

3. Describe some of the advantages and disadvantages of kidney transplantation over a life-time of kidney dialysis: