

Lecture Note		
Subject: HAP, 201T	SEM-2nd	UNIT-III
Submitted By:	Prasenjit Mishra	HCP-345-BBSR

Kidney Disorder

The sign of kidney disease are.

- High blood pressure
- Swelling of the face and ankles
- Puffiness around the eyes
- Frequently urinating (at night)
- Rusty or brown colour urine
- Back pain below ribs.

Types:

1. Inherited kidney disorders
2. Congenital kidney diseases
3. Acquired kidney diseases

RENAL DISEASE Terminology

Dysuria	Urethritis (inflammation of urethra) and Cystitis (inflammation of bladder due to infection)
Polyuria	(increased urine flow at night)
Nocturia	
Oliguria	Decreased urinary output i.e. < 300 ml/ day - hypotension, hypovolaemia decreased volume of circulating blood in body) - intrinsic renal disease - urinary tract obstruction
Haematuria	blood in the urine, arises anywhere in renal tract - micturition-urethral disease- tendency to urinate
Renal pain	dull constant pain in the loin. - renal obstruction, acute pyelonephritis, acute nephritic syndrome, polycystic kidney, renal infant.
Ureteric colic	Severe loin pain, waxes and wanes, low fever, vomiting, radiate to abdomen, groin, upper thigh. - Renal calculus, clot.

Kidney Failure or End-stage Renal Disease (ESRD)

Occurs when the kidneys do not function properly or sufficiently resulting in the accumulation of waste products and toxic materials may cause permanent and irreversible damage to body cells, tissues and organs

– kidneys that function <20% of required capacity

Symptoms • Decreased urination • Blood in the urine • Nausea and vomiting

• Swollen hands and ankles • Puffiness around the eyes • Itching • Sleep disturbances • High blood pressure • Loss of appetite

Treatment • Dialysis – Hemodialysis – Peritoneal Dialysis
• Transplant – the best means of treatment

Hemodialysis:- A process by which excess waste products and water are removed from the blood

Peritoneal Dialysis:- Dialysis solution flow into the peritoneal (abdominal) cavity through a catheter • Peritoneum acts as a filter

Kidney Transplant:- A kidney from either a living related or a brain dead person is removed and surgically placed into the kidney failure patient.

COMMON KIDNEY DISEASES

- Polycystic Kidney Disease
- Hypertensive Nephrosclerosis
- Glomerulonephritis / Glomerulosclerosis
- Urinary Tract Infection (UTI)
- Kidney Stones
- Diabetic Kidney Disease
- Analgesic nephropathy

Inherited kidney disorders

Polycystic kidney disease (PKD)

It is a genetic disorder marked by the growth of numerous cysts in the kidneys
These PKD cysts compress functioning kidney tissue; eventually replace much of the mass of the kidneys

Type: - Autosomal Dominant PKD
Autosomal Recessive PKD

Symptoms Hematuria
Blood in the urine
Liver and pancreatic cysts
Abnormal heart valves
High blood pressure

Diagnosed Ultrasound imaging computed tomography (CT scan)
Magnetic resonance imaging (MRI)

Treatment Not available, only symptomatic
Pain medications, surgery to shrink cysts
Urinary tract infections antibiotics

Hypertensive Nephrosclerosis

- Poorly controlled high blood pressure (hypertension) can lead to kidney failure – Thickening of blood vessels
- Headache • Giddiness (sometimes related to posture)
- Neck discomfort • Easily tired • Nauseous and/or vomiting
- Protein in urine

Treatment • Medications to control blood pressure (anti- hypertensive) • Lowering of dietary salt (2g/day) • Exercise regularly

Glomerulonephritis / Glomerulosclerosis

- Glomerulonephritis - An inflammatory condition that affects predominantly the glomeruli.
- Causes – IgA nephropathy – Streptococcus bacteria – Autoimmune
- Glomerulosclerosis - scarring of the glomeruli

Signs and Symptoms • Blood or protein in urine • Frothy urine (signifying protein in urine) • Dark or pink-coloured urine • Leg swelling • Systemic disease like diabetes or autoimmune disease will have systemic manifestations, e.g. weight loss, arthritis, or skin rash

Treatment Specific • Suppression of inflammation may be achieved by certain medications (eg steroids). General • Medications to decrease excretion of urinary protein • Control of blood pressure • Dietary modifications

Urinary Tract Infection (UTI)

- Disease of the urinary tract – Infection occurs when microorganisms attach themselves to the urethra and begins to multiply.
- May lead to infection of the kidneys (pyelonephritis) and cause permanent kidney damage, if left untreated.
- Women are especially prone to get urinary tract infection.
- Conditions that increases risk of UTI – Diabetes – Situations where a urine catheter is needed – Abnormalities of the urinary tract – Obstructed urine flow (large prostate or stone) – Being pregnant

Signs and Symptoms

- Painful urination (burning sensation)
- Hot and foul smelling urine • Blood in urine
- Fever (sometimes with chills)
- Painful lower abdomen • Increased urgency/frequency of wanting to pass urine
- Nausea and/or vomiting

Treatment • Appropriate antibiotics • Drink plenty of water

Kidney Stones

- Start as salt/chemical crystals that precipitate out from urine
 - Occurs when substance in urine that prevents crystalization are ineffective
44. Kidney Stones • Various forms of kidney stones - the most common is calcium in combination with either phosphate or oxalate
- More common in – Males – 20-40 yo

Signs and Symptoms • Extreme pain at the site where the stone is causing the irritation

- Blood in the urine (abrasion along the urinary tract as the stone travels)
- Painful and/or difficult urination
- Unable to pass urine if the stone is large enough to obstruct the outlet completely

Treatment • With plenty of water, most stones can pass through if small

- Pain-killers (as prescribed by the doctor)
- Some medications may help 'breakdown' larger stone
- Shockwave therapy (F-SWL) to break the stone
- Surgical intervention - cystoscopy or open surgery

Diabetic Kidney Disease

- Common in chronic and poorly controlled diabetics
- Diabetes damages blood vessels in the kidneys
- Occurs in both types of diabetes
- Occurrence of high blood pressure in diabetics is a strong predictor for diabetic nephropathy

Signs and Symptoms

- Frothy urine (signifying protein in urine)
- Leg swelling (worse after walking/standing)
- High blood pressure
- Itching
- Nausea and/or vomiting
- Losing weight
- Lethargy
- Increased need to urinate at night

Treatment

- Good control of diabetes
- Good control of blood pressure (aiming for < 130/85 or lower in younger patients)
- Medications to decrease protein excretion and preserve the function of kidneys
- Lower protein diet
- Treat any urine tract infection (which is common in diabetics).

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MICTURITION REFLEX

Micturition is the process by which the urinary bladder empties when it becomes filled.

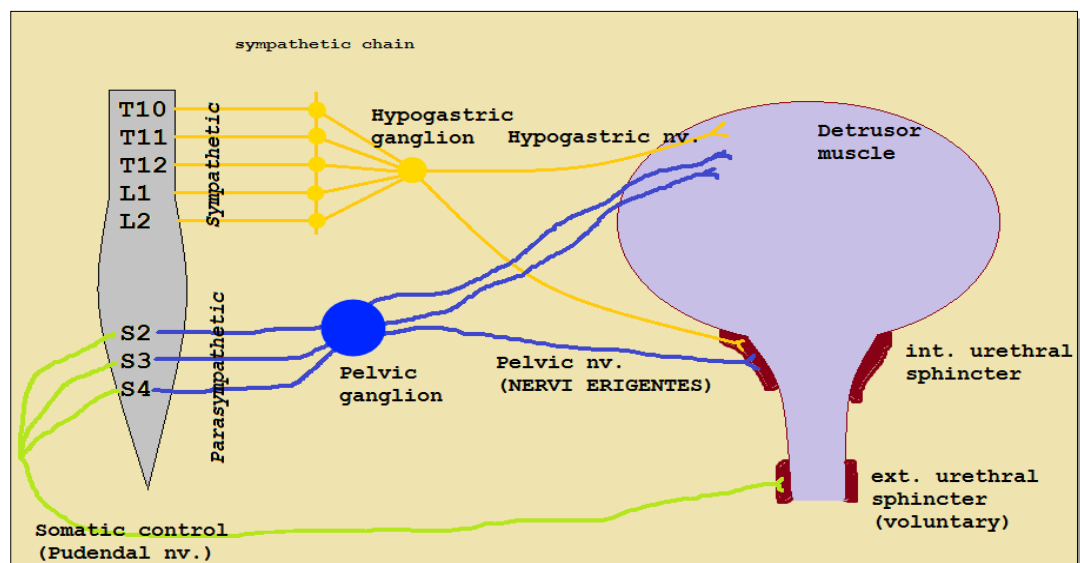
• This involves **two main steps**:

- First**, the bladder fills progressively until the tension in its walls rises above a threshold level;
- The second step**, which is a nervous reflex called the *micturition reflex* that empties the bladder or, if this fails, at least causes a conscious desire to urinate.

Although the micturition reflex is an autonomic spinal cord reflex, it can also be inhibited or facilitated by centers in the cerebral cortex or brain stem.

Innervation of the Bladder

- The principal nerve supply of the bladder is by way of the pelvic nerves, which connect with the spinal cord through the sacral plexus, mainly connecting with cord segments S-2 and S-3.
- Coursing through the pelvic nerves are both sensory nerve fibers and motor nerve fibers. The sensory fibers detect the degree of stretch in the bladder wall.
- The motor nerves transmitted in the pelvic nerves are parasympathetic fibers. These terminate on ganglion cells located in the wall of the bladder. Short postganglionic nerves then innervate the detrusor muscle.
- Skeletal motor fibers transmitted through the pudendal nerve to the external bladder sphincter - somatic nerve fibers that innervate and control the voluntary skeletal muscle of the sphincter.
- The bladder receives sympathetic innervation from the sympathetic chain through the hypogastric nerves, connecting mainly with the T-10-12, L-1-2 segment of the spinal cord. • These sympathetic fibers stimulate mainly the blood vessels - sensory nerve fibers also pass by way of the sympathetic nerves and important in the sensation of fullness and pain.



Transport of Urine.

Urine flowing from the collecting ducts into the renal calyces stretches the calyces and increases their intrinsic pacemaker activity, which in turn initiates peristaltic contractions that spread to the renal pelvis and then downward along the length of the ureter peristaltic contractions in the ureter are enhanced by parasympathetic stimulation and inhibited by sympathetic stimulation

The normal tone of the detrusor muscle in the bladder wall have a tendency to compress the ureter, thereby preventing backflow of urine from the bladder when pressure builds up in the bladder during micturition or bladder compression.

Micturition Reflex

- a) Micturition contractions are the result of a stretch reflex initiated by sensory stretch receptors in the bladder wall, especially by the receptors in the posterior urethra when this area begins to fill with urine at the higher bladder pressures.
- b) Sensory signals from the bladder stretch receptors are conducted to the sacral segments of the cord through the pelvic nerves and then reflexively back again to the bladder through the parasympathetic nerve fibers by way of these same nerves.
- c) When the bladder is only partially filled, these micturition contractions usually relax spontaneously after a fraction of a minute, the detrusor muscles stop contracting, and pressure falls back to the baseline.
- d) As the bladder continues to fill, the micturition reflexes become more frequent and cause greater contractions of the detrusor muscle.
- e) Once a micturition reflex begins, it is “self-regenerative.” initial contraction of the bladder activates the stretch receptors to cause a greater increase in sensory impulses to the bladder and posterior urethra, which causes a further increase in reflex contraction of the bladder cycle is repeated again and again until the bladder has reached a strong degree of contraction.
- f) Then, after a few seconds to more than a minute, the self- regenerative reflex begins to fatigue and the regenerative cycle of the micturition reflex stops, permitting the bladder to relax.

The micturition reflex is a single complete cycle of

- (1) Progressive and rapid increase of pressure
- (2) A period of sustained pressure
- (3) Return of the pressure to the basal tone of the bladder

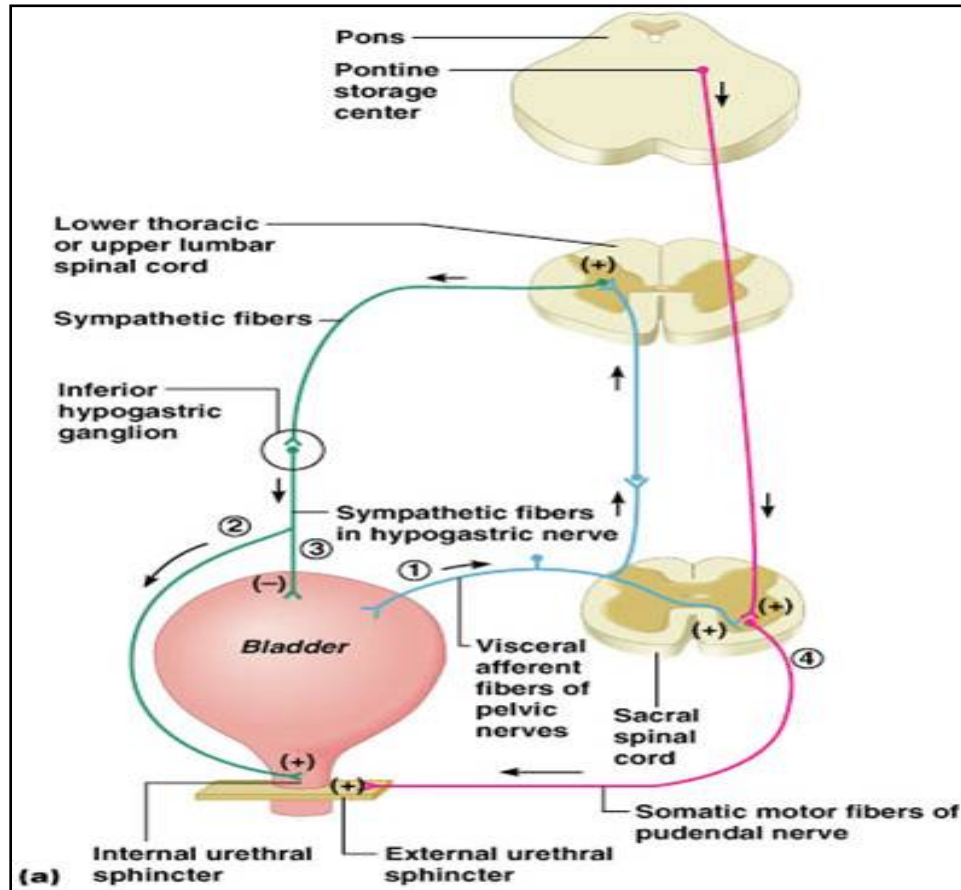
Once a micturition reflex has occurred

But has not succeeded in emptying the bladder, the nervous elements of this reflex usually remain in an inhibited state for a ***few minutes to 1 hour or more*** before another micturition reflex occurs. As the bladder becomes more and more filled, micturition reflexes occur more and more often and more and more powerfully.

Once the micturition reflex becomes powerful

It causes another reflex through the pudendal nerves to the external sphincter to inhibit it. If this inhibition is more potent in the brain than the in external sphincter, urination will occur.

If not, urination will not occur until the bladder fills & further micturition reflex becomes more powerful



What is Voluntary urination?

- I. First, a person voluntarily contracts his or her abdominal muscles, which increases the pressure in the bladder
- II. and allows extra urine to enter the bladder neck and posterior urethra under pressure, thus stretching their walls.
- III. This stimulates the stretch receptors, which excites the micturition reflex and simultaneously inhibits the external urethral sphincter.
- IV. Ordinarily, all the urine will be emptied, with rarely more than 5 to 10 milliliters left in the bladder.

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PHYSIOLOGY OF URINE FORMATION

The kidneys perform their most important functions by filtering the plasma and removing substance from the filtrate at variable rates, depending on the needs of the body.

The kidneys serve multiple functions, including-

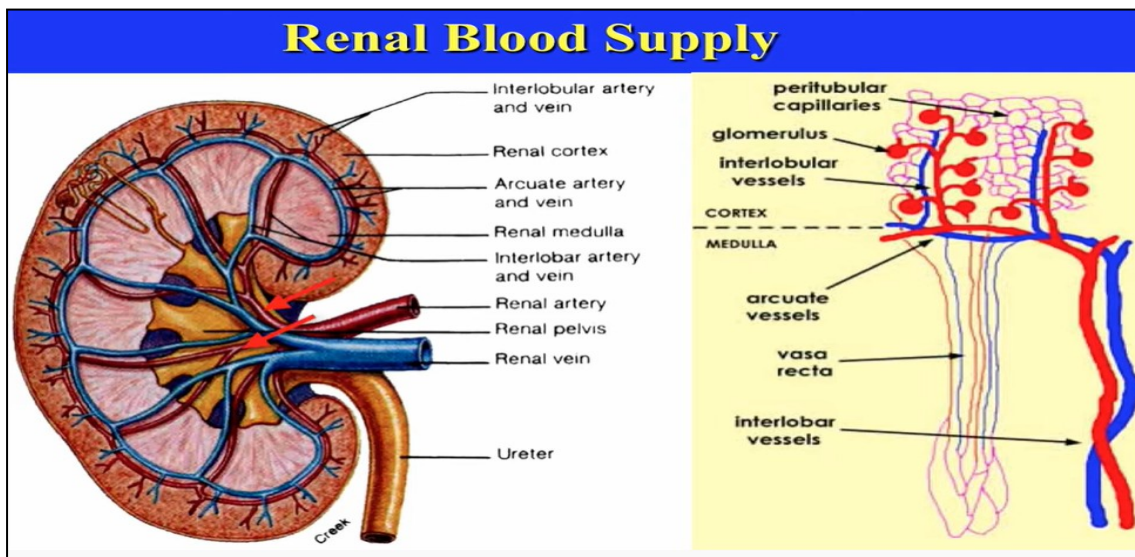
- i. Excretion of metabolic waste products and foreign chemicals,
- ii. Regulation of water and electrolyte balances,
- iii. Regulation of body fluid osmolality and electrolyte concentration,
- iv. Regulation of arterial pressure,
- v. Regulation of acid base balance,
- vi. Secretion, metabolism and excretion of hormones,
- vii. Gluconeogenesis.

Physiologic Anatomy of the Kidneys

- Two kidneys- on the posterior wall of the abdomen, outside peritoneal cavity.
- Each kidney- weighs 150 gms, size- clenched fist.
- Medial side- hilum (renal artery, vein, lymphatics, nerve supply and ureter)
- Capsule- tough fibrous, protects inner delicate structures.

Renal blood supply

- Blood flow to both kidneys- 22% of the cardiac output or 1100ml/ min.
- Renal artery, interlobar, arcuate, interlobular, afferent, glomerular capillaries, efferent arterioles.
- Peritubular capillaries, interlobular, arcuate, interlobar, renal.



Nephron- functional unit of the kidney

- Each kidney- 1 million nephrons.
 - Kidney can not regenerate new nephrons.
 - After 40 yrs- functioning nephrons decreases about 10% every 10 yrs.
 - Each nephron contains-
1. Glomerulus- tuft of glomerular capillaries, through which large amount of fluid filtered from the blood
 2. Long tubule- filtered fluid is converted into urine on its way to pelvis of the kidney.

URINE FORMATION

The rates at which different substances are excreted in the urine represent the sum of three renal processes:

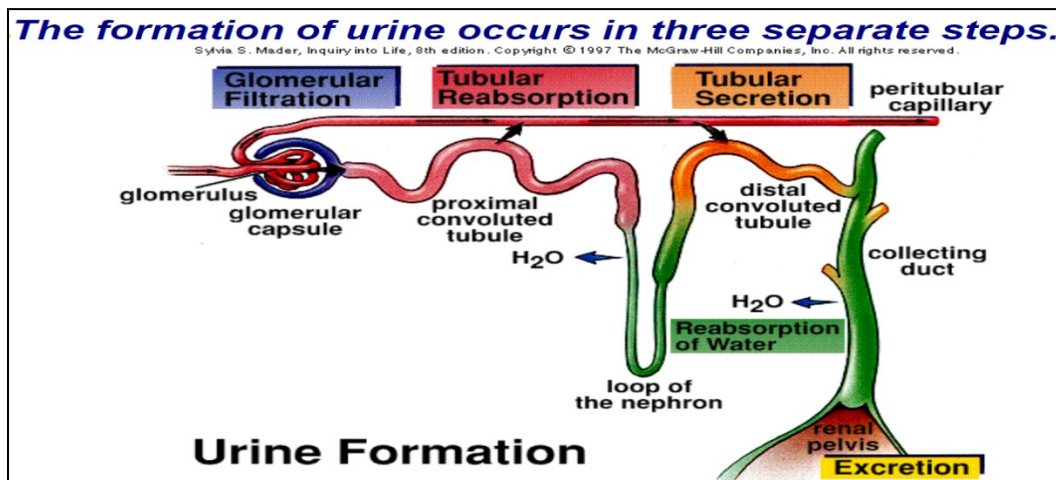
1. Glomerular filtration
2. Reabsorption of substances from the renal tubules into the blood
3. Secretion of the substances from the blood in the renal tubules.

Expressed mathematically

Urinary excretion rate= filtration rate- reabsorption rate + secretion rate.

1. GLOMERULAR FILTRATION

- Glomerular filtrate: the fluid that enters the capsular space. (female-150lit, male-180lit).
- Filtration fraction: the fraction of blood plasma in the afferent arteriole in the kidneys that become glomerular filtrate (0.16-0.2).



Filtration membrane

- The glomerular capillaries and the podocytes, which completely encircles the capillaries, form a leaky barrier known as filtration membrane.
- Substance filtered from blood crosses three filtration barriers: 1. Glomerular endothelial cells, 2. Basal lamina, 3. Filtration slit formed by podocytes.

Principle of filtration

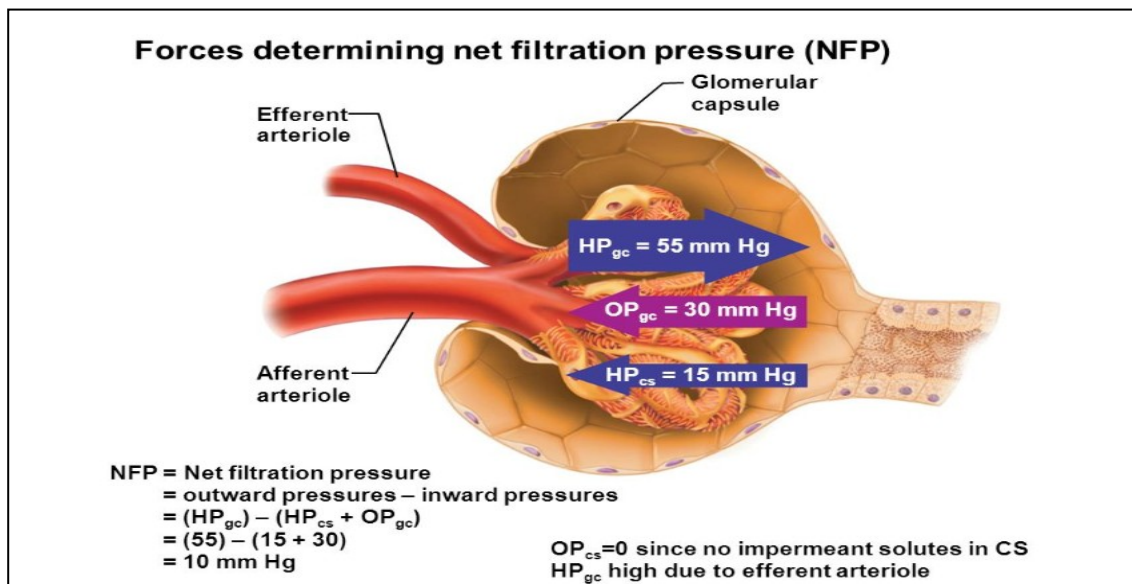
1. The use of pressure to force fluids and solutes through a membrane is same in glomerular capillaries and elsewhere in the body.
2. The volume of the fluid filtered in the renal corpuscle is much larger in other capillaries of the body for three reasons:
 - a. Larger surface area, mesangial cells relax increased GFR and contracts decreased GFR.
 - b. Filtration membrane- thin and porous, thickness- 0.1mm, 50 times leakier.
 - c. Glomerular capillary blood pressure is high.

Net filtration pressure

$$\text{NFP} = \text{Glomerular blood hydrostatic pressure (GBHP)} - [\text{capsular hydrostatic pressure (CHP)} + \text{blood colloid osmotic pressure (BCOP)}] = 10 \text{ mm Hg.}$$

Pressures which promotes filtration: GBHP, CHP.

Pressure which oppose filtration: BCOP.



Glomerular Filtration Rate • The amount of filtrate formed in all renal corpuscles of both the kidneys each minute is the GFR.

- Male- 125ml/min, female- 105ml/min.
- GFR- too high decreased reabsorption, too low increased reabsorption.
- Mechanism that regulates GFR operate in two main ways:
 1. By adjusting blood flow into and out of glomerulus,
 2. Altering the glomerular capillary surface area available for filtration.

Regulation of GFR: It is regulated-

- Myogenic mechanism
- Tubuloglomerular feedback
- Neural regulation of GFR
- Hormonal regulation of GFR

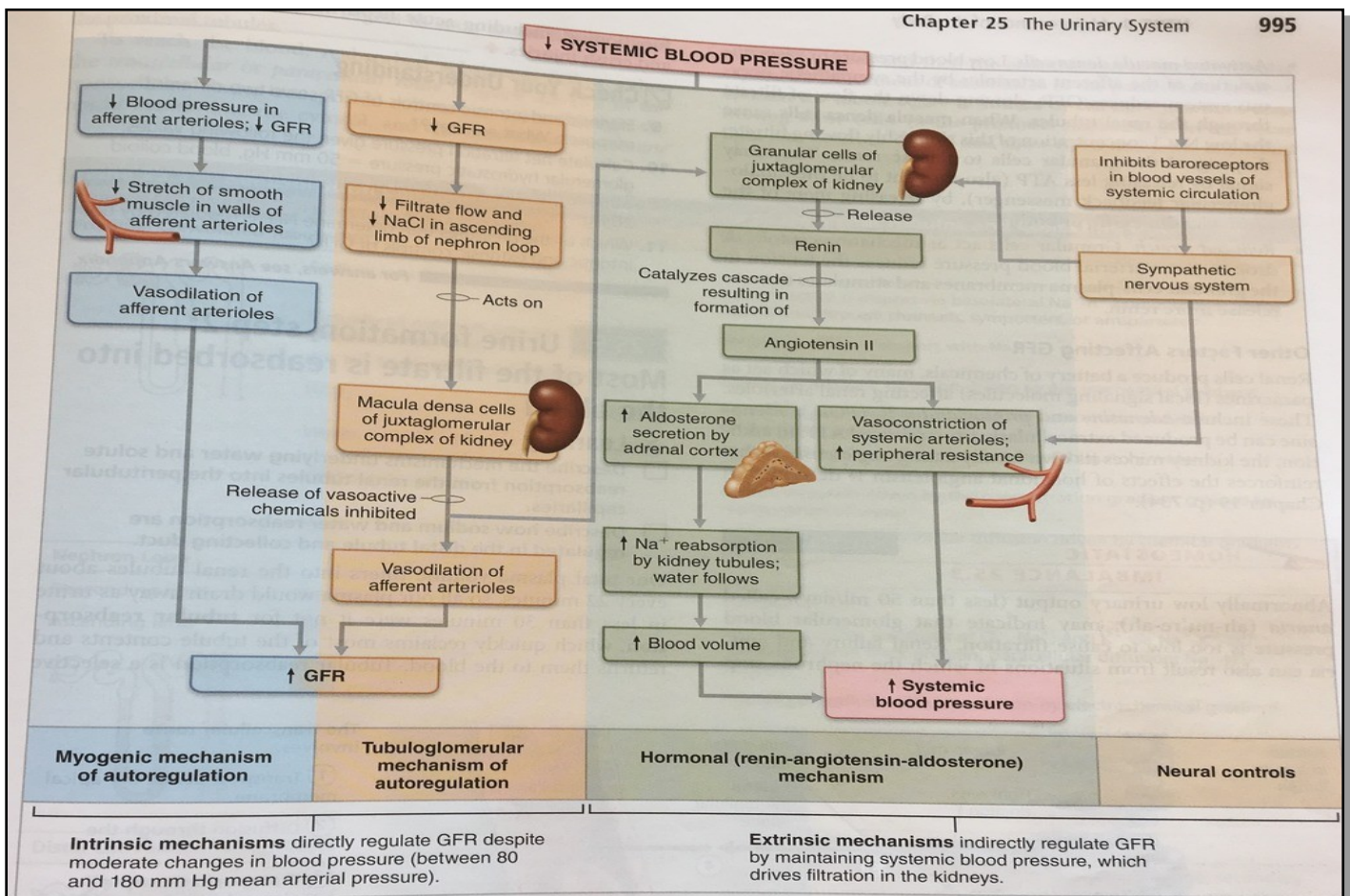


Figure 25.14 Regulation of glomerular filtration rate (GFR) in the kidneys. (Note that while the extrinsic controls are aimed at maintaining blood pressure, they also maintain GFR since bringing blood pressure back up allows the kidneys to maintain GFR.)

	TYPE OF REGULATION	MAJOR STIMULUS	MECH AND SITE OF ACTION	EFFECT ON GFR
Renal	Myogenic mech	Increased stretching of smooth muscle fibres in afferent arterioles walls due to increased BP	Stretched smooth muscle fibres contracts, narrowing lumen of the arterioles	Decrease
Renal	Tubuloglomerular feedback	Rapid delivery of Na and Cl to the macula densa due to high systemic BP	Decrease in release of NO by JGA causes constriction of the afferent arterioles	Decrease
Neural	Neural	Increase in the activity level of the renal sympathetic nerves releases norepinephrine	Constriction of afferent arterioles through activation of alpha 1 receptor and increased release of renin	Decrease
Hormone	Angiotensin II	Decrease blood volume or BP stimulates production of Angiotensin II	Constriction of afferent and efferent arterioles	Decrease
Hormone	ANP	Stretching of atria of heart stimulates secretion of ANP	Relaxation of mesangial cells in glomerulus increases capillary surface area available for	increase

TUBULAR REABSORPTION AND TUBULAR SECRETION

Renal Corpuscles: A renal corpuscle is the blood-filtering component of the nephron of the kidney.

GFR: 105-125ml/min of fluid that is isotonic to blood.

Filtered substances: water and all solutes present in the blood (except proteins) including ions, glucose, amino acid, creatinine, uric acid.

Proximal Convoluted Tubule.

Reabsorption (into blood) of filtered:

- Water- 65% (osmosis)
- Na- 65% (sod pot pumps)
- K-65% (diffusion)
- Glucose-100% (symporters and facilitated diffusion)
- Cl- 50% (diffusion)
- HCO₃- 80-90% (facilitated diffusion)
- Urea- 50% (diffusion)
- Ca, Mg- variable (diffusion)

Secretion:

- H- variable (antiport)
- NH₄- variable, increase in acidosis
- Urea- variable (diffusion)
- Creatinine- small amount

LOOP OF HENLE

Reabsorption (into blood) of:

- water- 15% (osmosis in descending limb)
- Na- 20-30% (symporters in ascending limb)
- K- 20-30% (symporters in ascending limb)
- Cl- 35% (symporters in ascending limb)
- HCO₃- 10-20% (facilitated diffusion)
- Ca, Mg- variable (diffusion)

Secretion: • Urea- variable (recycling from collecting duct)

Early Distal Convoluted Tubule

Reabsorption (into blood) of:

- Water- 10-15% (osmosis)
- Na- 5% (symporters)
- Cl- 5% (symporters)
- Ca- variable (stimulated by parathyroid hormone)

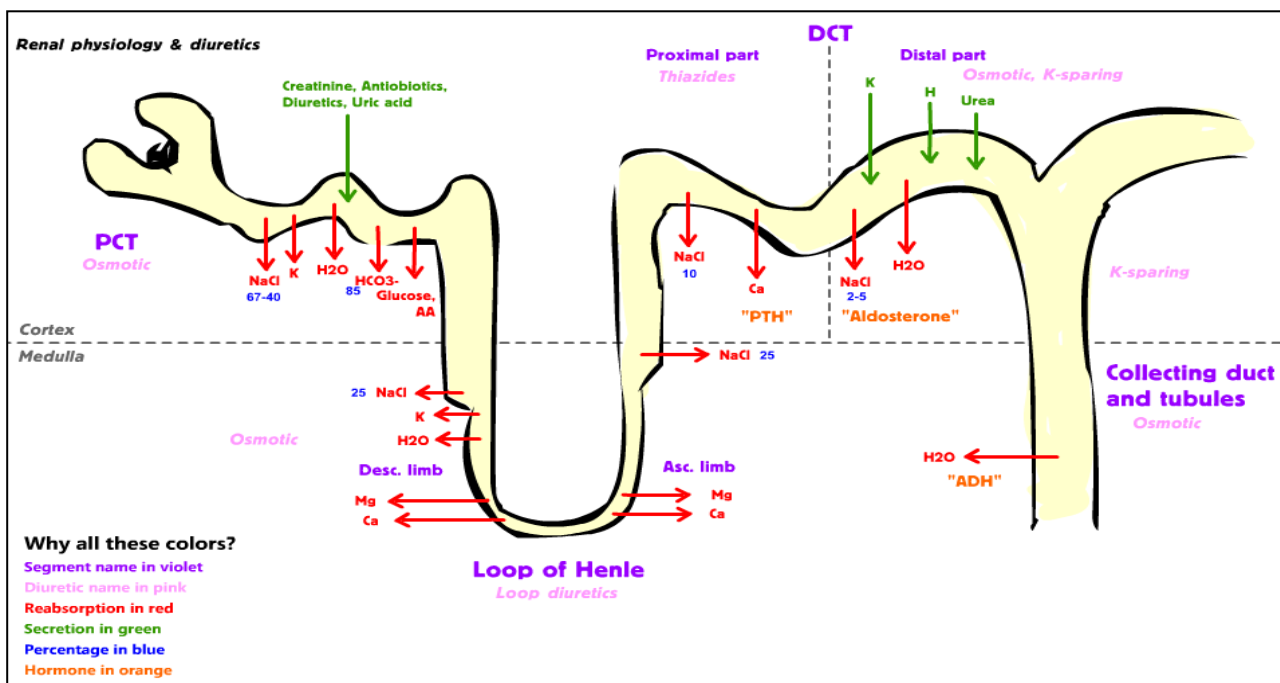
Late DCT And CD

Reabsorption (into blood) of:

- Water- 5-9% (insertion of water channel stimulated by ADH)
- Na- 1-4% (sod pot pumps and sod channel stimulated by aldosteron)
- HCO₃- variable amount depends on H secretion
- Urea- variable (recycling to loop of henle)

Secretion (into urine) of:

- K- variable amount to adjust for dietary intake (leaky channels)
- H- variable amounts to maintain acid base balance



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Renal Control of Acid Base Balance

- The kidneys control acid-base balance by excreting either acidic or basic urine
- Excreting acidic urine reduces the amount of acid in extracellular fluid
- Excreting basic urine removes base from the extracellular fluid

The kidneys regulate extracellular fluid H^+ concentration through three fundamental mechanisms:

- (1) Secretion of H^+
- (2) Reabsorption of filtered HCO_3^-
- (3) Production of new HCO_3^-

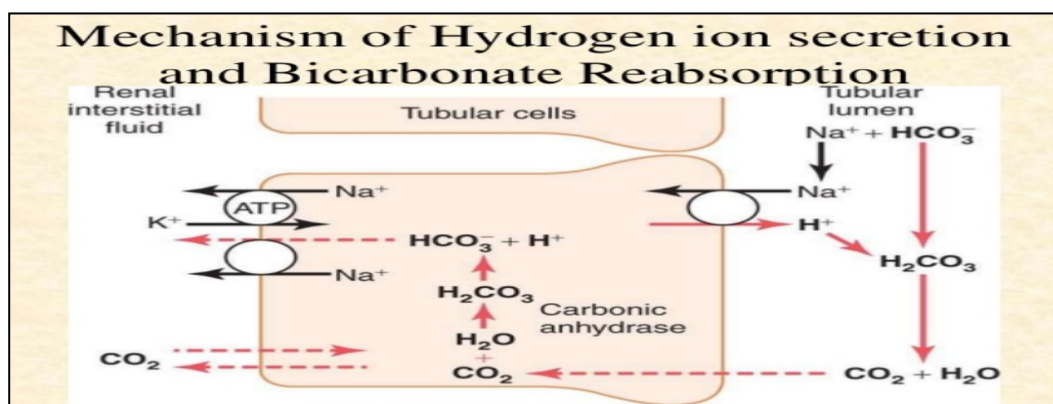
In acidosis, the kidneys do not excrete HCO_3^- into the urine but reabsorb all the filtered HCO_3^- and produce new HCO_3^- which is added back to the extracellular fluid. This reduces the extracellular fluid H^+ concentration back toward normal.

In alkalosis the kidneys fail to reabsorb all the filtered HCO_3^- thus increasing the excretion of HCO_3^-

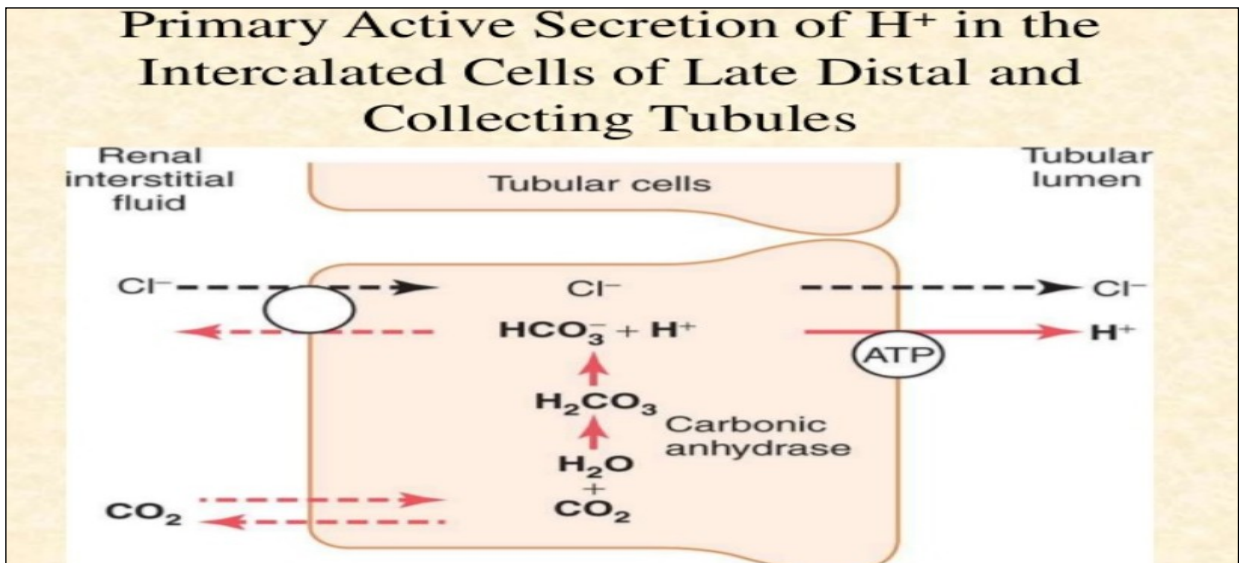
- Because HCO_3^- normally buffers H^+ in the extracellular fluid, this loss of HCO_3^- is the same as adding H^+ to the extracellular fluid.
- In alkalosis the removal of HCO_3^- raises the extracellular fluid H^+ concentration back towards normal.

About 80 to 90 percent of the bicarbonate reabsorption and H^+ secretion occurs in the proximal tubule

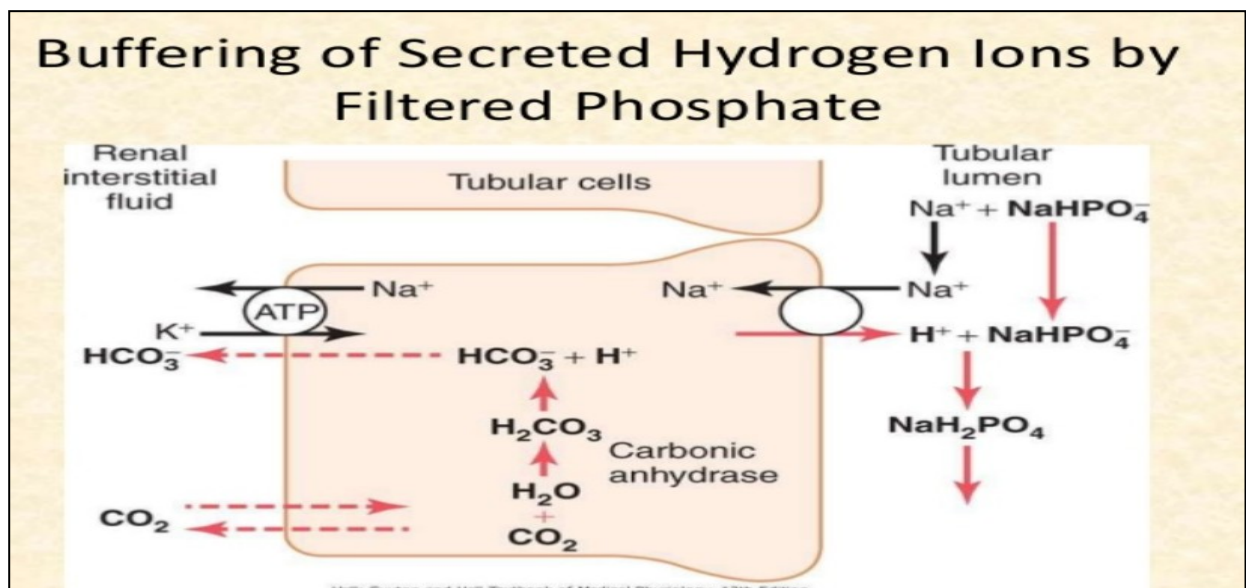
Mechanism of Hydrogen ion secretion and Bicarbonate Reabsorption.



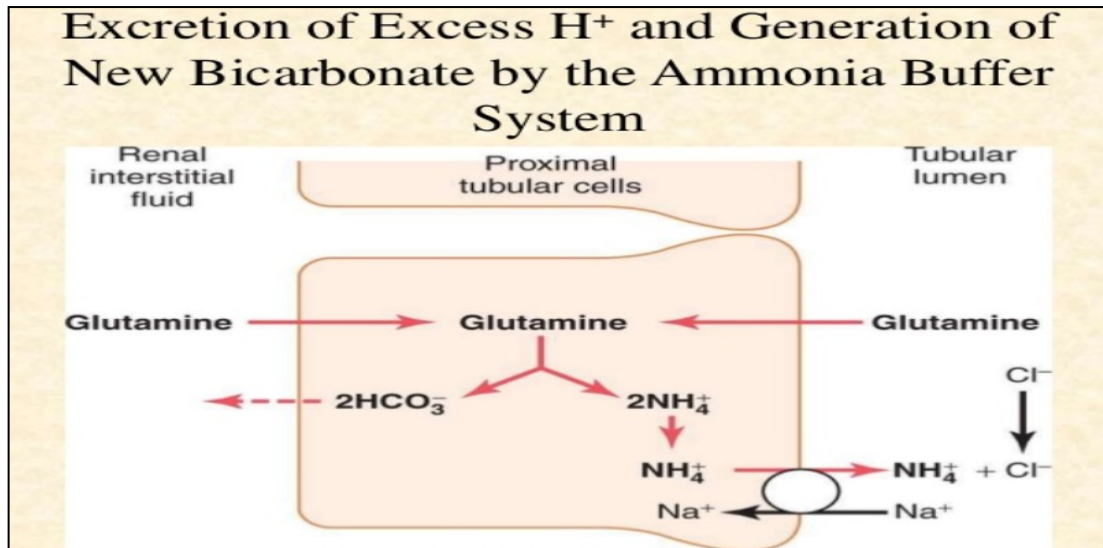
Primary Active Secretion of H⁺ in the Intercalated Cells of Late Distal and Collecting Tubules



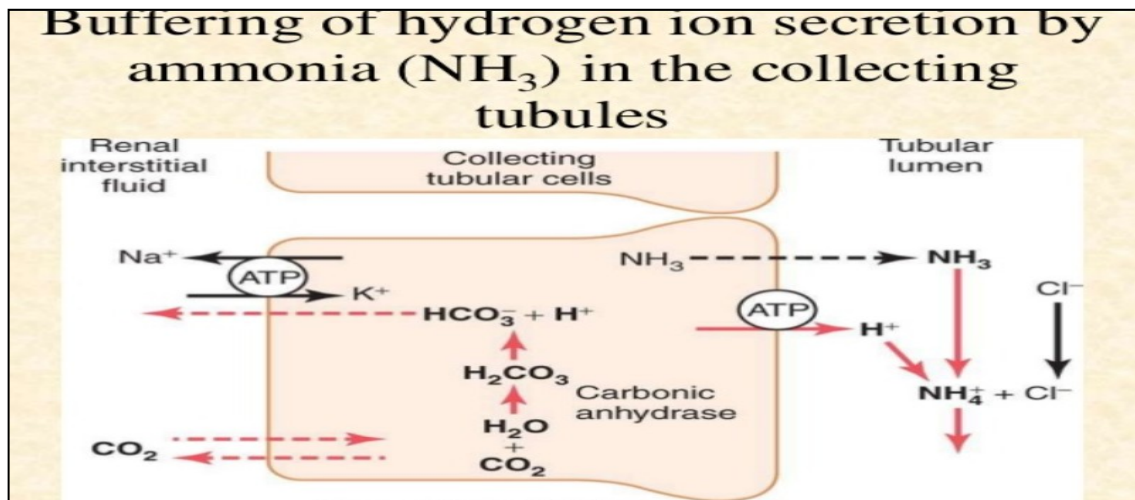
Buffering of Secreted Hydrogen Ions by Filtered Phosphate



Excretion of Excess H⁺ and Generation of New Bicarbonate by the Ammonia Buffer System



Buffering of hydrogen ion secretion by ammonia (NH₃) in the collecting tubules



Renal Correction of Acidosis-Increased Excretion of H⁺ and Addition of Bicarbonate to the ECF.

- Acidosis decreases the ratio of Bicarbonate/Hydrogen ion in Renal Tubular Fluid
- As a result, there is excess H⁺ in the renal tubules, causing complete reabsorption of bicarbonate and still leaving additional H⁺ available to combine with the urinary buffers (phosphate and ammonia)
 - Thus, in acidosis, the kidneys reabsorb all the filtered bicarbonate and contribute new bicarbonate through the formation of ammonium ions and titratable acid.

Renal Correction of Alkalosis-Decreased Tubular Secretion of H⁺ and Increased Excretion of Bicarbonate.

- Alkalosis increases the ratio of bicarbonate/hydrogen ion in renal tubular fluid
- The compensatory response to a primary reduction in PCO₂ in respiratory alkalosis is a reduction in plasma concentration, caused by increased renal excretion of bicarbonate.
- In metabolic alkalosis, there is also an increase in plasma pH and decrease in H⁺ concentration
 - The cause of metabolic alkalosis is a rise in the extracellular fluid bicarbonate concentration
 - This is partly compensated for by a reduction in the respiration rate, which increases PCO₂ and helps return the extracellular fluid pH toward normal
- In addition, the increase in bicarbonate concentration in the extracellular fluid leads to an increase in the filtered load of bicarbonate which in turn causes an excess of bicarbonate over H⁺ secreted in the renal tubular fluid
- The excess bicarbonate in the tubular fluid fails to be reabsorbed because there is no H⁺ to react with, and it is excreted in the urine.

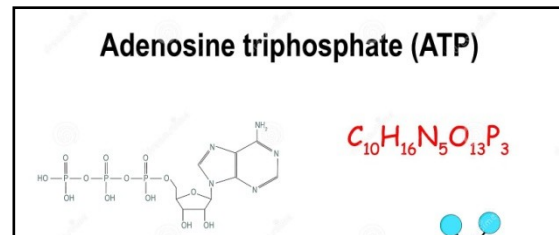
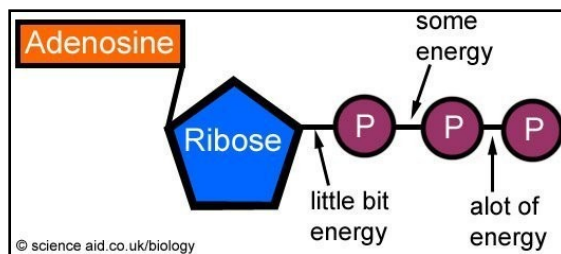
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ENERGETICS

ATP FORMATION:-

Before cells can use the energy of sunlight or energy /calories stored in carbohydrates, they must transfer the energy to molecules of ATP.

- ATP is composed of adenine, ribose, and three phosphate groups.
- ATP transfers energy to many different chemical reactions; almost all metabolic pathways directly or indirectly run on energy supplied by ATP.
- ATP can donate a phosphate group (phosphorylation) to another molecule, which then becomes primed and energized for specific reactions. (ready to be used for energy)



In human cells, cellular respiration releases energy from energy-rich organic molecules and changes ADP into ATP.

- Aerobic respiration is the main ATP- producing pathway
- Anaerobic respiration produces much less ATP (because no oxygen is involved) and can only be used for short periods of time, such as in vigorous muscle exercise.

AEROBIC RESPIRATION

Initial Breakdown of Glucose

- Glycolysis reactions occur in the cytoplasm (liquid stuff outside the nucleus) and results in the breakdown of glucose to pyruvate; small amounts of ATP are generated.

- Glucose is first phosphorylated in energy-requiring steps then split to form two molecules of PGAL.
- By substrate-level phosphorylation, four ATP are produced; but because two ATP were used previously, there is a net gain of only two ATP.
- Enzymes remove H^+ and electrons from PGAL to change NAD to NADH (which is used later in oxidative phosphorylation).

The end products of glycolysis are:

- two pyruvates,
- two ATP (net gain), and
- two NADH for each glucose molecule degraded.

THE KREBS CYCLE

Preparatory Steps of Krebs cycle (occurring in the mitochondria) degrades pyruvate to carbon dioxide, water, ATP, H^+ ions, and electrons.

Pyruvate (produced in the cytoplasm) enters the mitochondria and is converted to acetyl-CoA, which then joins oxaloacetate already present.

Krebs cycle serves three functions:

- H^+ and e^- are transferred to NAD^+ and FAD.
- Two molecules of ATP are produced by substrate-level phosphorylation.
- Most of the molecules are recycled to conserve oxaloacetate for continuous processing of acetyl-CoA.

The final stage of aerobic respiration occurs in the electron systems embedded in the inner membrane of the mitochondrion.

- Oxidation phosphorylation (which takes place on the cristae of the mitochondria) processes the H^+ ions and electrons to generate high yields of ATP.
- NADH and $FADH_2$ give up their electrons to transport (enzyme) systems embedded in the mitochondrial inner membrane.
- The actual ATP synthesis is accomplished when H^+ ions that have been pumped out of the inner mitochondrial compartment flow back through a channel protein called ATP synthase.

Oxygen joins with the "spent" electrons and H⁺ to yield water.

The production of ATP is completely dependent on the supply of oxygen that withdraws the electrons at the end of the transport systems.

Glucose Breakdown

The aerobic route is summarized: $C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$

Electron transport yields thirty-two ATP; glycolysis yields two ATP; Krebs yields two ATP for a grand total of thirty-six ATP per glucose molecule.

The actual yield can vary with cell type.

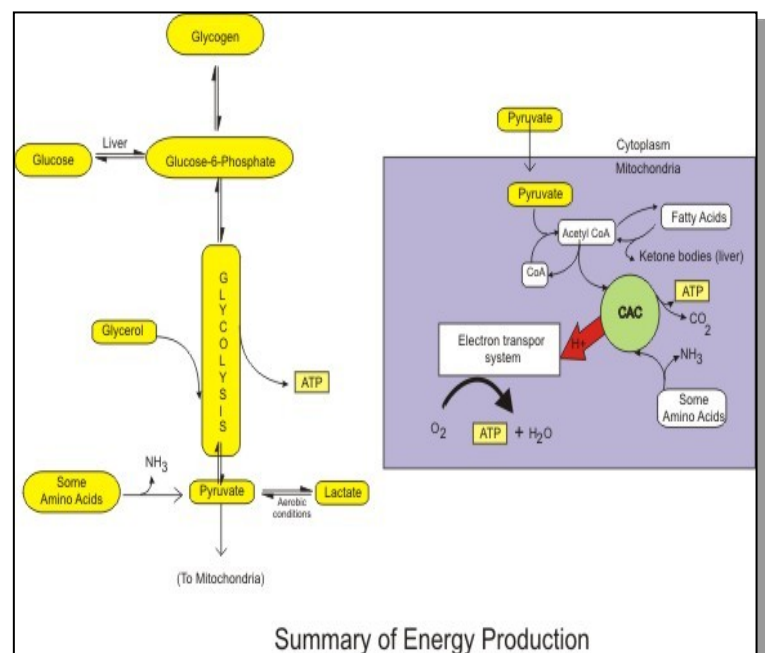
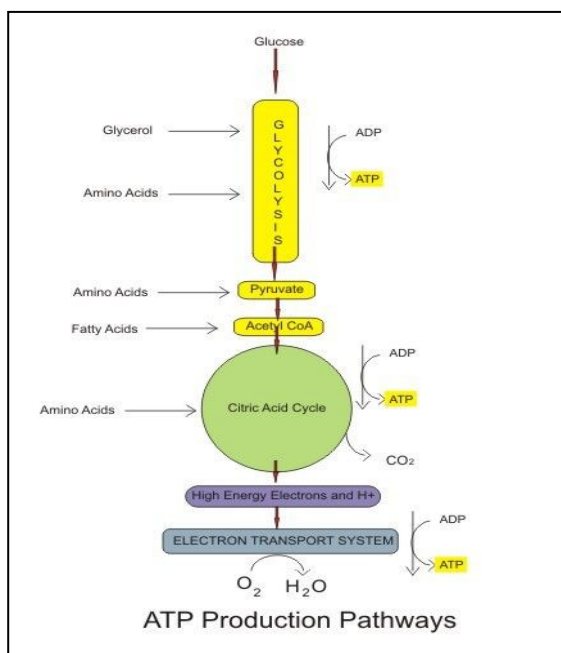
ATP From Anaerobic Pathways

Anaerobic pathways operate when oxygen is absent (or limited); pyruvate from glycolysis is metabolized to produce molecules other than acetyl-CoA.

In lactate fermentation, glycolysis produces two pyruvate, two NADH molecules, two ATP molecules, and two lactate, which tend to build up and cause temporary muscle cramps.

The ADP/ATP Cycle

The ADP/ATP cycle is a method for renewing the supply of ATP that is constantly being used up in the cell. Energy input couples inorganic phosphate to ADP to form energized ATP.



ATP (as a source of energy)

- a. ATP is the immediate energy source as its energy store is not long lasting due to the instability of the phosphate bonds
- b. Cells don't store large quantities of ATP however ATP is rapidly re formed from ADP and inorganic phosphate easily making it go further
- c. ATP is better than glucose as it releases **ROLES OF** smaller more manageable quantities of energy
- d. The hydrolysis of ATP to ADP is a single reaction releasing energy immediately whereas the process for glucose is much longer
- e. ATP cannot be stored so is continuously made in the mitochondria, cells such as muscle fibres contain large mitochondria due to the required energy
- f. Metabolic Processes: Forming polysaccharides from monosaccharides, Polypeptides from amino acids and DNA/RNA from nucleotides
- g. Movement: Provides energy for muscle contraction allowing the muscle filaments to slide over each other
- h. Active Transport: ATP provides energy to change the shape of carrier proteins in plasma membranes allowing molecules to move against the concentration gradient
- i. Secretion: Forms lysosomes needed for secretion of cell products
- j. Activation of molecules: When a phosphate molecule is transferred from ATP to another it makes it more reactive lowering activation energy. This allows enzyme catalysed reactions to occur more readily

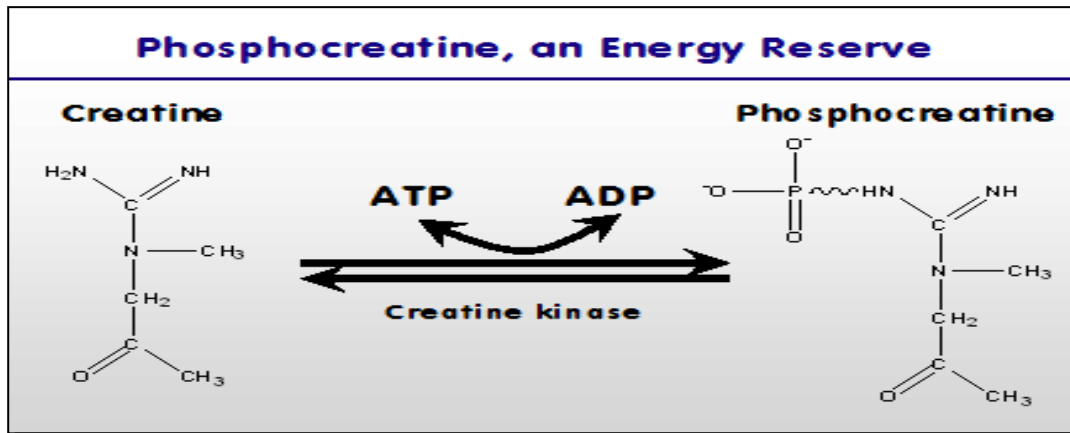
CREATININE PHOSPHATE

What is Creatine and Creatinine

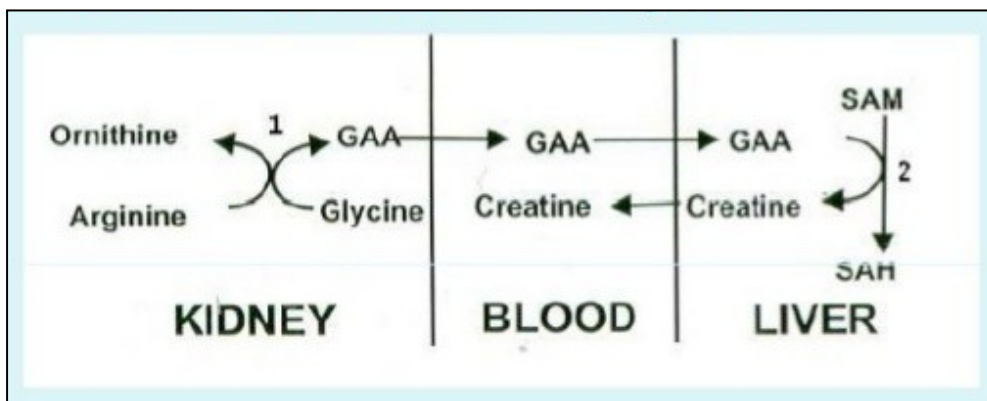
- Creatine and creatinine are not the same substance!
- Creatine is found in the muscles
- Creatinine is a break-down product (a waste product) of creatine phosphate and creatine in muscles, and is usually produced at a fairly constant rate by the body depending on muscle mass).

Structure

The creatine is an amino acid that does not found in proteins. Creatine is a nitrogenous organic acid. Three amino acids are required: Glycine Arginine Methionine (as S-adenosylmethionine)



Site of biosynthesis:



Distribution of body creatine

From liver, transported to other tissues (98% are present in skeletal and heart muscles)

In Muscle, gets converted to the high energy source creatine phosphate

What's the Relationship between Creatine and Creatinephosphate?

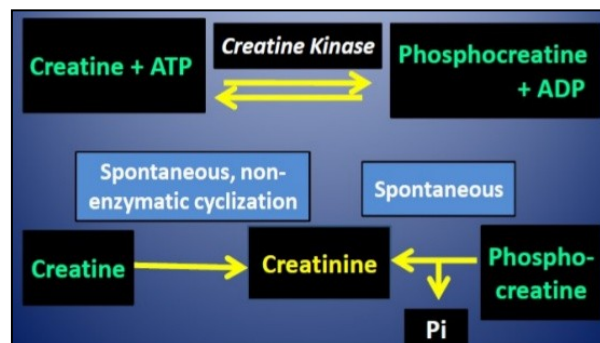
Creatine and creatine phosphate exist in a reversible equilibrium in skeletal muscle.

In skeletal muscle, approximately one-fourth of creatine exists as free creatine and threefourth exists as creatine phosphate.

Creatine Phosphate

- Is a high-energy phosphate compound
- Acts as a storage form of energy in the muscle
- Provides a small but, ready source of energy during first few minutes of intense muscular contraction

Formation:



Creatine Degradation

- Creatine and creatine phosphate spontaneously form creatinine as an end product
- Creatinine is excreted in the urine
- Serum creatinine is a sensitive indicator of kidney disease (Kidney function test)
- Serum creatinine increases with the impairment of kidney function.

Creatinine Excretion

The creatinine is a waste product of creatine phosphate and it will be excreted by the kidney in the urine at a rate of 1 to 2 g/day.

Creatinine Metabolism

- a. Every day about 2% of body creatine is converted to creatinine
- b. Creatinine is transport through the blood stream to kidney
- c. The kidney filter out most of the creatinine and excrete it in the urine.

Role of Creatinine Phosphate

1. *The Diagnostic Function of Creatinine*

- d. If the kidney are damaged or impaired and cannot work normally
- e. The amount of creatinine in urine goes down while its level in blood goes up
- f. Creatinine has been found to be a fairly reliable indicator of kidney function
- g. Serum creatinine level is an important diagnostic tool to asses renal function

2. *Estimate muscle mass*

The amount of muscle tissue in men tend to have higher levels of blood creatinine because they have more skeletal muscle tissues than women.

Normal serum creatinine level is 0.7 to 1.4 mg/dl and serum creatine level is 0.2 to 0.4mg/dl .The amount of creatinine excreted is proportional to the total creatine phosphate content of the body therefore can be used to estimate muscle mass.

3. *Creatine Kinase (CK) Diagnostic Value*

CK is required for conversion of creatine into creatine phosphate

CK has **3 isoenzymes: are tissue specific**

- a. CK-MM mainly in skeletal muscle
- b. CK-MB mainly in heart muscle
- c. CK-BB mainly in brain

Assaying for CK over a period of time is an diagnostic value for determination of tissue damage of organ like brain and muscle and heart.

Basal metabolic rate

BASIC METABOLIC RATE

Food is the fuel source of the body, the ingested food undergoes metabolism to liberate energy required for the vital activities of the body

Man consumes energy to meet the fuel demands of the three ongoing processes in the body

- i. Basal metabolic rate
- ii. Specific dynamic action
- iii. Physical activity

Basal Metabolic Rate:- It is the minimum amount of energy required by the body to maintain life at complete physical and mental rest in post absorptive state

Several functions within the body occurs at basal condition like

- working of heart and other organs
- conduction of nerve impulse
- reabsorption by renal tubules
- Git motility
- Ion transport across membranes

Normal values of BMR

- Adult man: 35-38 cal/sq.m/hr or 1600cal/day
- Adult woman: 32-35 cal/sqm/hr or 1400cal/day
- A BMR value between -15% and +20% is considered normal

Factors affecting BMR

- Surface area: directly proportional to surface area
- Sex: men have marginally higher BMR (5%)
- Age: in infants and growing children BMR is higher. In adults BMR decreases at the rate of 2% per decade of life
- Physical activity: increase with regular exercise
- Hormones: thyroid hormones increase BMR. Epinephrine, cortisol, sex hormones and growth hormone hormones increase BMR
- Environment: BMR is higher in cold climates compared to warm climates
- Starvation: during starvation a decrease in BMR up to 50% has been reported
- Fever: fever increases BMR. 10% increase for every 1°C rise in body temperature
- Disease status: BMR is elevated in infections, leukemia, cardiac failure hypertension etc.

Role of BMR

- BMR is important to calculate the caloric requirement of an individual and planning of diets
- Assessment of thyroid function
- BMR is below normal in starvation, under nutrition, in fever, diabetes insipidus, leukemia and Polycythemia, Addison's disease.