MSCU ANSWERS TO ASSORTED BIOCHEMISTRY SAQ'S FOR MBCHB AND BPHARM LEVEL 2

A TRIBUTE TO THE LATE PROF. HASSAN SAIDI. BSc (Anatomy), MBChB, MMed (Surg), FACS.

1. **List five major mechanism of antibiotic resistance.**
   (a) Enzymatic cleavage/ inactivation or modification of the antibiotic; (hydrolysis by beta lactamases and amino glycoside modding enzymes)
   (b) Altered receptors/ binding proteins preventing attachment to surface (Fails to bind to altered altered PBPs). An alteration in the target site of the antibiotic that reduces its binding capacity.
   (c) Altered permeability and efflux pumps stop through porins. The reduced intracellular antibiotic accumulation by decreasing permeability and/or increasing active efflux of the antibiotic.
   (d) Bypass of a metallic block TMP/SMX
   (e) The modification of metabolic pathways to circumvent the antibiotic effect
2. Make brief notes on the following;
   (a) Beneficial mutations
   (b) Spontaneous mutations
   (c) Glycosylation
   (d) Molecular tags
3. Briefly explain five genetic mutations that confer resistance to infection by the malarial parasite in endemic areas.
4. **State five reasons why parasites that live in micro-aerobic sites within the body have evolved anaerobic pathways for energy generation.**
5. Illustrate and briefly explain the following chromosomal alternations stating possible phenotypic effect:
   (a) Inversion
   (b) Reciprocal translocation
6. Define the following and give an example of each:
   (a) Aneuploidy
   (b) Multiple alleles in a population
7. State any four exceptions to the Mendelian original principal of inheritance.
8. If a child and its mother are both blood group B explain the possible blood group(s) of the father.
9. Using illustrations where appropriate, describe how the normal cellular protein PrP^{c} can in the presence of minute quantities of abnormal PrP^{sc} protein become infectious leading to cell death.
10. **Describe the mechanisms of action of:**
    (a) **Steroid hormones**

    Steroid hormones are lipid soluble and thus travel through blood with the help of a protein carrier. When they get to the target cell they detach from the carrier and traverse the cell membrane and enter the cell by simple diffusion. Receptors for steroid hormones are located inside target cells, in the cytoplasm or nucleus. The hormone will either bind to a cytoplasmic receptor and then enter the nucleus as a hormone-receptor complex or enter the nucleus to encounter its receptor. The receptors function as ligand-dependent transcription factors. That is to say, the hormone-receptor complex binds to promoter regions of responsive genes and stimulate or sometimes inhibit transcription from those genes.

Thus, the mechanism of action of steroid hormones is to modulate gene expression in target cells. By selectively affecting transcription from a battery of genes, the concentration of those respective proteins are altered, which clearly can change the phenotype of the cell. When hormone binds to receptor, a characteristic series of events occurs:

- *Receptor activation* is the term used to describe conformational changes in the receptor induced by binding hormone. The major consequence of activation is that the receptor becomes competent to bind DNA.
- *Activated receptors bind to "hormone response elements"*, which are short specific sequences of DNA which are located in promoters of hormone-responsive genes. In most cases, hormone-receptor complexes bind DNA in pairs, as shown in the figure below.
- *Transcription from those genes to which the receptor is bound is affected.* Most commonly, receptor binding stimulates transcription. The hormone-receptor complex thus functions as a transcription factor.

(b) Amine/peptide hormones

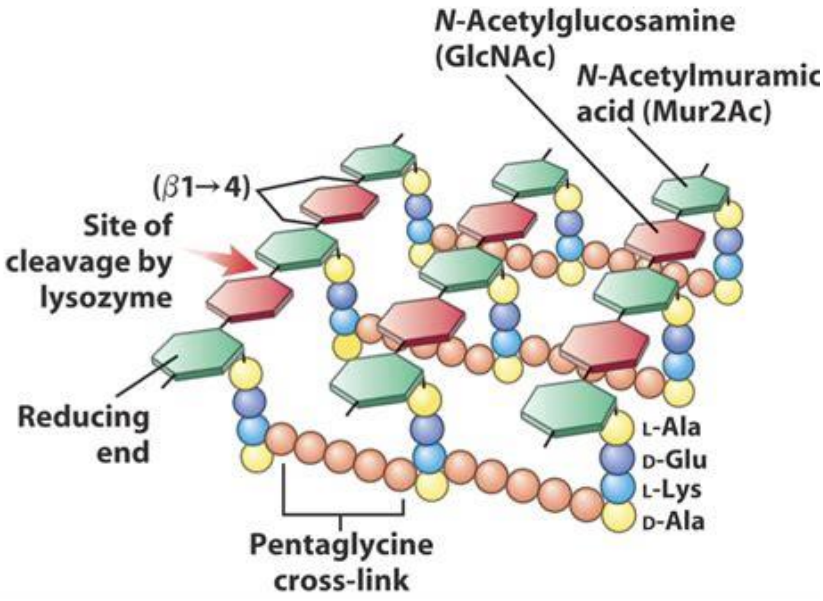
Peptide hormones are released from a cell via exocytosis as prohormones. Specific endopeptidases cleave the prohormone into a hormone before released into the bloodstream where they travel to the target cell. All peptide hormones are hydrophilic and are therefore unable to cross the plasma membrane alone but act on the cell via second messengers. Peptide hormone interact with specific receptor at the extracellular domain with through transmembrane domain activate the cytosolic domain to release intracellular signals. Binding of hormone leads to dimerization of the receptor. This then causes self-phosphorylation of cytosolic domain as well as other proteins in the cytosol. For some receptors, second messengers are also produced. Changes in activities of proteins in the cytosol as well as expression of new genes in the nucleus bring about changes in the cellular activities. Some peptide hormones also interact with intracellular receptors found in the cytoplasm or nucleus via intracrine mechanism.

11. Discuss the applications of Polymerase Chain Reaction (PCR) in modern science.
12. **Briefly discuss the major steps in the biosynthesis of peptidoglycan and outline the reasons why penicillin is an effective inhibitor of cell wall biosynthesis.**

Biosynthesis of the Peptido-glycan (5 Stages)

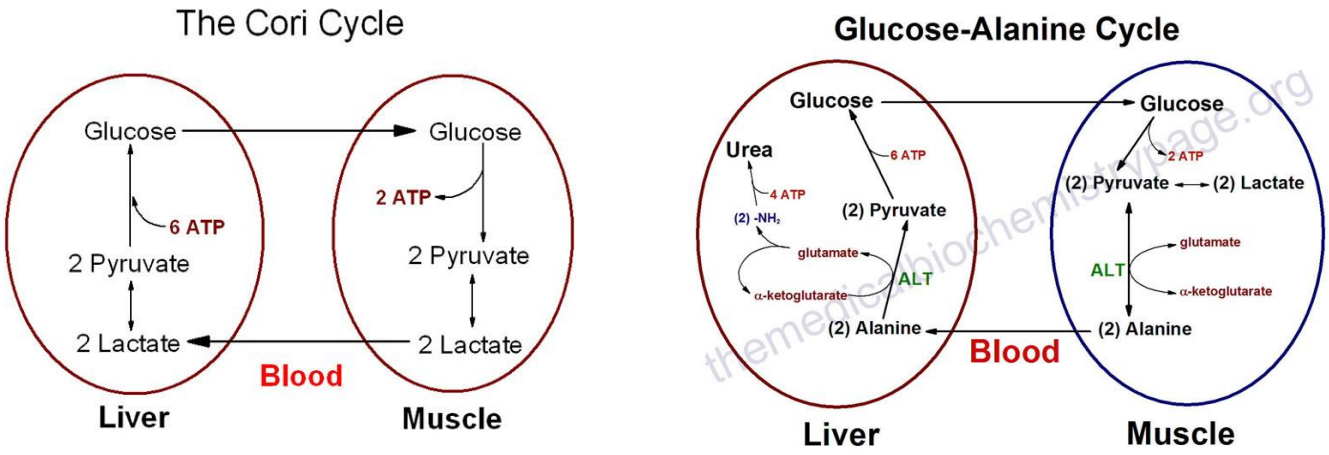
• Peptide built on NAM attached to UDP (NAM peptide transferred to carrier lipid (Bactoprenol) while product lies outside c-membrane precursors are made inside the cell)
• Lipid shuttle polar UDP across the c-membrane
• NAG and Penta-glycine bridge added to NAM peptide attached to lipid carrier
• Disaccharide peptide transferred from carrier lipid to growing polysaccharide chain
• Transpeptidation reaction of Penta-glycine bridge crosslink different polysaccharide strands

β-Lactam antibiotics such as penicillin inhibit the formation of peptidoglycan cross-links in the bacterial cell wall; this is achieved through binding of the four-membered β-lactam ring of penicillin to the enzyme DD-transpeptidase. As a consequence, DD-transpeptidase cannot catalyze formation of these cross-links, and an imbalance between cell wall production and degradation develops, causing the cell to rapidly die.



13. **The Cori cycle and the Glucose-Alanine cycle are two important cycles illustrating the metabolic cooperation between muscle and liver.**

(a) In form of a scheme show the (I) Cori cycle (ii) Glucose-Alanine cycle.



(b) Clearly differentiate between the role(s) of the two cycles.

The glucose-alanine cycle occurs in skeletal muscle to eliminate nitrogen while replenishing the energy supply for muscle. The amino group transported from the muscle to the liver in the form of alanine, is converted to urea in the urea cycle and excreted. The Cori cycle on the other hand describes the linked metabolic pathways by which muscles, even in the absence of oxygen, remain capable of functioning. This occurs as a result of the liver's ability to convert a muscle's chemical waste product back into its energy source.

14. **State one difference between plasmodium and human metabolism with regards to the following:**

(a) Glycolysis

They lack glucose stores and thus their source is directly from blood and they don't oxidize glucose completely to CO2 and H2O. Pyruvate is not the end product of glycolysis. Most of the pyruvate is converted to volatile products such as formate and acetate and lactate.

(b) Kreb's cycle

Plasmodium lack a functional Kreb's cycle since α-ketoglutarate dehydrogenase activity is absent.

(c) Haemoglobin metabolism

Plasmodium, digest the protein as a source of amino acids.

•Haemoglobin plays a central role during the blood stage of Plasmodium infections

•Haemoglobin consumption is achieved through several distinct mechanisms depending on the stage of parasite development.

Reactive heme group is released from the globin portion of the protein. The free heme is toxic hence it is detoxified by polymerization into crystals known as hemozoin.

•Hemozoin crystals are generated by polymerization of heme through the formation of a bond between the iron atom of one heme molecule and carboxylate of another.

• In humans, haemoglobin is briken down into bilirubin in the liver which is further converted to urobilinogen and urobilin. Urobilinogen is excreted in the kidney as urine while urobilin along with stercobilin are excreted in faeces.

(d) Folate metabolism

•Filaria can oxidise 5-methyl Tetrahydrofolate to 5,10 Methylene Tetrahydrofolate. This reaction doesn't occur in the host.

•This may be an adaptation with the parasite to provide them with an additional substrate other than folate. 5,10 Methylene Tetrahydrofolate is a substrate for thymidylate synthetase, which is involved in the conversion of dUMP to dTMP

•dTMP can be converted to dTTP required for nucleic acid synthesis.

•The reaction is very important for the parasites that can't synthesise the nucleotide de novo or salvage it.

•However, parasites employing de novo purine synthesis require 5,10 Methylene Tetrahydrofolate and such parasites include Filariae.

•Because of this importance of purine metabolism, interruption of folate supply in metabolism will inhibit growth and reproduction in parasites.

•Intracellular protozoa and pathogenic bacteria synthesise Tetrahydrofolate de novo from GTP, PABA and glutamate, whereas mammalian host don't have this pathway. Mammals get folate from their diet which they directly reduce to tetrahydrofolate.

•This substantial difference in the source of tetrahydrofolate has proved useful in chemotherapy since analogs of PABA competitively inhibit the enzyme dihydropteroate synthase (DHPS) and this diminishes the rate of tetrahydrofolate synthesis.

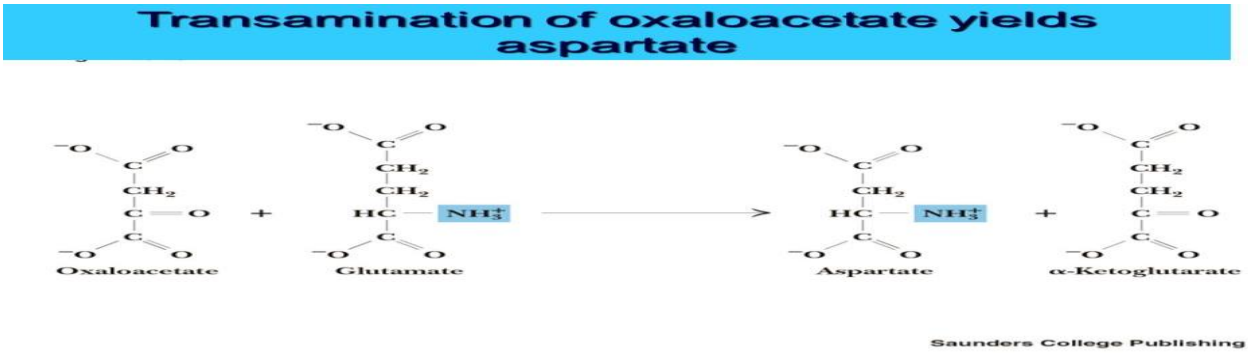
(e) Vitamin metabolism

The three biosynthetic pathways that produce vitamins B1, B6 and B9 are absent from the host, but are well established in P. falciparum.

15. Briefly describe the following mutation types:
    (a) Reversal mutation.
    (b) Transition mutation
    (c) Transversion mutation

(d) Back mutation
(e) Forward mutation
(f) Suppressor mutation

16. Briefly state and explain the application of bioinformatics.
17. Describe the three steps in PCR amplification.
18. Answer the following:
    (a) The initiation of DNA replication occurs at specific points called?- **Origins of replication**
    (b) DNA is unwound with the help of?- **DNA helicase**
    (c) Single stranded DNA produced during replication is stabilized through the binding of? - **Single stranded binding proteins.**
    (d) After replication, the RNA primer in okazaki fragments is removed and the gaps are filled in by **DNA ligase** and **DNA polymerase**?
    (e) The _____are the specific sequences on DNA template that regulate the transcription of one or more genes.
    (f) List two differences between replication and transcription.
19. Answer the following:
    (a) Give three main classes of RNA and state their role in protein synthesis.
    (b) A set of enzymes called _____are used to charge the tRNA with the proper amino acid.
    (c) The genetic code is _____since more than one codon is used for most amino acids.
    (d) The untranslated regions at the beginning and the end of mRNA are called _____and _____respectively.
20. A breed of dairy cattle is of **black coat** and **big body**. Occasionally, calves with recessive red coat are born. A dairy farmer purchased a prized **black big body** bull to improve on his livestock with the promise that it was a pure breeder. To his dismay, the bull produced a calf with recessive colour when mated to his undisputed pure breeding **black big body cow.** Using **R** for colour and **S** for body size,
    (a) What genotype did the farmer expect for the pure breeding prized bull?
    (b) What is the genotype of the above mentioned cow?
    (c) State the circumstances under which it was possible to get a **red calf** from the cross of the bull and the undisputed pure breeding cow?
    (d) If the bull mentioned above was mated with a true breeding **big red** cow, in a Punnet square show your phenotypes of the offspring (NB use the true genotypes for the bull: show all your genotypes clearly.
21. With the aid of illustrations, classify **eukaryotic chromosomes** on the basis of their size and centromere position. Identify one human chromosome that fits into each of the classes.
22. Briefly describe the asymmetric model of viroid replication.
23. Define the Wobble hypothesis and write the permitted anticodon-codon base pairing at the Wobble position.
24. With illustrations, briefly discuss the elongation cycle of prokaryotic protein biosynthesis.
25. **Using structural illustration and aspartate as an example describe the transamination process**. **Aspartate** transaminase. An enzyme that catalyzes the reversible transfer of an amino group from **aspartate** to α-ketoglutarate to form glutamate and oxaloacetate, requiring the coenzyme pyridoxal phosphate; it is normally present in serum and in various body tissues, especially in the heart and liver.



26. **Outline five fates of amino acids in the amino acid pool**
    - They are used to provide about 10-15 of the body's energy demand
    - They are used to synthesize nitrogenous products such as purines, pyrimidines and porphyrins
    - They are used to make carbohydrates and fats
    - They are used to make enzymes and hormones
    - They are used to make contractile proteins and immunoproteins
    - The glucogenic amino acids are used to form glucose
    - They are used to form tissue proteins and plasma proteins
27. **Describe the biochemical basis of the excitation-contraction coupling in a skeletal muscle.**

1. Nerve impulse arrives at neuromuscular junction (neuron to muscle cell communication).
2. Acetylcholine (ACh) is released from motor neuron and diffuses across to the motor end plate.
3. ACh binds with nicotinic receptors at the motor end plate (a specialized portion of sarcolemma). Receptors are linked to ligand gated ion channels, allowing Na^+ influx (plus a little bit of K^+ efflux), resulting in the depolarization of the muscle cell membrane. This results in a motor end plate potential, which becomes an action potential (AP) in muscle cells.
4. The impulse (AP) is spread very quickly throughout the cell by the transverse ("T") tubules. Located on the T-tubules are the dihydropyridine (DHP) receptors that are mechanically linked to the lateral sacs (terminal cisternae) of the sarcoplasmic reticulum (SR). When triggered by the change in membrane potential (AP) traveling down the t-tubules, the DHP receptors mechanically opens gates on the SR. This then causes the SR to release the Ca^{2+} it has stored there into the cytosol (sarcoplasm) of the skeletal muscle.
5. The increase in $[Ca^{2+}]_i$ binds to the regulatory protein troponin, causing it to change shape and move.
6. The movement of troponin then moves tropomyosin away from covering the active site on actin, thus exposing the myosin binding site on actin.
7. Due to the strong affinity between them, the **myosin head binds to the actin** (crossbridge).
8. Crossbridge formation stimulates ATPase activity, and allows the **power stroke** to occur. The power stroke is the 'pulling' of actin toward the M line by the pivoting of the myosin

head. The myosin head is going from a high energy state to a low energy state during the power stroke (PE converted to KE).

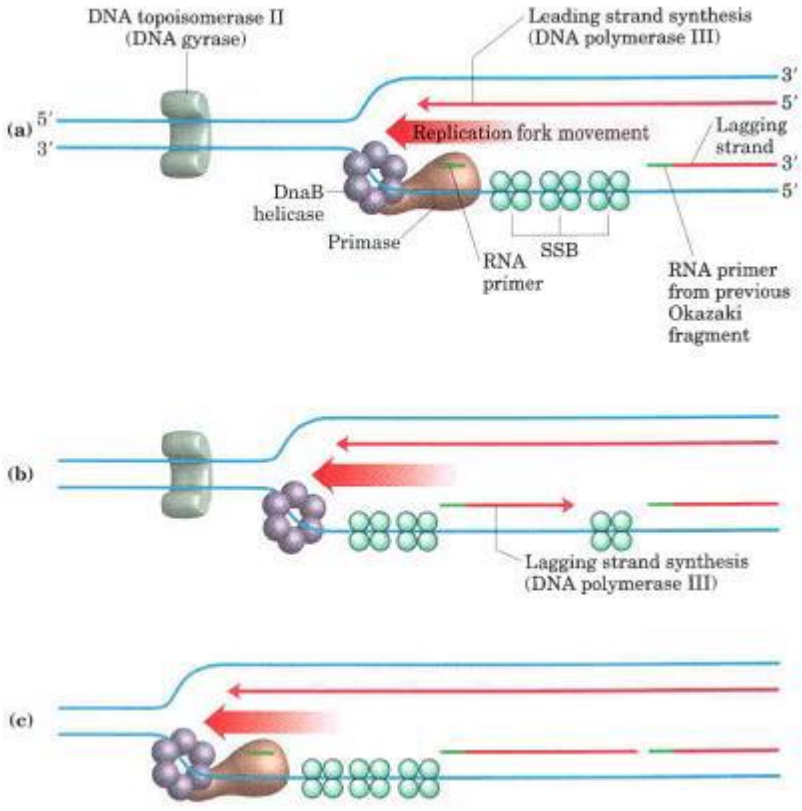
9. **If more ATP is available, then the crossbridge is broken and myosin releases actin**. This allows for the repositioning of the myosin head into the high energy state.
10. Then, if the nerve impulse is still present, steps 7 through 9 will be repeated.

This muscle contraction will continue until: **1)** the impulse stops or **2)** fatigue occurs.

If Nerve Impulse Stops:

1. Ca^{2+} will be pumped back into SR (re-sequestered) by active transport (Ca^{2+}ATPase).
2. Without the increased $[Ca^{2+}]_i$, troponin is no longer bound to Ca^{2+} and the tropomyosin then moves back over to cover the binding sites on actin. Thus **crossbridges formation cannot occur**.
3. When all the myosin heads detach, actin slides back to its original position and the muscle relaxes.

28. What is post-transcriptional regulation and how does it usually work?
29. **Name the following**
    (a) Full name of the two key enzymes of purine salvage pathways- **Ribose phosphate pyrophosphokinase and glutamine PRPP amidotransferase**
    (b) The intermediate product leading to both GMP and AMP in de-novo purine biosynthesis. **IMP inosine 5 monophosphate**
30. **Draw a clearly labelled diagram of a DNA replication fork.**



31. With regards to eukaryotic RNA polymerases, highlight on the main product of; and the effect of α-amanitin on;
    (a) Polymerase I
    (b) Polymerase II
    (c) Polymerase III
32. **Outline the major four enzymes responsible for protein degradation and list down two functions of HCL acid in digestion process.**
    In human digestion, proteins in food are broken down into smaller peptide chains by digestive enzymes such as pepsin, trypsin, chymotrypsin, and elastase, and into amino acids by various enzymes such as carboxypeptidase, aminopeptidase, and dipeptidase.
    HCL helps to convert inactive pepsinogen into pepsin and also creates an acidic environment for the enzyme pepsin to work efficiently.
33. **List the metabolic fuel/energy related pathways/processes which take place in the human hepatocyte in;**
    (a) Mitochondria – Krebs cycle, electron transport, oxidative phosphorylation, fatty acid oxidation, ketone body synthesis.
    (b) Cytosol – Glycolysis, pentose phosphate pathway, fatty acid synthesis
    (c) Both –Gluconeogenesis, urea synthesis.
34. Briefly explain the following terms;
(a) Inclusion cell disease
(b) Zellwerger syndrome
(c) Signal sequence
(d) Operon
(e) Operator
35. **Discuss the structural features of proteins which serve as signals for their degradation.**

36. **Briefly discuss the Aspartate-Arginosuccinate shunt that links Krebs-Henseleit Cycle and Citric Acid cycle and list four diseases associated with urea elimination.**

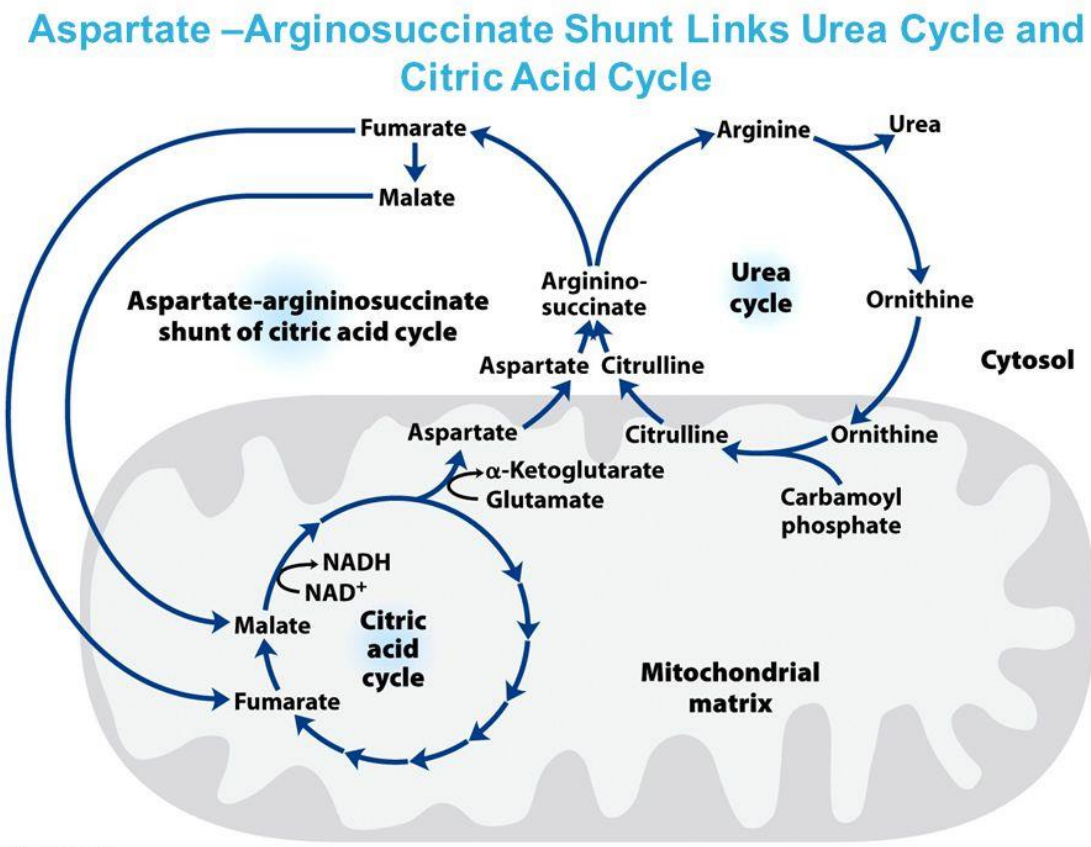


Figure 18-12

1. Hyperammonemia (elevated blood ammonia)
2. Uremia (presence of urea in blood)
3. Argininemia- arginine in the blood due to arginase deficiency
4. Carbamoyl phosphate synthetase deficiency
5. Orthinine transcarbomylase deficiency
6. Citrullinemia- deficiency of argininosuccinate synthetase deficiency

37. Discuss how prokaryotic organisms use lac operon to regulate gene expression in response to their environment.
38. Define the following terms and give an example in each case;
    (a) Multiple alleles
    (b) Codominance
39. Carefully study statements (a) and (b) below and answer the questions that follow; use clearly presented illustrations:
    (a) A woman has a daughter. There are three men whom she claims might have been the father of the child. The judge in the paternity court orders that all the three men, the child and the mother have blood tests. The results are: mother type A; daughter type O;
        - Man#1, Type AB

- Man #2, Type B
- Man #3, Type O

The mother claims that this proves that man #3 must be the girl's father.

(I) Is the mother correct? Why or why not?

(ii) The judge isn't satisified, so he asks for the medical records of the people involved. He

Discovers that the little girl is colour blind. Men #1 and 2 are also colour blind. Man #3 has normal colour vision, as does the mother (NB colour blindness is X-linked and recessive). Assuming that one of these three men must be the father, can you now determine which of the three it is?

(b) Three babies were mixed up in a hospital. After considerations of the data below, which of the following represent the correct baby and parent combinations?

	Couple#1	Couple#2	Couple#3
Parent's blood groups	A and A	A and B	B and O
Baby's blood group	B	O	AB

Assign the babies to the parents and justify, use clearly represented illustrations.

40. In the table below, fill in the information on chromosomal basis of sex determination in the animal kingdom.

	System used	Male chromosomes	Female chromosomes	Example?
1				
2				
3				
4				

41. Using illustrations, briefly explain the genetic basis of 'mosaic traits' in animals.
42. Differentiate between expressivity and penetrance in a dominant trait.
43. Draw a diagram illustrating how a retra-troposon moves within a genome.
44. In human genomes, name any three types of sequences that contributes to the non-coding DNA
45. Give the full names of the following; LINEs, FISH
46. Define the terms; genome length and genome complexity. (B) A genome is made up of the following sequences. 2.5Mb of unique sequences, 2500 copies of a moderately repeating sequences that is 1Kb long and 500,000 copies of a highly repeating sequence that is 50 base pairs long. Showing your work clearly determine (I) The genome length in base pairs(bp) (ii) The genome complexity in base pairs.
47. Answer the following.
    (a) Define $Cot_{1/2}$ value and state three factors that influence it.
    (b) Draw a clearly labelled illustration to show the theoretical Cot-curve of a human genome and mention the OD at which this is determined.
48. With regards to muscle contraction, list the functions of the following proteins;
    (a) Actin- activates myosin ATPase
    (b) Myosin- Cross bridge formation

(c) Tropomyosin- prevents actin from associating with myosin head
(d) Troponin- >I- inhibits actomyosin ATPase
>C- binds calcium ions
>T- binds tropomyosin

49. **Describe the process of DNA replication in E. Coli.**

The synthesis of a DNA molecule can be divided into three stages: initiation, elongation, and termination, distinguished both by the reactions taking place and by the enzymes required.
Initiation of replication
•**The initiation** of DNA replication occurs at specific points called origins of replication (e.g. OriC in E. coli). Once DNA synthesis has been initiated, two replication forks, extending in either direction from the origin of replication, proceed to allow the full replication of the genome. OriC is the binding site of proteins DNA A, B and C that promote the melting (opening) of the DNA helix, a process that is essential so that DNA replicating enzymes can read the base sequence. The polymerase can only function if a free 3OH group is present. This hydroxyl group is provided by an RNA primer (which is complementary to the DNA) that is 5–15 nucleotides long. The synthesis of the primer is directed by a form of RNA polymerase (called primase). DNA is unwound into the polymerase complex with the help of DNA helicases. Topoisomerase enzymes (e.g. DNA gyrase) are required to relieve tension in the helix that results as a consequence of the unwinding process. Single-stranded DNA produced during replication are stabilized through the binding of single-stranded binding proteins (SSBs)

Elongation

•The elongation phase of replication includes two distinct but related operations: leading strand synthesis and lagging strand synthesis. Leading strand synthesis begins with the synthesis by primase of a short (10 to 60 nucleotide) RNA primer at the replication origin. Deoxyribonucleotides are added to this primer by a DNA polymerase III. Leading strand synthesis then proceeds continuously, keeping pace with the unwinding of DNA at the replication fork. The lagging strand is formed so that nucleotide polymerization can occur on both template strands in a 5'to 3'direction. DNA ligase is then required to join the phosphodiester backbone of the Okazaki fragments to form a complete strand.
DNA synthesis on the leading and lagging strand
(a) At intervals, primase synthesizes an RNA primer for a new Okazaki fragment.
(b)Each primer is extended by DNA polymerase lll.
(c)DNA synthesis continues until the fragment extends as far as the primer of the previously added Okazaki fragment A new primer is synthesized near the replication fork to begin the process again. The synthesis of DNA fragment on lagging strand.
Each RNA primer is ~ 10 nucleotides. This primer is removed by a special DNA repair enzyme, RNAse H that recognises an RNA strand in RNA/DNA hybrid and cleaves it. The gaps are filled in by DNA Polymerase and DNA ligase. DNA polymerase has a 3'-5' proofreading exonuclease activity

Termination

•Termination occurs at defined DNA sequences (called terminator sequences) that act as binding sites for a protein called Tus (terminus utilization substance). The Tus-Ter complex can arrest a replication fork from only one direction.

50. Explain the difference between a missense mutation and a nonsense mutation

51. **Describe a frame shift mutation.**
    Mutation is a change in DNA base pair. In frame shift mutation, there is deletion or insertion of a base thus changing the reading frame of mRNA downstream. Incorrect amino acids are incorporated.
    Effects;
    (a) Shortens a protein by bringing a stop codon into the reading frame
    (b) Lengthens a protein by resulting in read through of stop codons.
52. Explain the genetic background and symptoms/appearance of the following;
    (a) Mosaicism
    (b) Klinefelter syndrome
53. **Write short notes on lactose intolerance in humans.**
    This is the inability to digest lactose into glucose and galactose due to low levels of the enzyme lactase in the duodenum. Lactase deficiency is more common in some races and increases with age. The symptoms are flatulence, nausea, boating and loose stool.
54. **Describe the mechanism of action of steroid hormones.**
    Steroid hormones are lipid soluble and thus travel through blood with the help of a protein carrier. When they get to the target cell they detach from the carrier and traverse the cell membrane and enter the cell by simple diffusion. Receptors for steroid hormones are located inside target cells, in the cytoplasm or nucleus. The hormone will either bind to a cytoplasmic receptor and then enter the nucleus as a hormone-receptor complex or enter the nucleus to encounter its receptor. The receptors function as ligand-dependent transcription factors. That is to say, the hormone-receptor complex binds to promoter regions of responsive genes and stimulate or sometimes inhibit transcription from those genes.
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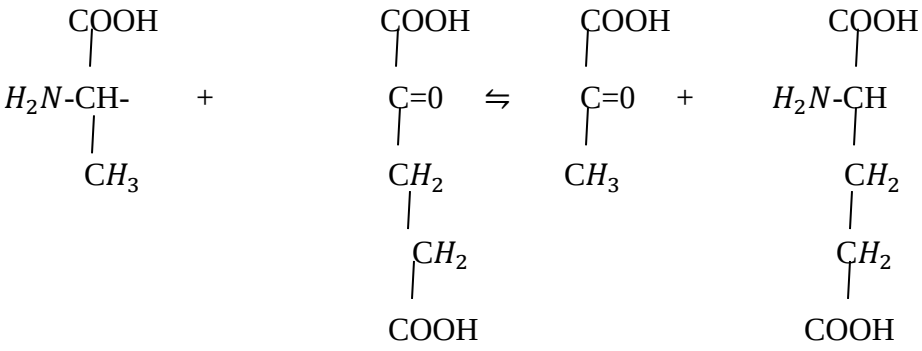
- *Transcription from those genes to which the receptor is bound is affected.* Most commonly, receptor binding stimulates transcription. The hormone-receptor complex thus functions as a transcription factor.

55. Using structural illustrations and alanine as an example describe the transamination process.

Transamination is a chemical reaction that transfers an amino group to a keto acid to form new amino acids. This pathway is responsible for the deamination of most amino acids. These essential amino acids to nonessential amino acids. It is accomplished by enzymes called transaminase or aminotransferases. Using alanine as an example:

L-Alanine +∝-ketoglutarate $\xleftrightarrow{Alanine\ transaminase}$ Pyruvate + L-glutamate



56. Briefly explain the Baltimore classification of viruses.
    Classification is based on relationship of viral genome to its mRNA.
    Classified into 7 classes.
    I. Double stranded DNA viruses
    II. Single stranded DNA viruses
    III. Double stranded RNA viruses
    IV. (+) single stranded RNA viruses
    V. (-) single stranded RNA viruses
    VI. Single stranded RNA-RT (Reverse Transcriptase)
    VII. Double stranded DNA-RT

57. Discuss the biochemical and functional differences between the red skeletal muscles and the white skeletal muscles in humans.

PROPERTIES	RED(SLOW)	WHITE (FAST)

Contraction time (onset)	75 msec (slow)	25 msec(fast onset)
Contraction duration	Longer	Shorter
Diameter of muscle Fiber	Small	Large
Myosin ATpase activity	Low	High
Glycogen storage	Low	High
1° ATP source(metabolism)	Oxidative Phosphorylation	Glycolysis
Mitochondrial content	High	Low
Blood supply	High	Low
Fatigue	Slow to fatigue	Fast to fatigue

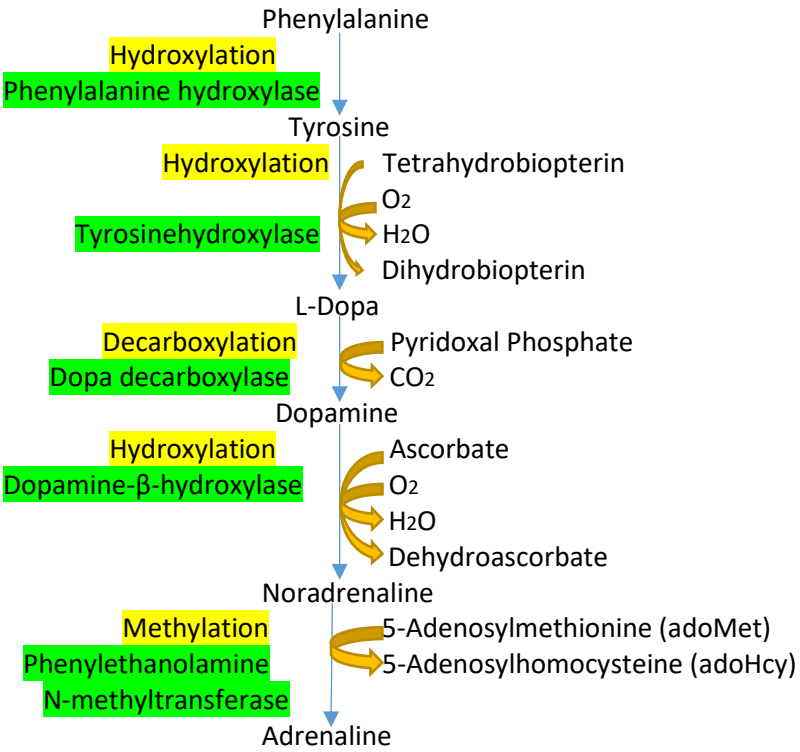
58. Answer the following;
    (a) List two infective stages of the plasmodium life cycle.
        - Sporozoites.
        - Merozoites.
    (b) The end product of glucose metabolism in bloodstream form of T. brucei is **glycerol & pyruvate** while the vector form of T. brucei is **succinate and acetate**.
    (c) Trichomonas vaginalis contain hydrogenosome which performs energy metabolism as **mitochondria** do in other protozoa and the major end product of this metabolism are hydrogen and **acetate, malate and carbon iv oxide**.
    (d) List two enzymes in folic acid synthesis that are targeted by chemotherapeutic agents in treatment of parasitic infections.
        - DHPS.
        - DHFR.
    (e) State the role of pentose phosphate pathways in parasitic protozoa.
        - Provides ribose sugars for nucleotide metabolism.
        - Provides NADPH for reductive biosynthesis (defends against ROS).
59. Answer the following;

(a) In control of gene regulation, DNA methylation inhibit transcription by?

(b) Describe the occurrence of inclusion cell disease and Zellwenger syndrome in relation to protein targeting.

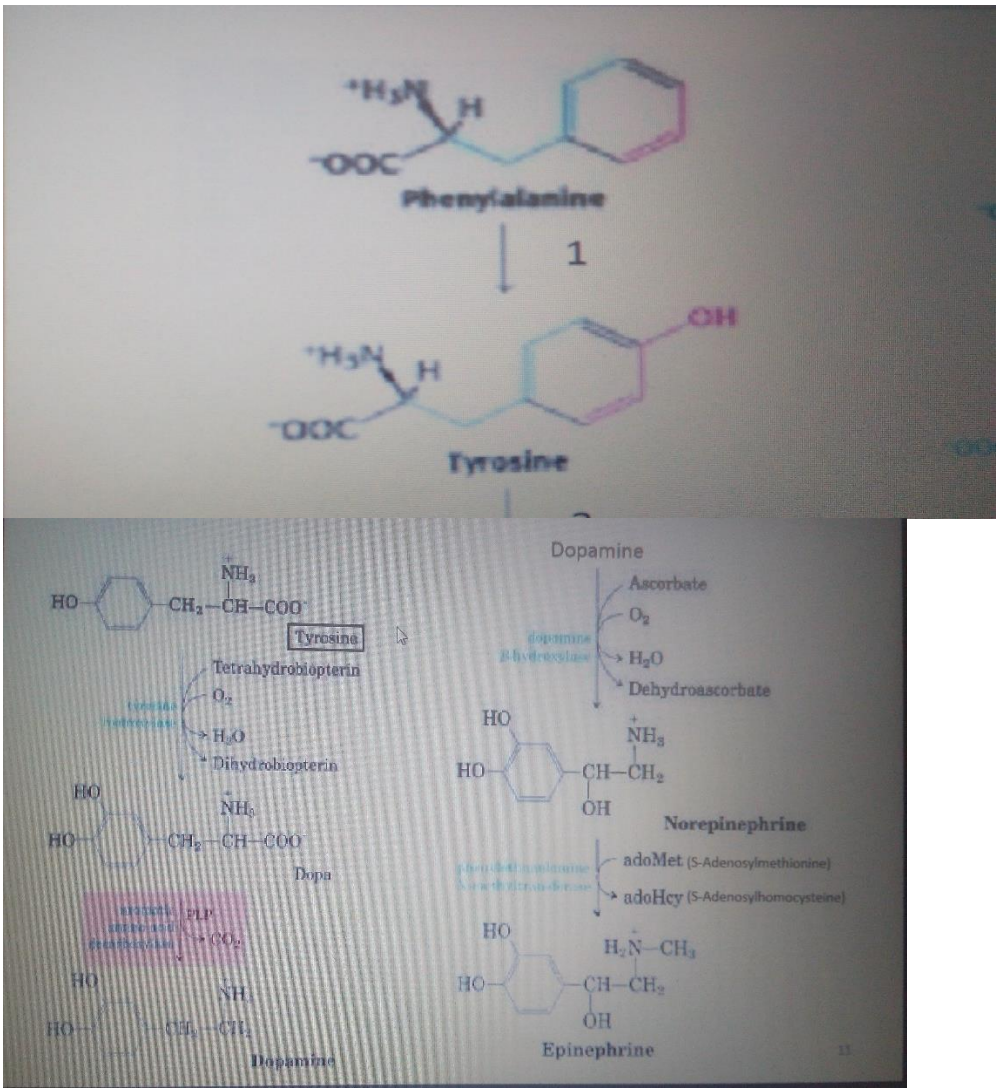
60. State five factors that distort the Mendelian inheritance ratio. (b) Explain why it is important to perform a test cross.
61. Outline the five major steps in biosynthesis of peptidoglycan.
62. (a) List the four phases of pharmacokinetics in their order.
    - Absorption.
    - Distribution.
    - Metabolism.
    - Excretion.

    (c) List six major modes of excretion of drugs.
    - Urine.
    - Faeces.
    - Sweat.
    - Breast milk.
    - Biliary.
    - Saliva
63. Describe the biosynthetic pathway of adrenaline from phenylalanine.



KEY

Green – Enzymes
Yellow – Processes



64. Describe the occurrence and causes of DNA mutation.
65. Outline five reasons why parasitic protozoa prefer anaerobic energy metabolism to aerobic metabolism.

Anaerobic parasitic protozoa are quite few those that have been studied, they include; *Giardia lamblia, Entamoeba histolytica, Trichomonadidae, Trichomonas vaginalis and Tritrichomonas foetus.*

i. Anaerobic parasitic protozoa do not have a mitochondria and hence rely on fermentative processes via an extended glycolytic pathway for ATP generation.
ii. Some attack/live in areas where there is reduced oxygen availability for instance GIT, reproductive tract

66. Outline five applications of bacteria in science and technology.

- Genetic Engineering. This is the manipulation of genes. The DNA revolution in which *Escherichia coli*, E. coli, was central in the theory as the first host of foreign DNA.
- Production of fuels and breaking down of wastes by bacteria that express a foreign fluorescent protein.
- Food Processing. The milk souring bacterium, *Lactobacillus bulgaris*, is used to make yoghurt and cheese. Bacteria are used to form organic acids in pickles and vinegar.
- Biotechnology. The use of microorganisms including bacteria and fungi in the manufacturing and service industries. Bacteria, in the chemical industries, is the most important in the production of pharmaceuticals.
- Fibre retting. Bacteria such as *Clostridium butyricum*, are used to separate fibres of jute, hemp and flax in the process of retting.
- Digestion. *Escerichia coli* that live in the human intestines synthesizes vitamin B and releases it for human use.
- Pest control. Bacteria can also be used in the place of pesticides in biological pest control. This is commonly uses *Bacillus thuringiensis*, BT, a Gram-positive, soil-dwelling bacterium. This bacterium is used as a Lepidopteran-specific insecticide under trade names such as Dipel and Thuricide. They are environmentally friendly due to specificity.

67. Outline five applications of polymerase chain reaction (PCR) on modern medicine.
68. Outline five factors that contribute to selective toxicity to chemotherapy in parasitic protozoa.
    (a) Metabolism
    (b) Excretion
    (c) Exposure rate
    (d) Distribution within the body
    (e) Dosage, especially dose-time relationship
    (f) Life stage such as infant, young adult or elderly adult.
    (g) Health of an individual including organ function and pregnancy, which involves physiological changes that could influence toxicity.
    (h) Presence of other chemicals, nutritional status.
69. Outline the three major reactions shared by branched chain amino acids degradation. (B) List the enzymes and co-factor involved in each reaction above.

Reactions	Enzymes	Co-factors
Oxidative decarboxylation	α-keto acid dehydrogenase	TPP, lipoamide,FAD
Transamination	Branched chain amino acid transaminase	
Dehydrogenation	Acyl co-A dehydrogenase	FAD

70. Outline the major diseases associated with the Krebs-Henseleit cycle and the enzymes involved.
71. Outline fates of amino acids in the amino acids pool.
72. Outline the effect of insulin and glucagon on the following

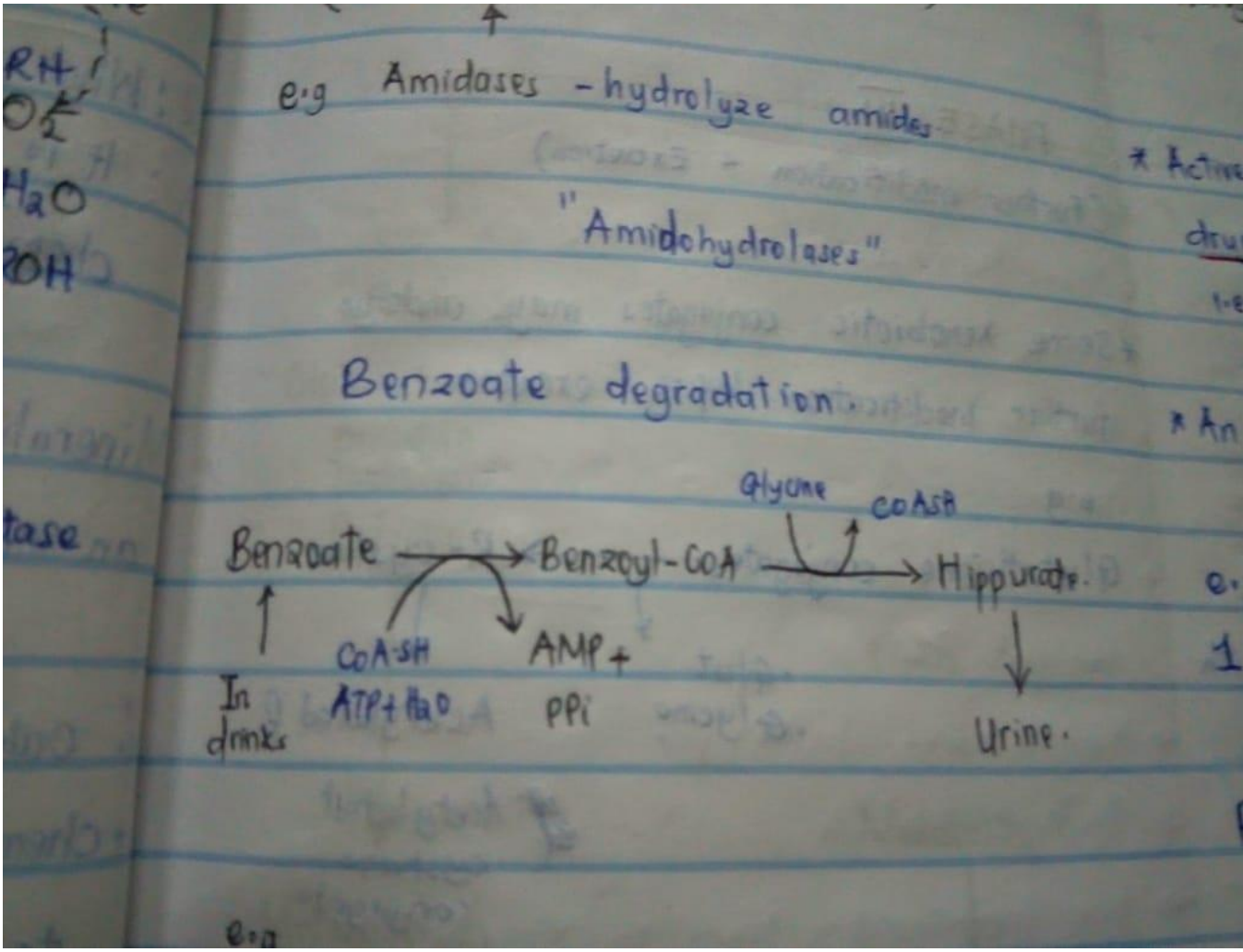
Metabolic action	Insulin	Glucagon
Glycogenolysis.		
Lipolysis		
Glycogenesis		
Ketogenesis		

Gluconeogenesis		
Amino acid uptake in the liver		
Glycogen synthase activity- Glycogen phosphorylase activity- Protein synthesis-		

73. (a) Briefly explain any 4 factors that are known to cause deviation from the normal Mendelian inheritance pattern. (b) Differentiate between euchromatin and heterochromatin.

74. **Describe how benzoate (found in cordial juices as preservative) is metabolized and excreted in humans.**

Metabolizing this compound by living organisms can ultimately make an active compound that reacts with DNA, changes the genetic structure of cells and has adverse effects on cell division. Sodium benzoate in the mitochondria of liver cells is metabolized by binding to amino acid glycine and later excreted as hippuric acid from the urine.



75. **Describe the mechanism of action of peptide hormone**.

Protein and peptide hormones, catecholamines like epinephrine, and eicosanoids such as prostaglandins find their receptors decorating the plasma membrane of target cells. Binding of

hormone to receptor initiates a series of events which leads to a generation of so called second messengers within the cell (the hormone is the first messenger).The second messenger the triggers a series of molecular interactions that alter the physiologic state of the cell. Another term for used to describe this entire process is **signal transduction**.

76. Describe the mechanism by which introns are removed from nuclear pre-mRNA
77. Explain how multiple mRNAs can arise from one pre-mRNA
78. **Differentiate between pathogenicity and virulence, briefly describe the mechanism of pathogenicity**

    Pathogenicity is the ability to cause disease by overcoming the defenses of the host while **Virulence**–the degree or extent of pathogenicity. Virulence factors –the various traits or features that allow or enhance the microorganism's ability to cause disease.

    MECHANISMS OF PATHOGENICITY

    1. PORTALS OF ENTRY

    To cause disease, most pathogenic bacteria must gain access to the host including skin and mucus membranes cuts, surgical procedures, catheters, etc. may allow bacteria entrance into the host

    2. PORTALS OF EXIT

    Many pathogens have preferred portals of entry that are necessary for disease production
    If they gain entrance via another portal, disease may not occur for instance; Salmonella typhi produces disease when swallowed but not if rubbed on the skin

    3. ADHERENCE.

    Means attachment. A necessary step in pathogenicity. Attachment between pathogen and host is accomplished by means of adhesins or ligands.

    4. INVASION

    • Once attached to target cells, many bacteria can then invade the cell. Not all bacteria are invasive. Invasive organisms attach and enter host cells by a number of mechanisms; Production of surface proteins called invasins or enzymes

    5. HOW BACTERIA DAMAGE HOST CELLS

    Direct damage or through the production of Toxins (Endotoxins or exotoxins). Toxins are not required for growth and genes for toxins are usually on plasmids

79. Interferons mediate anti-viral activity by three pathways;
    (a) List these three pathways
    (b) Describe how any two of these pathways bring about the antiviral activity.
80. Discuss post-transcriptional modification of mRNA
81. (a) Draw a diagram illustrating how retra-troposons move within genomes
    (b) define genomic imprinting (c) in human genome, name any three types of sequences that contributes to the non-coding DNA (d) LINEs mean?
82. Outline the functions of the following;

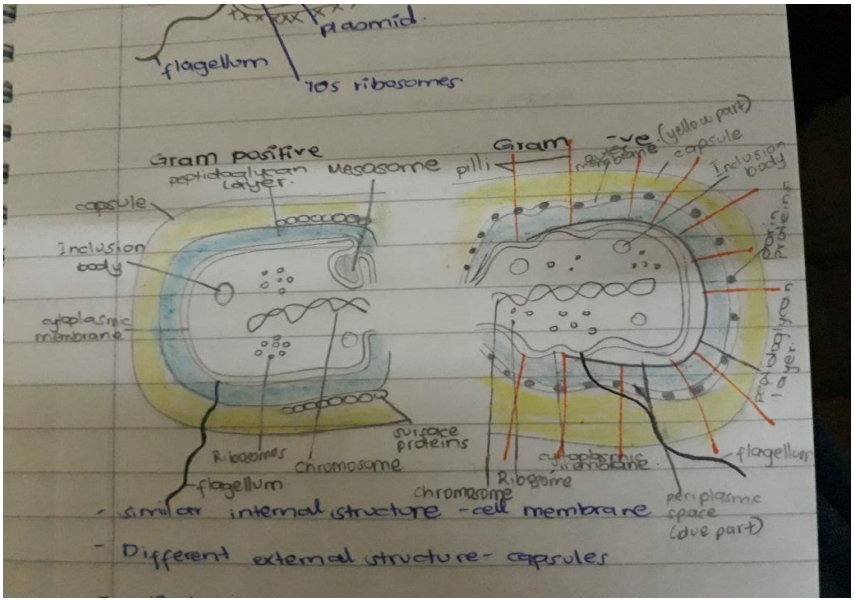
(a) RNA polymerase I
(b) RNA Polymerase II
(c) Taq polymerase
(d) Photolyase
(e) DNA ligase

83. **Based on your knowledge of bacterial Biochemistry;**

(a) Outline the components of a cell wall

-Peptido-glycan Polymer (amino acids + sugars)
•Sugars; NAG & NAM (N-acetylglucosamine, N-acetymuramic acid)
•D form of Amino acids used not L form (Hard to break down D form)
•Amino acids cross link NAG & NAM
-Lipoteichoic acid and teichoic acids
-Polysaccharides
-Lipopolysaccharides
-Lipoproteins

(b) List down the differences between gram positive and negative

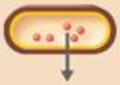


A comparison between Gram positive and Gram negative cell wall

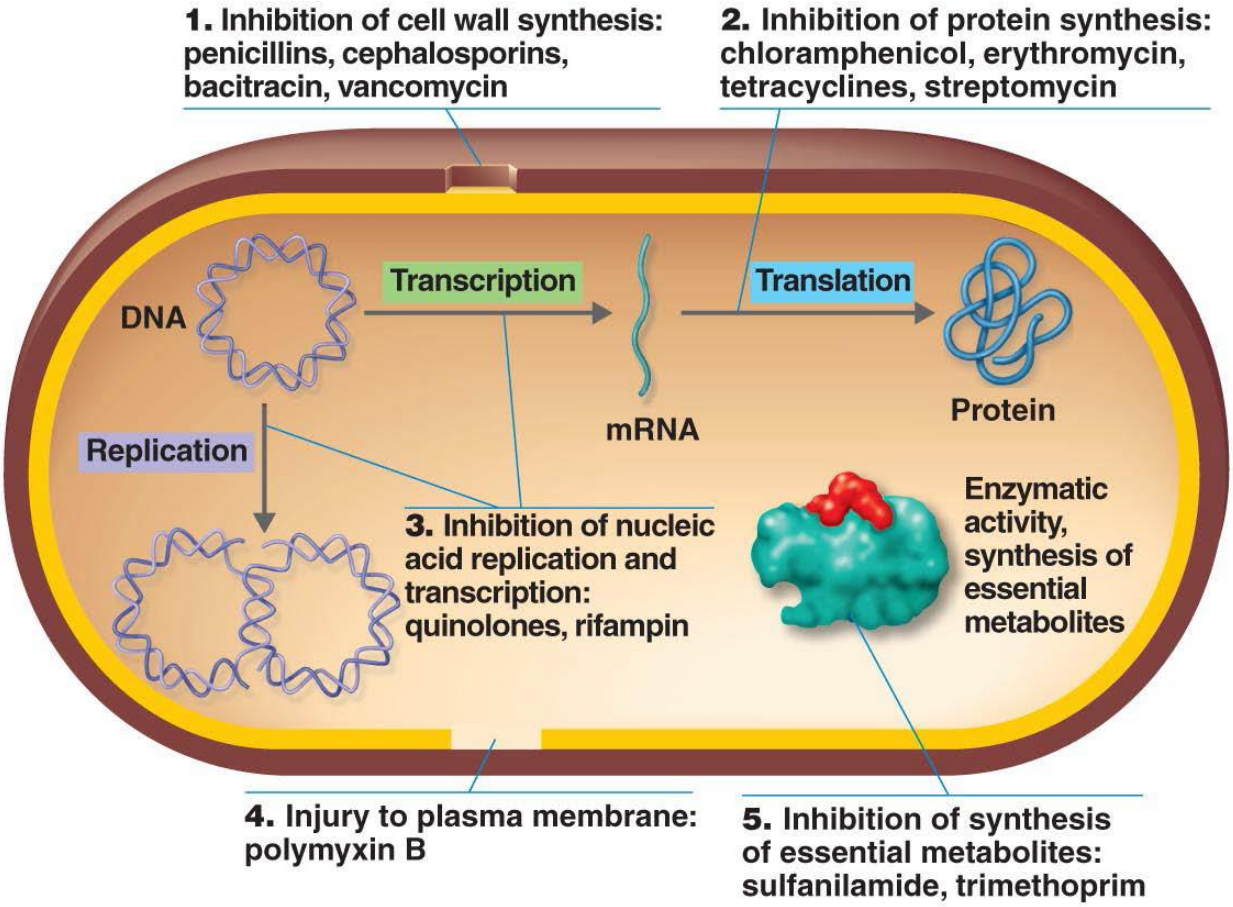
Item	Gram positive	Gram negative
Peptidoglycan layer	Thick (multilayered)	Thin (single-layered)
Teichoic acids	Present	Absent
Periplasmic space	Absent	present
Lipopolysaccharide (LPS) content	Virtually none	High
Lipid and lipoprotein content	Low	High
Resistance to physical disruption	Low	High
Inhibition by basic dyes	Low	High
Susceptibility to anionic detergents	Low	High
Resistance to drying	Low	High
Gram reaction	Retain crystal violet dye and stain dark violet	Can be decolorized to accept counter stain

(c) List down the differences between endotoxins and exotoxins

Table 15.3 Exotoxins and Endotoxins

Property	Exotoxin	Endotoxin
		
Bacterial Source	Mostly from gram-positive bacteria	Gram-negative bacteria
Relation to Microorganism	Metabolic product of growing cell	Present in LPS of outer membrane of cell wall and released with destruction of cell or during cell division
Chemistry	Proteins, usually with two parts (A-B)	Lipid portion (lipid A) of LPS of outer membrane (lipopolysaccharide).
Pharmacology (Effect on Body)	Specific for a particular cell structure or function in the host (mainly affects cell functions, nerves, and gastrointestinal tract)	General, such as fever, weaknesses, aches, and shock; all produce the same effects
Heat Stability	Unstable; can usually be destroyed at 60–80°C (except staphylococcal enterotoxin)	Stable; can withstand autoclaving (121°C for 1 hour)
Toxicity (Ability to Cause Disease)	High	Low
Fever-Producing	No	Yes
Immunology (Relation to Antibodies)	Can be converted to toxoids to immunize against toxin; neutralized by antitoxin	Not easily neutralized by antitoxin; therefore, effective toxoids cannot be made to immunize against toxin
Lethal Dose	Small	Considerably larger
Representative Diseases	Gas gangrene, tetanus, botulism, diphtheria, scarlet fever	Typhoid fever, urinary tract infections, and meningococcal meningitis

(d) Giving an example in each case, outline the various mechanisms of action of antimicrobial drugs.

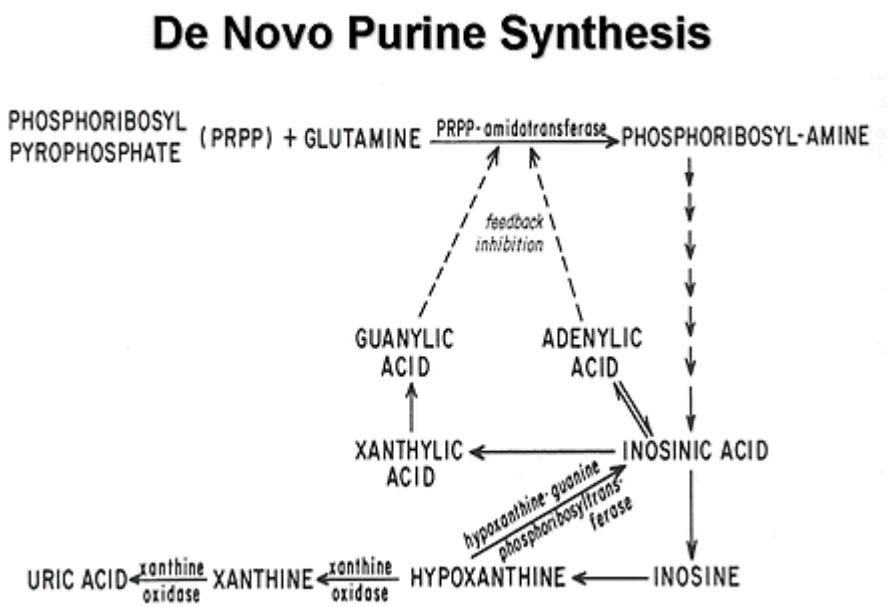


84. State five mechanisms of how an individual's genetic background can increase resistance to malarial infection in endemic areas.
85. State the Mendelian 1st and 2nd laws. State five factors that cause deviation from Mendel's original principle of inheritance.
86. With regards to protein biosynthesis, illustrate and name the components of an initiation complex. Mention the accessory factors involved in this step and their roles.
    (a) Briefly describe the three steps of the elongation cycle of protein biosynthesis with the enzymes involved.
    (b) Give any three inhibitors of prokaryotic protein biosynthesis and mention their mode of action.
87. **Distinguish between de novo and salvage biosynthesis and highlight two key differences between de novo purine and pyrimidine biosynthesis.**

    In De Novo pathways, the nucleotide bases are assembled from simpler compounds. The framework for a pyrimidine (= thymine and cytosine or uracil) base is assembled first and then attached to ribose. The framework for a purine (= adenine and guanine) base is synthesized piece by piece directly onto a ribose-based structure. **In salvage pathways**, preformed bases are recovered from nucleotide breakdown and reconnected to a ribose unit.

De Novo purine synthesis	De novo Pyrimidine synthesis
All enzymes are found in the cytosol	Only some of the enzymes are found in the cytosol
IMP serves as a common precursor of AMP and GMP.	UMP which serves as a common precursor
Pyrimidine ring is added later after formation of PRPP	The pyrimidine ring is formed first and then ribose 5-phosphate is added via PRPP
Synthesis takes place in the cytosol	Synthesis takes place in the cytosol and mitochondria

88. **Describe de novo purine biosynthesis in humans and highlight on the regulation of different pathways; whether activation or feedback inhibition.**



Feedback inhibition of de novo pathway occurs from the products of salvage pathway.

89. **Describe in detail the active methyl cycle (methionine cycle).**
90. Identify three key differences between DNA replication and transcription. Highlight on the supramolecular assembly in which proteins are synthesized.
91. Outline five features that enhance microorganism's ability to cause diseases.
92. **Attempt the following;**
    (a) List two genetic factors that promote gout.
    •**Increased PRPP synthetase activity**: results in increased intracellular levels of PRPP.
    •**Partial decrease in HGPRTase activity**; Since there is decreased salvage of hypoxanthine and guanine, PRPP is not consumed by the HGPRTase reaction and PRPP can activate glutamine–PRPP amidotransferase activity. With decreased salvage of hypoxanthine and

guanine, IMP and GMP are not formed via this pathway so that regulation of the PRPP amidotransferase step by IMP and GMP as negative effectors is compromised.

•**Glucose 6phosphatase deficiency**. Loss of glucose 6phosphatase activity results in more glucose 6phosphate being shunted to the HMP shunt. Hence more ribose 5phosphate is generated and the intracellular level of PRPP is increased.

(b) **What causes neurological disorder in Lesch-Nyhan? -** In the brain, lack of HGPRTase could lead to decreased levels of intracellular GTP due to decreased salvage of guanine. Since GTP is a precursor of tetrahydrobiopterin, a required cofactor in the biosynthesis of neurotransmitters, low levels of GTP during development could be the triggering factor in the observed neurological manifestations.

(c) **What is the role of folic acid in deoxythymidilate synthesis?** Folic acid (N5,N10 methylene tetrahydrofolate) is used to donate a one carbon unit to 2 deoxyuridine 5 monophosphate (dUMP) and simultaneously reduced to a methyl group to form Deoxythymidylate (dTMP).

(d) List two amino acids required in pyrimidine synthesis.- glutamine, glycine and aspartate

(e) Azaserine is a powerful inhibitor of glutamine amidotransferases. If growing cells are treated with azaserine, what intermediates of nucleotide biosynthesis will accumulate? Explain. - 5-phosphoribosyl-1-pyrophosphate (PRPP) will accumulate. This is because glutamine amidotransferases catalyse the transamination of glutamine to PRPP to form 5-phosphoribosylamine.

93. **Describe in detail the process of DNA replication.**

The synthesis of a DNA molecule can be divided into three stages: initiation, elongation, and termination, distinguished both by the reactions taking place and by the enzymes required.

Initiation of replication

•The initiation of DNA replication occurs at specific points called origins of replication (e.g. OriC in E. coli). Once DNA synthesis has been initiated, two replication forks, extending in either direction from the origin of replication, proceed to allow the full replication of the genome. OriC is the binding site of proteins DNA A, B and C that promote the melting (opening) of the DNA helix, a process that is essential so that DNA replicating enzymes can read the base sequence. The polymerase can only function if a free 3OH group is present. This hydroxyl group is provided by an RNA primer (which is complementary to the DNA) that is 5–15 nucleotides long. The synthesis of the primer is directed by a form of RNA polymerase (called primase). DNA is unwound into the polymerase complex with the help of DNA helicases. Topoisomerase enzymes (e.g. DNA gyrase) are required to relieve tension in the helix that results as a consequence of the unwinding process. Single-stranded DNA produced during replication are stabilized through the binding of single-stranded binding proteins (SSBs)

Elongation

•The elongation phase of replication includes two distinct but related operations: leading strand synthesis and lagging strand synthesis. Leading strand synthesis begins with the synthesis by primase of a short (10 to 60 nucleotide) RNA primer at the replication origin. Deoxyribonucleotides are added to this primer by a DNA polymerase III. Leading strand synthesis then proceeds continuously, keeping pace with the unwinding of DNA at the replication fork. The lagging strand is formed so that nucleotide polymerization can occur on both template strands in a 5'to 3'direction. DNA ligase is then required to join the phosphodiester backbone of the Okazaki fragments to form a complete strand.

DNA synthesis on the leading and lagging strand
(a) At intervals, primase synthesizes an RNA primer for a new Okazaki fragment.
(b)Each primer is extended by DNA polymerase lll.
(c)DNA synthesis continues until the fragment extends as far as the primer of the previously added Okazaki fragment a new primer is synthesized near the replication fork to begin the process again. The synthesis of DNA fragment on lagging strand.
Each RNA primer is ~ 10 nucleotides. This primer is removed by a special DNA repair enzyme, RNAse H that recognises an RNA strand in RNA/DNA hybrid and cleaves it. The gaps are filled in by DNA Polymerase and DNA ligase. DNA polymerase has a 3'-5' proofreading exonuclease activity
Termination
•Termination occurs at defined DNA sequences (called terminator sequences) that act as binding sites for a protein called Tus (terminus utilization substance). The Tus-Ter complex can arrest a replication fork from only one direction.

94. A gene is made up of the following nucleotide sequence;
    Coding strand; GCC-AGT-CGA-ATG-CTA
    Anti-sense strand; CGG-TCA-GCT-TAC-GAT
    (a) Write down the mRNA sequence clearly showing its 5' and 3' ends.
95. Given the DNA duplex below;
    3' ATGACTCTCTAGTCCAT- sense strand
    5' TACTGAGAGATCAGGTA- anti-sense strand
    (a) Write the sequence of the mRNA
    (b) Write all the base sequences of the first three anticodons of the cognate tRNA
96. **Using a diagram differentiate between the structures of Gram positive and negative bacteria**

TRIBUTE TO THE LATE PROFFESOR HASSAN SAIDI

PROF. SAIDI WAS A CELEBRATED GENERAL AND LAPARASCOPIC SURGEON AT KENYATTA NATIONAL HOSPITAL AND AGA KHAN HOSPITALS, A FELLOW OF THE AMERICAN COLEGE OF SURGEONS AND MEMBER OF THE KENYA MEDICAL ASSOCIATION. CHAIRMAN DEPARTMENT OF HUMAN ANATOMY, PRESIDENT SURGICAL SOCIETY OF KENYA, EDITOR IN CHIEF OF THE ANNALS OF AFRICAN SURGERY JOURNAL, ASSOCIATE DEAN SCHOOL OF MEDICINE UNIVERSITY OF NAIROBI, BOARD CHAIR NARIOBI SURGICAL SKILLS CENTRE.

We celebrate his life legacy for being an excellent teacher of Anatomy, with a thirty-year experience in instruction and teaching Human Anatomy at the University of Nairobi, Aga Khan University Nairobi and University of Pennsylvania. He has mastery of Embryology, Gross Anatomy, Histology and molecular biology, with surgical anatomy as his pet subject. Having taught over 4000 undergraduate medical students, supervised over 40 B.Sc. Anatomy students, 30 Master of Medicine Surgery students, and 4 Master of Anatomy students. He mentored many renowned surgeons, doctors and clinical officers.

Prof. Hassan Saidi was able to publish over 60 high impact peer reviewed articles in local and international journals. His research activity focused on clinical anatomy in all its aspects, trauma, oncology and surgery of the digestive tract. He published a book on histology and was in the process of publishing a text book of Surgical Anatomy. Prof. Hassan Saidi held many leadership roles in the University of Nairobi, initially as a course coordinator and rising to become the chairman of thematic areas within the department. He was the substantive Chairman of the Department of Human Anatomy until the time of his death. Prof. Hassan Saidi was also the associate dean, Preclinical departments of the University of Nairobi. During his tenure as a chairman, he shepherded the establishment of the Nairobi Surgical Skills Centre, publication of the Kimani's Histology Text and Atlas, Establishment of the Anatomy Journal of Africa, supported staff development, training and promotion as well as supporting many local and international staff retreats.

Prof Hassan indeed had many friends. He definitely did not know all of them, but yet he would never deny any genuine person seeking assistance. Taking time to engage with different age groups and this he did effortlessly. An opportunity to watch football, play some basketball or just have a 'chat' (always very insightful and refreshing) over some coffee snack was a sought-after opportunity by many. In his 36hr day, he would still find time to call up and catch up with his friends, his objective to savour every moment with friends to improve them in one way or another. What better HE WAS!

Prof. Hassan Saidi was married, with three sons. He was actively involved in charity and volunteer activities through HAIBA foundation and other charity groups. He was a mentor, a great teacher, researcher and a surgeon.He surely fought a good fight and finished the race. He will be missed by many but his legacy lives on forever in our hearts and lives, till always and forever!!!

TRIBUTE TO THE LATE PROFFESOR HASSAN SAIDI

WHAT ARE YOU DOING TO EMULATE THE KIND OF LIFE PROF. SAIDI LIVED? IN ALL THE ABOVE CITED ACHIEVEMENTS, AND THE IMPACT HE GENERATED IN ALL WALKS OF LIFE, DO YOU THINK IT'S POSSIBLE TO LEAVE A TRAIL OF THE SAME MAGNITUDE OF EXQUISITION?

YES IT IS! START WITHIN YOUR SPHERE OF INFLUENCE. LOOK FOR A WAY TO BLESS AND MOULD YOUR FELLOW MEDICS. STUDY MEDICINE WITH PASSION, TRANSFORMATIVE PURPOSE AND PURSUE EXCELLENCE WITH DISTINCTIONS IN ALL YOU DO. ABOVE IT ALL, PURSUE GOD WITH ALL OF YOUR BEING, WHILE PLUGGING INTO HIS SOURCE TO HELP YOU ACHIEVE IT ALL IN KEEPING PROF. SAIDI'S LEGACY ALIVE!!!

ALL THE BEST IN YOUR STUDIES AND UPCOMING EXAMS AS GOD LEADS YOU INTO THE GREAT DOCTORS HE ORCHESTRATED YOU TO BE!!!

WHERE GOD LEADS, HE PROVIDES. WHERE HE GUIDES, HIS GRACE IS SUFFICIENT!