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Applied Microbiology and Infection Control & Safety

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Section Outline

PART I

APPLIED MICROBIOLOGY

CHAPTER 1

Introduction to Microbiology

CONCEPTUAL THEORY

Terminology

Fermentation: A process which involves conversion of carbohydrate into alcohol or other organic acids with release of carbon dioxide, under the anaerobic conditions, by the action of yeast or bacteria.
Genus: A group of organisms with similar features.
Species: Subdivision of a genus including identical organisms.
Spontaneous generation: A hypothesis saying that living organisms arise spontaneously from non-living matter.

INTRODUCTION TO MICROBIOLOGY

- Microbiology is the study of living organisms of microscopic size.
- The term "Microbiology" was introduced by French chemist Louis Pasteur.

HISTORICAL PERSPECTIVE

Antony van Leeuwenhoek	• Antony van Leeuwenhoek is known as Father of Microbiology. • Invented simple microscope
Louis Pasteur	• Developed vaccines against cholera, anthrax, and rabies. • Coined the term "Microbiology" and "Vaccine" • Proposed germ theory of disease • Introduced pasteurization to prevent souring of wine • Introduced sterilization techniques such as hot air oven and autoclave • Discovered microorganisms such as *Staphylococcus, Streptococcus* and *Pneumococcus.*
Edward Jenner	• Discovered the small pox vaccine • Known as Father of Immunology
John Needham	Supported and put forth the theory of spontaneous generation
Robert Koch	• Father of Bacteriology • Developed hanging drop method • Suggested Koch postulates
Paul Ehrlich	• Father of chemotherapy • Proposed " side chain theory " of antibody production
Selman Waksman	Coined the term "antibiotic" and developed "streptomycin"
Joseph Lister	• Marked the use of carbolic acid as an aerosol during surgery • Formulated the guiding principle of antisepsis for good surgical practice • Regarded as the Father of Modern Antiseptic Surgery

Contd...

PRINCIPLES OF MICROBIOLOGY

- Robert Koch was a German physician well known for his contributions to the field of medical techniques, and is called Father of Microbial Techniques and Father of Medical Microbiology.
- **Contributions of Robert Koch**
  - Robert Koch brought perfection in bacteriological techniques, *staining methods*, *pure culture techniques*, use of *solid media to culture* microorganisms.

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- **Koch's Postulates:** Koch's postulates serve as a guideline to prove a relationship between the disease and the causative organism.
  - **Postulate I—Association:** The microorganism must be present in the body of suffering animal and should not be found in healthy animal. A particular microorganism should be associated with a particular disease.
  - **Postulate II—Isolation:** The causative organism must be isolated from the body of diseased animal. This isolated organism must be cultured in laboratory to get a *pure culture*. Its growth characteristics and biochemical characteristics must be noted down.
  - **Postulate III—Inoculation:** The isolated organism from pure culture *must produce similar disease* in a healthy laboratory animal.
  - **Postulate IV—Reisolation:** The microorganism must be reisolated from the inoculated laboratory animal and identified as causative microorganism. The reisolated microorganism must show the same growth and biochemical characteristics as recorded in second step.
- **Limitations of Koch's Postulates:**
  - Not applicable to viruses, fungi, parasites.
  - Inability to study virus-induced illnesses because they were not easy to cultivate in lab.
- **Modern Concepts of Koch's Postulates:**
  - These are based on the nucleic acid of the pathogenic organism and say:
    - The nucleic acid must be present in diseased organ when anatomically observed.
    - The nucleic acid sequence of a pathogen should establish association with disease.
    - The results obtained from nucleic acid sequences must be reproducible in other labs.
    - Koch brought perfection in bacteriological techniques, heat fixing of the smear, staining methods, pure culture techniques, use of solid media to culture microorganisms.
    - He isolated anthrax bacillus (1876), *Mycobacterium tuberculosis* (1882) and *Vibrio cholerae* (1883).
    - He introduced tuberculin test which is a hypersensitivity reaction.

MICROBIOLOGY IN NURSING

During the interaction of a nurse with patient, knowledge of microbiology helps a nurse:

- To know how to handle a patient, clinical samples, and belongings without infecting oneself.
- To sterilize instruments such as metal instruments, surgical knives, blades, scissors, and needles, boiling at high temperature for sufficient time is enough.
- To use antiseptics to minimize septic conditions.
- To apply universal hand washing technique as fundamental principle to reduce/remove the load of microorganisms and prevent transmission of hospital-acquired infections.
- In diagnostic laboratory, where immunological and serological tests, hypersensitivity tests, blood grouping and antibiotic sensitivity tests aim at targeted treatment.
- To follow sterilization processes and aseptic procedures in OTs and minor.
- To successfully conduct mass immunization by following all precautions and guidelines of immunology and microbiology.
- To follow biomedical waste management system according to the principles of microbiology.

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CONCEPTUAL EXERCISES

LONG ANSWER QUESTIONS

1. What are the principles of microbiology in nursing? *(DU, RUHS, MGR)*

Answer

- **Development of microbiology as a scientific discipline:** Microbiology developed as an independent scientific discipline after the collective efforts made by scientists such as Leeuwenhoek, Pasteur, Koch, Lister and others to name a few. Starting with animalcule to aerobic and anaerobic and then to viruses and further to immunization, it all helped to evolve microbiology as an independent discipline.
- **Methods for studying microorganisms:** Discovery of various organisms and their association with different diseases made it necessary to develop new drugs and for this the microbial structure and its behavior is studied. Different techniques are used for this such as microbial physiology, cellular metabolism, molecular biology, microbial genetics, replication, growth, etc. The methods to identify the organisms were developed as a need such

as staining techniques, culture methods, and biochemical methods to identify the microorganisms, and microscopy too got advanced.

- **Control of microbial growth:**
  - The opportunistic pathogens, and fungi, etc. need to be controlled in the healthcare environment to protect the clients and healthcare personnel from the harms of these pathogen. For this sterilization of equipment and tools, devices like autoclave and hot air oven are used. Besides, radiations and ultrasonic waves; the methods to conduct procedures under aseptic ways; use of personal protective equipment following universal guidelines; use of disinfectants to keep control on the load of microorganisms in a hospital such as using formaldehyde vapors to sterilize operation theater are also used. Universal hand washing technique followed by all nurses is based on the fundamental principle of microbiology as hand washing reduces/removes the load of microorganisms and prevents transmission of hospital-acquired infections too. Using antiseptic ointments or liquids minimizes septic conditions that may be caused due to growth of microorganisms in the wounds.
  - The aseptic procedures followed in operation theaters and minor OTs are based on the principles of sterilization—both gaseous and liquid states of sterilizing agents are used in this process.
- **Clinical diagnosis:** Medical microbiology is mainly concerned with etiology, pathogenesis, lab diagnosis and treatment of infection along with the epidemiology and control of infection in the community. In order to manage a bacterial infection in a patient, first step is to establish a *clinical diagnosis* then the causative agent of the disease is isolated from the clinical sample. The antibiotic susceptibility test is determined in lab to give specific treatment before giving appropriate antibiotic. The whole therapeutic strategy is monitored. If antibiotic therapy is not successful then antimicrobial agents are observed in body fluids. Confirmation of bacterial cure is indicated by disappearing of signs and symptoms of the disease. Different blood groups are also identified in labs based on the knowledge of immunology, which is a necessary task before blood transfusion. Hypersensitivity reactions like Mantoux test is used to check tuberculosis.
- **Sterilization:** Water is sufficient to kill microorganisms when boiled to high temperature. This knowledge is applied to sterilize instruments in hospitals like metal instruments, surgical knives and blades, scissors and needles.
- **Biomedical waste management:** Biomedical waste management is necessary part of the hospital. Collection, segregation, transportation and disposal of biomedical waste are based on the principles of microbiology.
- **Immunology concept:**
  - **Immunological tests:** The knowledge about reactions between specific antigens and antibodies is fundamental for the tests like Radioimmunoassay (RIA), Complement Fixation Test (CFT), Enzyme-Linked Immunosorbent Assay (ELISA), and immunodiffusion and agglutination reactions—these tests are useful in diagnostic labs.
  - **Immunization programs:** The mass immunization programs are based on the knowledge of microbiology and immunology. These immunization drives have helped in eradicating dreadful diseases like smallpox and providing protection for diseases like mumps, hepatitis, diphtheria, etc.

2. Write about the contributions of Louis Pasteur to Microbiology. *(RUHS, MGR)*

Answer

Contributions of Louis Pasteur to Microbiology

- Pasteur is called the progenitor of modern immunology.
- His discoveries are substantiated as foundations for microbiology and immunology.
- He performed a series of experiments to prove that the solutions could be made free of microorganisms by boiling. If no air is left to come in contact with solutions, there is no emergence of microbial life.

Rejected the Theory of Spontaneous Generation

Swan neck experiment: Pasteur took broth in long necked flask and softened the neck of flask under the flame and molded it in the shape of a swan neck. Broth was boiled until steaming and then cooled. This solution of broth did not show growth of microorganisms when kept for long periods because the microbes were not able to reach the broth. This further rejected the theory of spontaneous generation. The microbes could not enter the broth due to peculiar shape of the neck of flask. This experiment supported germ theory of disease.

Pasteurization

Pasteurization involves moderate heat treatments of the product to kill microorganisms. This process is now backbone of wine industry. Nowadays, pasteurization is widely used in milk industry, food and beverage industries. The pasteurization process is based on the use of one of the following time and temperature relationships.

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- **High temperature short treatment (HTST):** This process uses higher heat for less time to kill pathogenic bacteria, e.g., milk is pasteurized at 161°F (72°C) for 15 seconds. HTST causes less damage to the nutrient composition and sensory characteristics of food as compared to low temperature long treatment (LTLT).
- **Low temperature long treatment (LTLT):** This process uses lower temperature for a longer time to kill pathogenic bacteria. For example, *milk* is pasteurized by this method by exposing it to 145°F (63°C) for 30 minutes.
- **Flash pasteurization:** In order to pasteurize food, 'Flash pasteurization' method is used. It involves HTST in which *pourable products* like juices are heated for 3–15 seconds at a temperature of 74°C which destroys harmful microorganisms. After heating, the product is cooled and packed. Most drink boxes and pouches are pasteurized in this way because it allows *extended unrefrigerated storage*.
- **Steam pasteurization:** This technology uses heat to control or reduce harmful microorganisms in *beef/meat*. Beef is exposed to pressurized steam for approximately 6–8 seconds. The steam raises the surface temperature of beef to 191°–200°F (88°–93°C). The carcasses are then cooled with a cold water spray. This process kills microorganisms like *Escherichia coli, Salmonella* and *Listeria.*
- **Irradiation pasteurization:** *Poultry products, red meat, spices, fruits and vegetables* are all subjected to small amounts of gamma rays. This process effectively kills vegetative bacteria and parasitic food-borne pathogens. Shelf life of food items is also increased.

Cause of Fermentation

- Pasteur discovered that fermentation of a substrate is caused by microorganisms.
- He found that there was a gray material growth in the substrate used for manufacturing alcohol. This microorganism growing in alcoholic product was the cause of souring of wine.

Pasteur Effect—Aerobic and Anaerobic

- While studying involvement of specific organisms in fermentation, Pasteur discovered that the fermentation process could be arrested by passing air or oxygen known as Pasteur Effect.
- He concluded that the reason for this was that presence or absence of oxygen affects the existence of microorganisms.
- He used the terms like *aerobic* for those organisms that can live in the presence of oxygen and *anaerobic* for those organisms that prefer to live in the absence of oxygen.
- He further suggested that putrefaction was due to the growth of anaerobic microorganisms.

Vaccines

He introduced attenuate live vaccines for prophylactic use. He developed vaccines against pox (Pasteurella now), anthrax and rabies, which were very deadly diseases at that time. Later, he applied this principle of attenuation to other diseases too to introduce immunization. First Rabies vaccination was introduced by Pasteur in 1885.

Discovered Causative Microorganisms and Isolated Them

Pasteur Discovered

- Silkworm disease known as pébrine and isolated the causative microorganisms of this disease.
- He discovered Staphylococcus, Streptococcus and Pneumococcus.
- He isolated microorganisms responsible for cholera and rabies. He demonstrated that the causative agents of these diseases were too small to be seen through microscope and it could pass through filters. Later on this filterable agent of disease was known as virus.

Molecular Asymmetry

- Pasteur tried to find the answer to the discovery by German chemist Eilhardt that tartrates rotated the plane of polarized light, whereas paratartrates did not, although both have identical chemical properties.
- Pasteur noted that tartrate crystals had asymmetric forms and that was the reason for this before-mentioned behavior. This discovery proved as foundation of stereochemistry.

Sterilization Techniques

- He introduced sterilization techniques and developed steam sterilization method, hot air oven and autoclave. These methods are backbone of the sterilization techniques and are widely used in healthcare industry, food and beverage industry.
- He suggested methods to control cross infections in hospitals.

3. Discuss the process of replication of virus. *(DU)*

Answer

- Viruses multiply in the host cells and totally depend on the host cell's biochemical machinery for replication and they have complete genetic information but the necessary enzymes are absent.

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- The viral components are made in host cell and after assembly released from the host cell.
- The whole process of viral replication can be divided into the following five phases:

1. **Adsorption:** The viruses adhere to a host cell. For this, they come in contact with cell by random collision and get attached to the cell with the help of specific receptors located on the surface of host cell. The viruses have ligands that recognize these receptors.
2. **Penetration:** The viruses enter the cells by different mechanisms depending on the type of host cell. In case of bacteria, the bacteriophage is unable to penetrate it. The reason lies in the special composition of bacterial cell wall and its rigidity. The virus introduces only its nucleic acid into the bacterial cell. The animal and human cells have no cell walls so whole viral particle penetrates the cell by a process known as *viropexis.* When the enveloped viruses penetrate a host cell, the envelope fuses with the cell membrane of host cell and nucleocapsid is released into the cytoplasm of host cell.
3. **Uncoating:** Under this process, viral capsid of a virus is removed, leading to the relegated of the viral genomic nucleic acid into the cells. In uncoating, the lysosomal enzymes secreted by the host cell and proteolytic enzymes secreted by the virus help in this process. In the end, the viral nucleic acid is released into the cell.
4. **Biosynthesis:** Viral nucleic acid and capsid are synthesized during this phase. Enzymes and regulatory proteins needed in the various stages of the replication are also synthesized. The regulatory proteins shut down the normal metabolism of the cell and direct it to produce the viral components. With the exception of poxviruses, DNA viruses synthesize nucleic acid in the nucleus of host cell and other components are synthesized in host cell cytoplasm.

   RNA viruses synthesize their components in host cell cytoplasm with an exception of orthomyxoviruses and a few paramyxoviruses which synthesize some components in host cell nucleus.

   In a nutshell, the whole phase of biosynthesis can be compiled as:
   - Transcription of early messenger RNA from the viral nucleic acid. This gets transported into the cytoplasm and early proteins are synthesized.
   - Translation of mRNA into early (nonstructural) proteins that are necessary for synthesizing viral components.
   - Early proteins help in making viral DNA too, so are transported back to nucleus and synthesize many copies of viral DNA.
   - Viral DNA now acts as template and viral nucleic acid replicates.
   - Early mRNA is transcripted into late mRNA and is transported back into the cytoplasm for translation into late proteins.
   - Late (structural) proteins are synthesized. These are the components of daughter virion capsids. The late proteins are then transported back into the nucleus.
5. **Assembly:** After the replication of viral proteins, nucleic acids and other parts or assembly of components occur in the cytoplasm or nucleus of the host cell.

   Picornaviruses and poxviruses are assembled in nucleus whereas herpesviruses and adenoviruses are assembled in cytoplasm.

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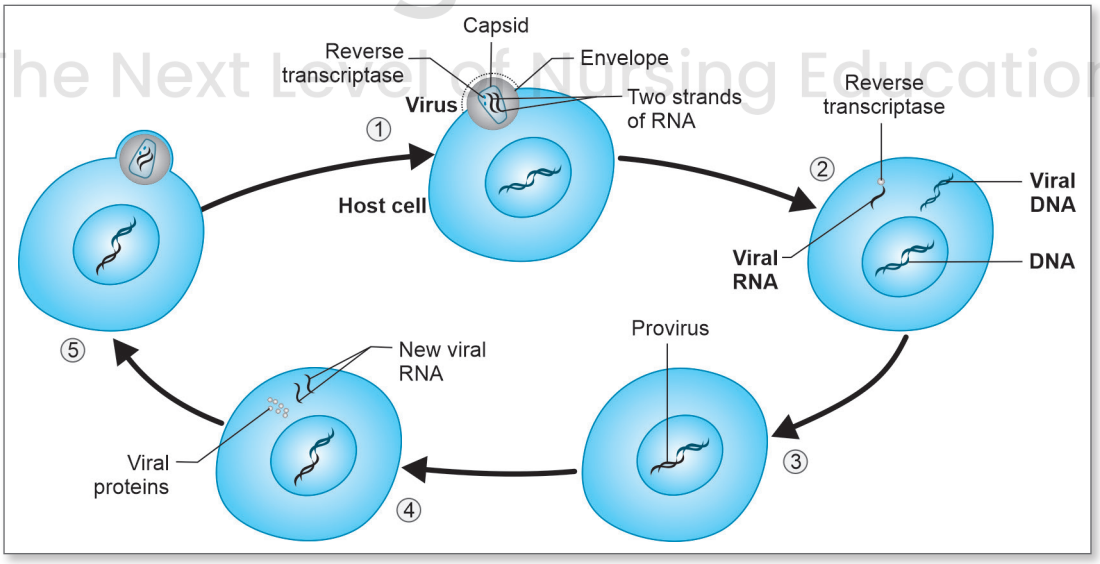

Figure 1.1: Replication of viruses

SHORT NOTES

1. Write a note on barrier nursing. *(DU)*

Answer

Barrier nursing is a term that is used for a set of stringent infection control techniques used in nursing.

Uses

It helps:

- To address highly contagious diseases.
- To manage diseases which have no existing cure.
- To create a barrier to isolate contagious patient.
- To protect other patients and medical personnel from getting infected.

Each of the following points given below briefly.

- Personal Protective Equipment (PPE)
- Hand Hygiene
- Aseptic techniques
- Isolation
- Biomedical waste disposal
- Cleaning and disinfection
- Signage and education
- Staff health check
- Risk assessment
- Linen handling
- Spill management
- Restricting visitors

Risk Management

- Routine care = Minimal risk
- Low risk requires gloves and plastic apron.
- For high risk contact, splash of body fluid specimens, waste disposal, wear gloves, mask, apron, eye protection.

2. Write a note on use of terminology. *(MGR)*

Answer

Use of Terminology in Microbiology

Clear and precise terminology is crucial in microbiology to ensure effective communication, accurate understanding, and consistency in research, clinical practice, and education. Some key considerations for using terminology in microbiology includes the following:

Standardization: Microbiology relies on standardized terminology to facilitate communication among researchers, healthcare professionals, and educators. Standardized terminology ensures consistency and clarity in describing microorganisms, microbial processes, and related concepts.

Taxonomy and nomenclature: Microorganisms are classified based on taxonomy, which involves organizing them into hierarchical categories such as domain, kingdom, phylum, class, order, family, genus, and species. The nomenclature system, governed by international bodies like the International Committee on Systematics of Prokaryotes (ICSP), assigns scientific names to microorganisms following standardized rules (e.g., binomial nomenclature).

Specificity: Microbiological terminology should be specific and unambiguous, avoiding vague or misleading terms. Precise terminology helps accurately describe microbial characteristics, behaviors, interactions, and clinical manifestations.

Avoidance of jargon: While microbiology has its specialized vocabulary, excessive use of technical jargon can hinder understanding, especially for non-experts. Clear explanations and definitions should accompany technical terms to facilitate comprehension.

Contextualization: Terminology should be used in the appropriate context, considering factors such as microbial diversity, pathogenicity, and host-microbe interactions. Contextual understanding enhances the accurate interpretation and application of microbiological concepts.

Education and communication: Effective teaching and communication in microbiology require the use of terminology that is accessible to learners and relevant to the audience's level of expertise. Providing clear definitions, examples, and illustrations can aid comprehension and retention of microbiological concepts.

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3. Write about contributions of Robert Koch. *(MGR)*

Answer

Contributions of Robert Koch

Robert Koch has contributed in various ways to the field of microbiology. Some of these are mentioned here:

- Before Koch, it was emphasized that the disease begins spontaneously. With his experiments, he *proved the germ theory of disease* and explained that disease is not due to curse but it originates from germs.
- His four postulates are a guideline when an association between disease and causative microorganism is to be established.
- In order to study morphology of an organism, he introduced *staining techniques*.

- Nowadays, we all are familiar with *heat fixing of the smear* before staining. This was also introduced by Koch.
- He introduced the dyes for staining microorganisms like *aniline dyes* which are easy to work with, fast to act and give good results.
- Technique to obtain *pure cultures* of microorganism was developed by him.
- Agar is used in many European dishes as a solidifying agent from a long time. Koch was first to use agar as solidifier in culture media. This facilitated a scientist to observe colonial morphology of an organism when grown in labs.
- He introduced a skin test for diagnosing tuberculosis which is a hypersensitivity reaction.

4. Write a short note on Louis Pasteur. *(RUHS)*

Answer

In 1856, Pasteur was called by wine makers of Lille to investigate the cause of souring of alcohol being produced. He investigated and found that there was a gray material growth in the substrate used for manufacturing alcohol. This microorganism growing in alcoholic product was the cause of souring of wine. He found that these undesirable microorganisms could be killed by heating the wine at 50°–60°C for a short period of time. This method is now popularly known as *Pasteurization* and involves moderate heat treatments of the product to kill microorganisms. This process is now the backbone of wine industry. Nowadays, pasteurization is widely used in milk industry, food and beverage industries.

We can summarize his contributions as follows:

- Pasteur discovered that *fermentation of a substrate is caused by microorganisms*.
- Pasteur performed *Swan neck experiment* to disapprove the theory of spontaneous generation.
- He was the first one to use terms like *aerobics* for those organisms that can live in the presence of oxygen and *anaerobic* for those organisms that prefer to live in the absence of oxygen.
- He discovered the process of *pasteurization* that is used nowadays to keep the food products for a long time, i.e., to increase shelf life of the product.
- He *developed vaccines* against cholera, anthrax and rabies, which were very deadly diseases at that time.
- He *discovered silkworm disease* known as pébrine and isolated the causative microorganisms of this disease.
- He *introduced sterilization techniques* and developed steam sterilization method, hot air oven and autoclave. These methods are backbone of the sterilization techniques and are widely used in healthcare industry, and food and beverage industry.
- He *isolated microorganisms responsible pox and rabies*. He demonstrated that the causative agents of these diseases were too small to be seen through microscope and these could pass through filters. Later on this filterable agent of disease was known as virus.
- He *suggested methods to control cross infections in hospitals*.
- He *introduced attenuated live vaccines* for prophylactic use.
- He *discovered microorganisms such as Staphylococcus, Streptococcus and Pneumococcus.*

SHORT ANSWER QUESTIONS

1. What is simple microscope? *(MGR)*

Answer

A simple microscope is a basic optical instrument used to magnify small objects or details that are otherwise difficult to see with the naked eye. It consists of a single lens, typically a convex lens, which bends light to produce an enlarged image. Simple microscopes are often used in educational settings, laboratories, and hobbyist applications. They are relatively easy to use and are effective for viewing objects such as cells, small organisms, or microscopic structures. However, they have limitations in magnification compared to compound microscopes, which utilize multiple lenses and more complex optical systems.

2. Write about contributions of Alexander Fleming. *(MGR)*

Answer

- Sir Alexander Fleming discovered the wonder drug Penicillin from mold "Penicillium notatum" in 1929.
- He is also known as Father of Antibiotics.
- Fleming, Florey and Chain was awarded Noble prize for the discovery of Penicillin in 1945.

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3. Write the contributions of Joseph Lister to the field of microbiology. *(DU)*

Answer

- In 1860, Joseph Lister applied a phenolic compound for dressing the surgical wounds and found that it was effective in preventing surgical wound infections.
- He is also known as *"Father of Antiseptic Surgery"*.
- On getting good results by the application of phenol on wounds, he also introduced spray of carbolic acid in operation theaters (OTs) so that the growth of microorganisms could be prevented.

4. Enumerate Koch postulates. *(MGR)*

Answer

Robert Koch gave the following four postulates:

1. The microorganism or other pathogen must be present in all cases of the disease.
2. The pathogen can be isolated from the diseased host and grown in pure culture.
3. The pathogen from the pure culture must cause the disease when inoculated into a healthy, susceptible laboratory animal.
4. The pathogen must be reisolated from the new host and shown to be the same as the originally inoculated pathogen.

5. Write about Fluorescent microscope. *(MGR)*

Answer

- The phenomenon of fluorescence was first described in 1852 by Sir George G Stroke. Fluorescence microscope uses fluorescent labeled dyes, like auramine O.
- The technique is based on the absorption of light and then re-emission of it by the microorganisms or other objects, which results in fluorescence of an object.
- This technique is useful in examining *Mycobacterium tuberculosis* and is widely used for detection of an antigen and antibody in the field of immunology.
- Nowadays, fluorescence microscope is *widely used* in the field of biomedical science in the research and diagnostic labs.

6. Mention contributions of Edward Jenner. *(MGR)*

Answer

Jenner **pioneered the concept of vaccines**, and invented vaccination with cowpox to replace the fearful dangers of inoculation with smallpox. This development resulted in immunity to smallpox and ushered in the era of preventive measures for contagious diseases.

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CONCEPTUAL REVISION

Golden Points

- Microorganisms were first seen in 1675 by a Dutchman Antony van Leeuwenhoek.
- Pasteur suggested methods to control nosocomial infections and introduced attenuated live vaccines for prophylactic use. Pasteur is called the progenitor of modern immunology.
- Joseph Lister used phenolic compound for dressing to prevent surgical wound infections. He is also known as Father of Antiseptic Surgery.
- Tyndallization was discovered by John Tyndall for sterilizing substances.
- Koch is well known for his contributions to the field of medical techniques, and is called Father of Microbial Techniques and Father of Medical Microbiology.
- Koch introduced the aniline dyes for staining, pure culture techniques, agar as solidifying agent and skin test for diagnosing tuberculosis.
- Sir Alexander Fleming discovered the wonder drug Penicillin in 1929.
- The first human disease of viral origin was yellow fever discovered by Sir Walter Reed in 1902.
- Ruska in 1934 discovered electron microscope.
- Metchnikoff discovered phenomenon of phagocytosis.

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MULTIPLE CHOICE QUESTIONS

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1. Louis Pasteur is associated with all, except:
a. Vaccination of smallpox
b. Germ theory
c. Pasteurization
d. Vaccination of rabies

Ans. a. Vaccination of smallpox

2. Robert Koch's assistant advise him to use agar instead of gelatin culture media for cultivation of bacteria as:
a. Agar is cheaper
b. Gelatin melts at 27°C
c. Agar has more nutrition
d. Gelatin is not easily available

Ans. b. Gelatin melts at 27°C

3. Theory of web causation was given by:
a. MacMahon and Pugh
b. Pettenkoffer
c. John Snow
d. Louis Pasteur

Ans. a. MacMahon and Pugh

4. All are Koch's postulates, except:
a. A microorganism should be constantly associated with the lesions of the disease.
b. It should be possible to isolate the bacterium in pure culture from the lesions.
c. Inoculation of such pure culture into laboratory animals should reproduce the lesions.
d. Administration of broad spectrum antimicrobial agent dependably eradicates the organisms and cures the diseases

Ans. d. Administration of broad spectrum antimicrobial agent dependably eradicates the organisms and cures the diseases

5. Leeuwenhoek is associated with:
a. Telescope
b. Microscope
c. Stains
d. Immunization

Ans. b. Microscope

6. Which scientist first disproved the theory of spontaneous generation by showing that maggots only appear on decaying meat that has been exposed to flies?
a. Francesco Redi
b. Joseph Lister
c. Louis Pasteur
d. Robert Hooke

Ans. a. Francesco Redi

7. The Alpha helical structure of DNA was discovered by:
a. Edward Tatum
b. Eile Metchnikoff
c. James Watson and Francis Crick
d. Oswald Avery, Maclyn McCarty, and Colin McLeod

Ans. c. James Watson and Francis Crick

8. The event that triggered the development and establishment of microbiology as a science is the:
a. Development of microscope
b. Germ theory of disease
c. Spontaneous generation
d. Use of disinfectants

Ans. a. Development of microscope

9. Which of the following pioneers of Microbiology is credited with the discovery of microorganisms using high-quality magnifying lenses (early microscopes)?
a. Antonie Van Leeuwenhoek
b. Louis Pasteur
c. Robert Hooke
d. Robert Koch

Ans. a. Antonie Van Leeuwenhoek

10. Match the following scientists with their contribution:

I. Elie Metchnikoff	1. Discovery of Transposons (jumping genes)
II. Martinus Beijerinck	2. Discovery of Arsphenamine (salvarsan) against syphilis
III. Barbara McClintock	3. Cellular immunity (phagocytes)
IV. Paul Ehrlich	4. Discovered viruses (called *Contagium vivum fluidum*) in a filtrate

a. I-4, II-3, III-2, IV-1
b. I-3, II-4, III-1, IV-2
c. I-3, II-1, III-2, IV-4
d. I-4, II-3, III-1, IV-2

Ans. b. I-3, II-4, III-1, IV-2

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Section Outline

CHAPTER 10

Drugs Acting on Urinary System

CONCEPTUAL THEORY

Terminology

Acidifiers and alkalinizes: The agents, which are used or can be used to acidify or alkalinize the urine, respectively as per requirement.
Antidiuretic hormone: It is synthesized in the supraoptic and paraventricular nucleus of hypothalamus and secreted by the posterior pituitary along with oxytocin.
Antidiuretics: The drugs that reduce urine volume. Their primary indication is *diabetes insipidus*.
Cholinergic drugs: The drugs which produce acetylcholine-like actions on different organ systems.
Diuretics: The drugs, which increase the excretion of urine by their action on the kidneys (specifically nephrons).

RENIN-ANGIOTENSIN SYSTEM

- **Composition:** Drugs in this category include angiotensin-converting enzyme (ACE) inhibitors (e.g., enalapril, lisinopril) and angiotensin II receptor blockers (ARBs, e.g., losartan, valsartan).
- **Action:** These drugs regulate blood pressure and fluid balance by affecting the renin-angiotensin-aldosterone system, leading to vasodilation and reduced blood volume.
- **Dosage:** Dosage varies based on the specific drug and the patient's condition.
- **Route:** Usually oral
- **Indications:** Hypertension, heart failure, diabetic nephropathy
- **Contraindications:** Hypersensitivity, pregnancy (especially ACE inhibitors)
- **Drug interactions:** Potential interactions with potassium-sparing diuretics and nonsteroidal anti-inflammatory drugs (NSAIDs)
- **Side effects:** Hypotension, cough (common with ACE inhibitors), hyperkalemia
- **Adverse effects**: Renal impairment, angioedema (rare but serious)

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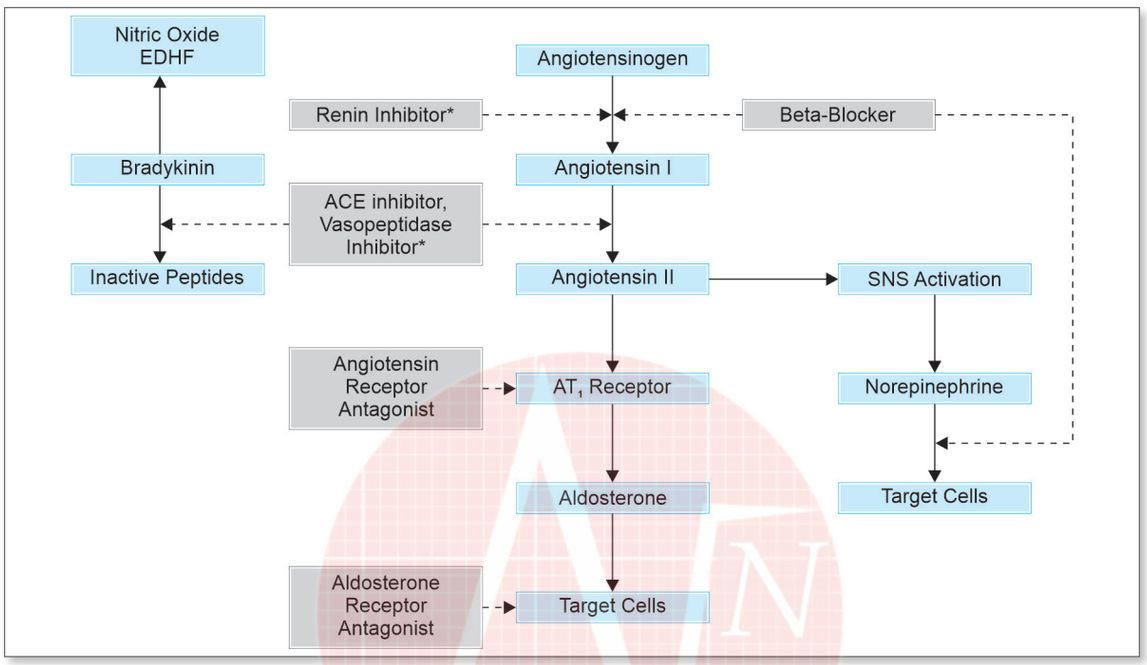

Figure 10.1: Drugs acting on renin-angiotensin-aldosterone system

DIURETICS

- Diuretics ("water pills") are the drugs which increase the urine output or urine volume by their action on kidneys (mainly nephrons).
- These diuretics are very effective in the treatment of conditions like chronic heart failure, nephrotic syndrome, chronic hepatic diseases, hypertension, pregnancy associated edema and cirrhosis of the liver.

Therapeutic Approaches

Two important functions of the kidney are as follows:

1. To maintain a homeostatic balance of electrolytes and water.
2. To excrete water soluble end products of metabolites.

Classification of Diuretics

According to Types

- **High ceiling (Loop diuretics)**
  - Furosemide
  - Torsemide
- **Thiazide diuretics**
  - Chlorothiazide
  - Hydrochloride thiazide
  - Benzthiazide
- **Osmotic diuretics:** Mannitol
- **Carbonic anhydrase inhibitors:** Acetazolamide
- **Potassium sparing diuretics**
  - Spironolactone
  - Amiloride

According to Efficacy

- **High efficacy diuretics**: Furosemide, torsemide, bumetanide, etc.
- **Medium efficacy diuretics:** Hydrochlorothiazide, chlorthiazide, chlorthalidone, indapamide, xipamide, etc.
- **Weak diuretics**: Carbonic anhydrase inhibitors, osmotic diuretics, potassium sparing diuretics.

Mechanism of Action

Theses drugs primarily act on the site II or the thick ascending limb of Henle's loop.

- **Loop diuretics**: They show their action by reducing absorption of sodium at the level of loop of Henle. For example Furosemide, Torsemide.
- **Potassium sparing**: Causes retention of potassium ions while maintaining the diuretic effects. Preferably given along with loop diuretics to prevent the potassium loss. e.g., Spironolactone.
- Drugs of this class primarily act on the site III or cortical diluting segment of loop of Henle or early distal convoluted tubule. The drugs inhibit Na^+Cl^- symporter at site III and inhibit the reabsorption of NaCl out of the tubule into the

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interstitial space thus increasing the loss of NaCl with water in the form of urine.

Example: Hydrochlorothiazide, chlorthiazide, clopamide, etc.

- **Thiazide:**
  - Mainly act in the PCT and the descending limb of loop of Henle.
  - The drugs inhibit the normal water reabsorption by their osmotic effects and lead to increased urine excretion.

  Example: Mannitol, isosorbide and glycerol
- **Osmotic:** It inhibits reabsorption of water and sodium. For example Mannitol.
- **Anhydrase inhibitor:** They suppress the activity of Carbonic Anhydrase, and result is excretion of alkaline urine due to retention of HCO_3^- in the tubular lumen.
- **Example:** Acetazolamide.
  - The drug decreases intraocular pressure,
  - pH and raises CO_2 in brain; resulting in sedation and seizures.

Indication and Uses

- **Loop diuretics:** Edema, Acute pulmonary edema (Acute LVF, MI), cerebral edema, hypertension, hypercalcemia and renal calcium stone.
- **Thiazide:** Mild to moderate edema (Cardiac failure, Nephrotic syndrome), HTN, Diabetes insipidus, Hypercalciuria/ Calcium stone, Premenstrual tenses.
- **Osmotic:** Acute renal failure during prolonged surgery or trauma to prevent or treat increase ICP, glaucoma.
- **Carbonic anhydrase inhibitor:** Glaucoma, epilepsy, acute motion sickness, periodic paralysis.
- **Potassium sparing:** Hyperaldosteronism, HTN, CHF, edema, combine with furosemide, thiazide to reduce potassium loss produce by these agents.

Drug Examples and Doses

S. No.	Drugs	Doses
1.	Furosemide	20–80 mg
2.	Torsemide	5–10 mg orally or IV OD
3.	Chlorothiazide	500–100 mg PO or IV OD or BID
4.	Hydrochlorothiazide	25–50 mg OD
5.	Benzthiazide	25 mg
6.	Mannitol	50–100 g IV
7.	Acetazolamide	125–250 mg orally IV
8.	Spironolactone	25–200 mg/day in 1 or 2 divided doses
9.	Amiloride	5–10 mg OD

Adverse Effects

- **Thiazide:** Hypokalemia, metabolic alkalosis, hyponatremia, dehydration, hypotension, hypercholesterolemia, hyperuricemia, azotemia (in renal disease patient)
- **Loop diuretic:** Hypokalemia, metabolic alkalosis, hyperuricemia, hypomagnesemia, dehydration (Hypovolemia), hypotension, ototoxicity (Dose related hearing loss)
- **Osmotic:** Electrolyte imbalance, increase circulatory load and may cause congestive heart failure.
- **Potassium sparing :** Hyperkalemia, metabolic acidosis, gynecomastia, aldosterone antagonist, gastric problems including peptic ulcer.
- **Carbonic anhydrase:** Hypokalemia, metabolic acidosis, skin rash.

Nursing Responsibilities

- Monitor urine output, blood pressure and hourly check for electrolyte imbalance.
- Obtain vital signs.
- Monitor laboratory values of Potassium or Sodium (diuretics can cause electrolyte imbalance).
- Observe for changes in level of consciousness, dizziness, fatigue and postural hypotension.
- Monitor hearing and vision (Loop diuretic are ototoxic).
- **Instruct patient to:**
  - Immediately report any severe shortness of breath, profound fatigue, edema in extremities, potential signs of heart failure or pulmonary edema.
  - Avoid excessive heat which contributes to fluid loss through perspiration.
  - Stop medication, if severe hypotension exists.
  - Immediately report any change in consciousness, specially feeling like fainting.
  - Change position slowly.
  - Receiving loop or thiazide diuretic to eat food high in potassium.
  - Receiving potassium—Sparing diuretic to avoid foods high in potassium.

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ANTIDIURETICS

Antidiuretics are the agents that reduce urine volume, opposing diuresis.

Divided into three groups:

1. Antidiuretic hormone [Antidiuretic hormone, argenine vasopressin (AVP)], lypressin, terlipressin, desmopressin.
2. Thiazides and amiloride.
3. **Other drugs:** Indomethacin, chlorpropamide, carbamazepine.

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Antidiuretic Hormone

- Causes long-term blood pressure control by increasing the water reabsorption from the collecting duct.
- It can raise blood pressure by constricting the blood vessels, hence also called vasopressin.

Thiazide Diuretics and Amiloride

- Thiazides causes induction in electrolyte depletion so that glomerular filtrate is more completely reabsorbed iso-osmotically in PT.
- Drugs also reduce glomerular filtration rate (GFR) and thus the fluid load on tubules

Other Drugs

- **Indomethacin** reduces renal prostaglandin synthesis
- **Carbamazepine** is an anticonvulsant agent. It reduces the volume of urine in central or neurogenic diabetes insipidus.
- **Chlorpropamide** acts on the pancreatic beta cell of islets, promotes insulin secretion, and produces hypoglycemic effect.

Mechanism of Action

Reduces urine flow by acting reabsorption of water by kidney tubules.

Indications and Uses

- Cranial diabetes insipidus
- Primary nocturnal enuresis (bed wetting)
- Nocturia associated with multiple sclerosis

Examples of Drug and their Doses

S. No.	Drugs	Doses
1.	Antidiuretic Hormone (Vasopressin)	5–10 units IM/SC
2.	Desmopressin	100–400 mcg orally 1–4 mcg IV.

Adverse Effects

Nasal irritation, rhinitis, abdominal cramps, urge to defecate, fluid retention, congestion, ulceration, nausea, pallor, backache in females (due to uterine contraction)

Nursing Responsibilities

- Monitor electrolyte imbalance.
- Monitor vital signs and BP regularly.
- Observe for signs of hypersensitivity reactions.
- Monitor laboratory values.
- Stop medication, if hypertension exists.

URINARY ANTISEPTICS

These are the drugs used for urinary tract infections which kill or inhibit the growth of microorganisms.

Mechanism of Action

- These are bacteriostatic drugs.
- These antimicrobials are orally administered which attain good antibacterial concentration only in urine, with little or no systemic antibacterial effects.

Indications and Uses

Used in the treatment of urinary tract infections associated with increased frequency of micturition, urgency, burning micturition (associated with cystitis), chills, fever, flank pain, and tenderness (associated with acute pyelonephritis).

Adverse Effects

Fever, rash, crystalluria, nausea, vomiting, photosensitivity reaction, Stevens-Johnson syndrome

Examples of Drug and their Doses

S. No.	Drugs	Doses
Sulphonamides		
1.	Cotrimoxazole	Cotrimoxazole (Trimethoprim/ Sulfamethoxazole) 80 mg – 400 mg
2.	Sulfadiazine	500–1000 mg
3.	Sulfamethoxazole	1–2 g orally every 6 hourly
Miscellaneous		
4.	Fluoroquinolones	Ciprofloxacin—250–500 mg, Levofloxacin 250–500 mg
5.	Methenamine	1 g orally
6.	Nalidixic acid	Nalidixic acid 500 mg
7.	Nitrofurantoin	50–100 mg orally

Nursing Responsibilities

- Assess the signs and symptoms of urinary tract infections.
- Advise the patient for the intake of fluid 2000–3000 mL/day to reduce crystalluria.
- Teach the patient proper hygiene measures to reduce the risk of reinfection.
- Monitor the patient's urinary elimination patterns.
- Instruct the women who are taking oral contraceptives to use an alternative method such as barrier method during the entire course of therapy.

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CONCEPTUAL EXERCISES

LONG ANSWER QUESTION

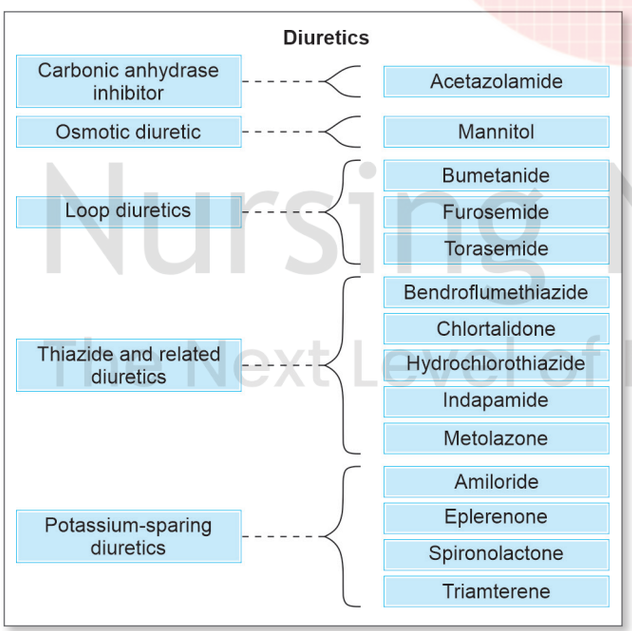
1. **Classify diuretics with suitable examples. Write the mechanism of action, uses, adverse effects contraindications and nursing management of furosemide.** ***(KUHS, MGR)***

Answer

Diuretics

- Diuretics increase the production of urine from the body and promote removal of excess sodium and water through kidneys.
- Diuretics are among the most widely prescribed drugs in clinical practice.
- They are used in a wide variety of medical conditions such as hypertension, heart failure, edema, liver cirrhosis, etc.

Classification



Furosemide

Furosemide is a loop diuretic which is prescribed to treat conditions like fluid retention and hypertension.

Mechanism of Action

- Furosemide, like other loop diuretics, acts by inhibiting the luminal Na^+-K^+-Cl^- cotransporter in the thick ascending limb of the loop of Henle, by binding to the Na^+-K^+-$2Cl^-$ transporter, thus causing more sodium, chloride, and potassium to be excreted in the urine.
- Furosemide is the prototype member of this class. It is a rapid acting and highly efficacious diuretic.

Target	Actions	Organism
A Solute carrier family 12 member 1	**Inhibitor**	Humans
N Carbonic anhydrase 2	**Inhibitor**	Humans
U G-protein coupled receptor 35	**Agonist**	Humans

- It acts on ascending limb of the loop of Henle where it inhibits Na^+-K^+-Cl^- cotransport.

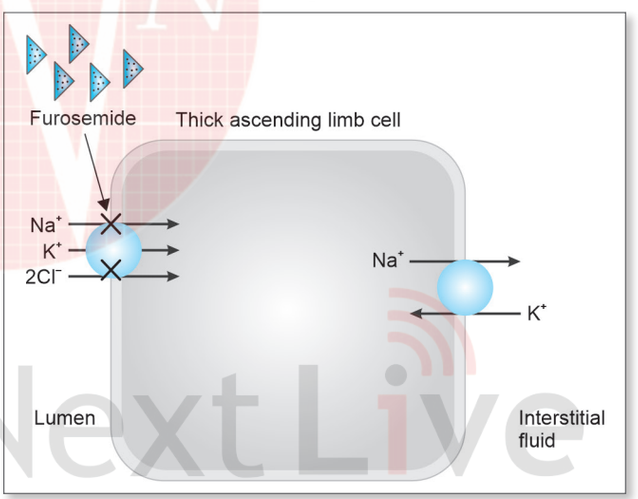


Figure 10.2: Mechanism of action

Therapeutic Uses

- **Edema:** They can be used in cardiac, hepatic, or renal edema. They can be used in nephrotic and other forms of resistant edema.
- **Acute pulmonary and cerebral edema:** Vasodilator action preceded the saluretic action, thus prompt relief is perceived in acute pulmonary edema. Osmotic diuretics are preferred in cerebral edema but furosemide can be given by intramuscular route.
- **Hypertension:** Only when it is complicated by:
  - Chronic renal failure
  - Coexisting refractory congestive heart failure (CHF)

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- Resistant to combination regimens containing a thiazide
- Marked fluid retention attributed to potent vasodilators

- Symptomatic congestive heart failure
- **Forced diuresis:** It can be used as an alternative to mannitol.

Adverse Effects

- **CNS:** Headache, dizziness, vertigo, paresthesia, restlessness, weakness
- **CVS:** Orthostatic hypotension, thrombophlebitis after IV administration.
- **Eye and ENT**: Blurred vision, yellow vision, transient deafness, hearing impairment, tinnitus
- **GIT:** Nausea, vomiting, abdominal pain, diarrhea, constipation.
- **Hepatic:** Increased liver enzymes, jaundice, hepatic dysfunction.
- **Hematologic:** Leukopenia, thrombocytopenia, aplastic anemia, agranulocytosis
- **Metabolic:** Volume depletion and dehydration, hypokalemia.
- **Skin:** Rash, pruritus, urticaria, dermatitis, photosensitivity reactions, erythema, toxic epidermal necrolysis.
- **Others:** Hypersensitivity reactions, anaphylactic reactions, interstitial nephritis, muscle spasm.

Contraindications

- Hypersensitivity to furosemide
- Severe sodium and volume depletion
- Patients with anuria
- Use with caution in lactation as drug appears in breast milk and may inhibit lactation.

Nursing Management

- Assess fluid status.
- Monitor daily weight, intake and output ratios, amount and location of edema, lung sounds, skin turgor, and mucous membranes.
- Notify health care professional if thirst, dry mouth, lethargy, weakness, hypotension, or oliguria occurs.
- Monitor BP and pulse before and during administration.
- Check for drug related complication or adverse effects.

SHORT NOTES

1. Write a short note on Furosemide as a diuretic. *(MGR)*

Answer

For Ans, Refer Long Question 1, Pg. No. 343

2. Write a short note on diuretics and their classification. *(MGR, RUHS, RUHS)*

Answer

Refer to Synopsis, Pg. No. 340

3. Write a note on complications of diuretic therapy. *(MGR)*

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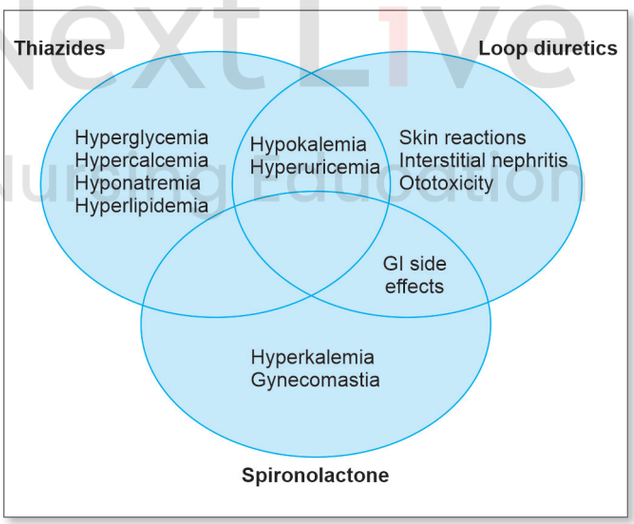
Answer

Complications of Diuretic Therapy

- Loop agents and thiazides may lead to hyponatremia, which, in the case of thiazides, may cause permanent neurologic damage. Dose-related reversible or irreversible ototoxicity may complicate treatment with loop agents.
- The most common adverse effect for any diuretic is mild hypovolemia, which can lead to transient dehydration and increased thirst.
- When there is an over-treatment with a diuretic, this could lead to severe hypovolemia, causing hypotension, dizziness, and syncope.
- Diuretic-related side effects can be separated into several categories, including those with well worked-out mechanisms, such as electrolyte defects and/or metabolic abnormalities and occurrences, such as impotence, which are mechanistically less well understood.



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4. Write a short note on acidifiers and alkalinizers. *(RUHS)*

Answer

Acidifiers

- The drugs, which are used to treat acid-base imbalance in the body.
- Basically they are used for the treatment of metabolic alkalosis.
- These are the agents used to neutralize the pH which has been increased due to certain causes like excess alkali intake.
- For example, Ammonium chloride, Ascorbic acid and Phenezopyridine
- They are widely used in metabolic alkalosis.

Alkalinizers

- The agents or drugs, which are used to neutralize the pH, which has been decreased due to certain causes like metabolic acidosis
- **Examples are:** Sodium bicarbonate, Sodium citrate, Potassium citrate, etc.

Pharmacokinetics

- Alkalinizers are given orally in tablet form or solution form.
- Excreted via renal route in the form of bicarbonates. Less than 5% is excreted in unchanged form.
- Alkalinizers when given in a dose of 10–15 mL QID: maintain a urine pH of 6.5–7.4 and when given in a dose of 15–20 mL QID maintain a urine pH of 7.0–7.6.

Indications

- Treatment of urinary tract infection along with antimicrobials.
- Used in treatment of cystitis and urethritis
- Treatment of systemic acidosis for shorter duration
- Treatment and prevention of uric acid and calcium oxalate stones.

5. What are diuretics? Name them. Explain why potassium sparing diuretic is combined with thiazides for the treatment of hypertension. *(RUHS)*

Answer

Diuretics

- Diuretics are drugs that cause a net loss of salt and water in the urine.
- Diuretics are among the most widely prescribed drugs in clinical practice.
- They are used in a wide variety of medical conditions such as hypertension, heart failure, edema, liver cirrhosis, etc.
- Diuretics are commonly classified into:
  - **Carbonic anhydrase inhibitors:** Acetazolamide.
  - **Loop diuretics:** Furosemide, bumetanide, torasemide, ethacrynic acid, etc.
  - **Osmotic diuretics:** Mannitol, isosorbide, glycerol, etc.
  - **Potassium sparing diuretics:** Amiloride, etc.
  - **Thiazide diuretics:** Hydrochlorothiazide, chlorthiazide, clopamide.

Potassium sparing diuretic is combined with thiazides for the treatment of hypertension:

- A combination of a potassium sparing diuretic with a thiazide diuretic is used to reduce edema due to salt and water retention in disorders of the heart, kidneys, liver or lungs.
- They are used commonly in treatment of hypertension.
- The combination of thiazides (particularly at higher doses) with potassium-sparing diuretics increases their BP-lowering effectiveness with less potassium depletion.

6. Differentiate between Hydrochlorothiazide and Furosemide *(KUHS)*

Answer

Differences between Hydrochlorothiazide and Furosemide

Features	Hydrochlorothiazide	Furosemide
Type or class	It is thiazide diuretic	It is high ceiling diuretic or loop diuretic.
Mode of action	It inhibits NaCl symport in distal convoluted tubule	It inhibits Na^+ - K^+- $2Cl^-$ cotransporter in ascending loop of Henle
Uses	Prescribed for high blood pressure, edema, osteoporosis, diabetes insipidus, nephrocalcinosis	Prescribed for edema, heart failure, ascites, high blood pressure, hypercalcemia, nonobstructive oliguria, oliguria, pulmonary edema, renal failure, renal transplant.
Efficacy	Less	More
Side effects	Weakness, low blood pressure, abdominal pain, nausea, anaphylaxis, etc.	Dehydration, electrolyte depletion, ringing in the ears, pancreatitis, diarrhea, dizziness, increased uric acid levels, photophobia, etc.

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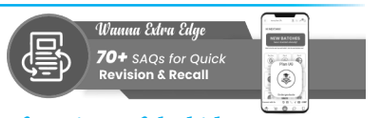
SHORT ANSWER QUESTIONS



1. Write any three main functions of the kidney.

Answer

Three main functions of the kidney:

1. **Excretory functions:** Excretion of nitrogenous wastes such as urea, uric acid and creatinine
2. **Regulatory functions:** It regulates and maintains the balance of fluid and electrolyte mainly
3. **Hormonal functions:** Production of erythropoietin and renin, activation of vitamin D.

2. Write the classification of Diuretics with examples.

Answer

Classification of Diuretics

Type of diuretic	Examples
Thiazide diuretics	Hydrochlorothiazide, Chlorthalidone
Loop diuretics	Furosemide, Bumetanide, Torsemide
Potassium-sparing diuretics	Spironolactone, Amiloride, Triamterene
Carbonic anhydrase inhibitors	Acetazolamide
Osmotic diuretics	Mannitol, Urea

3. Write the mechanism of action of loop diuretics.

Answer

Mechanism of Action of Loop Diuretics

- Loop diuretics inhibit Na^+/K^+ cotransport at site II and inhibit the reabsorption of NaCl out of the tubule into the interstitial space.
- Thus, the increased Na^+/Cl^- reach the distal tubule and promote the loss of H^+ and K^+ along with increased loss of water causing profuse diuresis

4. Enumerate any two indications of Thiazides.

Answer

Thiazides

- **Thiazide diuretics:** Include chlorothiazide, chlorthalidone, hydrochlorothiazide, indapamide, metolazone, and polythiazide
- **Indications of Thiazides:**
  1. **Edema**:
     - Thiazides can be employed for mild-to-moderate edema cases.
     - Not preferred for mobilization of edema fluid, but may be considered for maintenance therapy
     - Act most effectively in cases of cardiac edema; but are less effective in hepatic or renal edema
  2. **Hypertension:** Thiazides and related diuretics, especially chlorthalidone and hydrochlorthiazide are one of the first-line drugs in hypertension in elderly.

5. What are urinary antiseptics?

Answer

- Urinary antiseptics are antimicrobial agents which are orally administered and attain good antibacterial concentration only in urine, with little or no systemic antibacterial effects.
- It is equal to a form of local therapy and mainly used in lower urinary tract infections.
- **Examples:** Nitrofurantoin, Nalidixic acid and Methenamine, etc.

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CONCEPTUAL REVISION

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Golden Points

- Urine formation involves mainly three processes: Glomerular filtration, Selective tubular reabsorption and Tubular secretion
- Acetazolamide is a noncompetitive reversible inhibitor of both membrane-bound and cytoplasmic forms of carbonic anhydrase in PCT.
- Inhibition of carbonic anhydrase enzyme causes increased excretion of bicarbonates with Na+, K+ and water.
- Drugs that primarily act on the site II or the thick ascending limb of Henle's loop are called loop diuretics or high ceiling diuretics
- The relative potency order of loop diuretics is: Bumetanide > torsemide > furosemide > ethacrynic acid = Indacrinone
- The relative potency of Thiazides and thiazide-like diuretics is: Indapamide > Bendroflumethiazide > Metolazone > hydrochlorthiazide = Chlorthalidone > chlorthiazide
- Thiazides and related diuretics, especially chlorthalidone and hydrochlorthiazide are one of the first-line drugs in hypertension in elderly.
- Antidiuretics are the drugs that reduce urine volume. Their primary indication is diabetes insipidus.
- Antidiuretic drugs are divided into three groups:
  1. Antidiuretic hormone
  2. Thiazides and amiloride.
  3. Other drugs: Indomethacin, chlorpropamide, carbamazepine.
- Loop diuretics and spironolactone enhance the digitalis toxicity by causing hypokalemia.
- Urine pH play a pivotal role for the action of antimicrobial agents.
- The drugs which produce acetylcholine-like actions on different organ systems are known as cholinergic drugs.
- Acidifiers and alkalinizers are the agents, which are used or can be used to acidify or alkalinize the urine, respectively as per requirement.
- The AMAs which work better in acidic pH are: Nitrofurantoin, tetracyclines, cloxacillin, etc.
- The AMAs which work better in alkaline pH are: Cephalosporins, fluoroquinolones, aminoglycosides, cotrimoxazole, etc.

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MULTIPLE CHOICE QUESTIONS

1. Mannitol (Osmitrol), an osmotic diuretic, is contraindicated to which conditions?

1. Pulmonary edema
2. Heart failure
3. Hyponatremia
4. Narrow-angle glaucoma

a. If 1, 2, 3 are correct
b. If 1 and 3 are correct
c. If 2 and 4 are correct
d. If all four (1, 2, 3, and 4) are correct

Ans. a. If 1, 2, 3 are correct

2. The client at highest risk for nephrotoxicity with aminoglycoside use is a:

a. Female with past history of cystitis on 5 days of therapy
b. Male with a creatinine of 1.7 and BUN of 52 on a 10-day regimen
c. Male with history of kidney stones on 8 days of therapy
d. Female with BUN of 12 and creatinine of 0.8

Ans. b. Male with a creatinine of 1.7 and BUN of 52 on a 10-day regimen

3. Which drugs will be used to treat the patient with CKD for mineral and bone disorder?

1. Cinacalcet
2. Calcium acetate
3. Sevelamer
4. IV 10% calcium gluconate

a. If 1, 2, 3 are correct
b. If 1 and 3 are correct
c. If 2 and 4 are correct
d. If all four (1, 2, 3, and 4) are correct

Ans. b. If 1 and 3 are correct

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4. Superficial bladder cancer can be treated by direct instillation of the antineoplastic antibiotic agent Mitomycin. This process is termed:

a. Intraventricular administration
b. Intravesical administration
c. Intravascular administration
d. Intrathecal administration

Ans. b. Intravesical administration

5. In diabetes insipidus, diuretic showing paradoxical antidiuretic activity is:

a. Thiazide
b. Triamterene
c. Spironolactone
d. Furosemide

Ans. a. Thiazide

6. Potassium sparing diuretics act on:

a. Na^+ K^+ pump
b. Aldosterone receptor
c. Carbonic anhydrase
d. Na^+ Cl^- symporter

Ans. b. Aldosterone receptor

7. Desmopressin can be used for all of the following conditions; except:

a. Neurogenic diabetes insipidus
b. Nephrogenic diabetes insipidus
c. Bedwetting in children
d. Bleeding due to hemophilia

Ans. b. Nephrogenic diabetes insipidus

8. The drug that can be used for producing alkalinization of urine is:

a. Hydrochlorothiazide
b. Furosemide
c. Acetazolamide
d. Spironolactone

Ans. c. Acetazolamide

9. Epleronone:

a. Is an aldosterone antagonist
b. Can cause hyperkalemia in predisposed patients
c. Is a diuretic
d. All of the above

Ans. d. All of the above

Pathology and Genetics

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Section Outline

PART I PATHOLOGY

Chapter 1 Introduction to Pathology

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Chapter 3 Systemic Pathology (Part-B)—Kidney and Urinary Tract, Female Genital System, Male Genital System, Breast, Central Nervous System

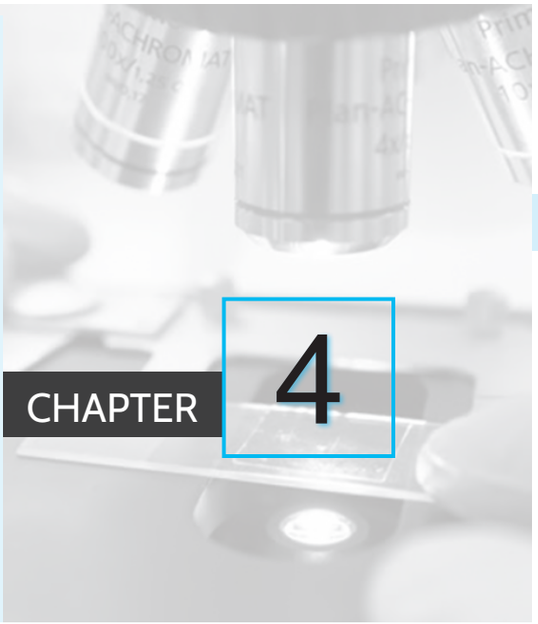
Chapter 4 Hematological Test for the Diagnosis of Blood Disorders

Chapter 5 Clinical Pathology

PART II GENETICS

Chapter 6 Genetics

- Basics of Genetics
- Maternal, Prenatal and Genetic Influences on Development of Defects and Diseases
- Genetic Testing in Neonates and Children
- Genetic Conditions of Adolescents and Adults
- Services Related to Genetics



CHAPTER 4

Hematological Test for the Diagnosis of Blood Disorders

CONCEPTUAL THEORY

Terminology

Bleeding time: It is the time taken for bleeding to stop from a superficial skin wound.
Clotting time: It is the time from the puncture of the blood vessel to the formation of a fibrin thread.
Complete blood count (CBC): It is also known as full blood count or blood panel. It is a test requested by a doctor or other medical professional that gives the information about the blood cells in a patient's blood.
Crossmatching: A test to confirm the donor-recipient compatibility by crossmatching patient's serum against donor red cells.
Erythrocyte sedimentation rate (ESR): A test measuring the rate at which erythrocytes settle.
Hemoglobin: It is the main constituent of the red blood cells and transport oxygen from lungs to various parts of the body.

BLOOD TESTS

Hemoglobin

- Hemoglobin is the main oxygen carrying component of red blood cell.
- It transports oxygen into our body through blood.

Structure and Types of Hemoglobin

- Hemoglobin is made up of a simple protein called globin and heme that contains iron.
- Heme molecule is composed of protoporphyrin with an iron (Fe^{++}) atom.
- The globin chain consists of two pairs of different polypeptide chains.

The types of hemoglobin

Type	Chain present
Hemoglobin A_1	$\alpha_2 \beta_2$
Hemoglobin A_2	$\alpha_2 \delta_2$
Fetal hemoglobin	$\alpha_2 \gamma_2$

Methods of Hemoglobin Estimation

- **Photoelectric colorimeter method:** Recommended method for hemoglobin estimation. Reliable and standard method of hemoglobin estimation.
- **Sahli's acid hematin method:** Formed acid hematin fades as soon as it is formed.
- **Oxyhemoglobin method:** Indirect method of hemoglobin estimation.
- **Alkali hematin method:** Less accurate method.
- **Tallquist's hemoglobin comparative chart:** This method is based on color comparison.

Normal Values

In general, the normal range of hemoglobin is as follows:

- 13.5 to 18.0 g/dL in men
- 12.0 to 15.0 g/dL in women
- 11.0 to 16.0 g/dL in children

BLOOD COMPONENTS

Blood is composed of formed elements known as "blood cells" and fluid matrix called "plasma".

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Blood Cells

Formed element	Numbers present per microliter (μL) and mean (range)	Appearance in a standard blood smear	Summary of functions	Comments
Erythrocytes (red blood cells)	5.2 million (4.4–6.0 million)	Flattened biconcave disk; no nucleus; pale red color	Transport oxygen and some carbon dioxide between tissues and lungs	Lifespan of approximately, 120 days
Leukocytes (white blood cells)	7000 (5000–10,000)	Obvious, dark-staining nucleus	All function in body defenses	Exit capillaries and move into tissues; lifespan of usually a few hours or days
Platelets	350,000 (150,000–500,000)	Cellular fragments surrounded by a plasma membrane and containing granules; purple stain	Hemostasis plus release growth factors for repair and healing of tissue	Formed from megakaryocytes that remain in the red bone marrow and shed platelets into circulation

Plasma

Components	Water	Salts Sodium, potassium, calcium, magnesium,chloride, bicarbonate	Plasma proteins Albumin Fibrinogen Immunoglobulins	Nutrients (e.g., glucose, waste products of metabolism, respiratory gases (O_2 and CO_2)
Functions	Solvent	Osmotic balance, pH buffering, regulation of membrane potentials	Osmotic balance, pH buffering, clotting, immune responses	Hormones Heat

Total Leukocyte Count

- A blood test to measure the number of white blood cells (WBCs) in the blood.
- Leukocytes are measured in blood by:
  - Manual method using Neubauer chamber
  - Using electronic cell counter
- Normal TLC:
  Adults: 4000–11000 cells/mL
  At birth: 8000–28000 cells/mL
  Pregnancy: Upto 15000 cells/mL

Causes of Altered Leukocyte Count

Leukocytosis	Leukocytopenia
Acute bacterial infections, especially by pyogenic organism, chronic infections, leukemoid reaction, leukemia, physioloical-pregnancy, etc.	Aplastic anemia, drug induced, radiation therapy, typhoid, hepatitis A and B, rheumatoid arthritis, malaria, etc.

Red Cell Count

Red cell counts are done by the following methods:

- Manual estimation—Using RBC pipette, Hb estimation and hematocrit.
- Electronic cell counter/auto analyzers

Normal Range

- **Adult male:** 4.7–6.1 million/mL
- **Adult female:** 4.2–5.4 million/mL
- **At birth:** 4.0–6.0 million/mL

Causes of Altered Red Cell Count

Increased red cell count	Decreased red cell count
Polycythemia vera, kidney tumor, congenital heart disease, sleep apnea, etc.	Anemia, cirrhosis, myelodysplastic syndromes, etc.

Platelet Count

- Platelet count is usually done by manual method or in a cell counter
- **Normal range:** 1.5–4.0 lakhs/mL

Thrombocytosis	Thrombocytopenia
Chronic myeloid leukemia, post hemorrhage, etc.	Acute ITP, chronic ITP, hypersplenism, DIC, drug induced, etc.

Packed Cell Volume/Hematocrit

- It is the volume (in percentage) occupied by the red blood cells obtained after the centrifugation of whole blood sample.

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- **Estimation by two methods:**
  1. Macrohematocrit or Wintrobe tube method
  2. Microhematocrit method
- **Normal value (males):** 40–55%
- **Normal value(female):** 35–48%
- **Infants:** 45–60%
- **Increases in:** Polycythemia vera rubra and secondary polycythemia states, dehydration, etc.
- **Decreases in:** Anema.

Erythrocyte Sedimentation Rate (ESR)

- ESR is a measure of the settling of red blood cells in a tube of blood during one hour.
- ESR is performed to assess the prognosis of inflammatory activity in the body.
- **Normal values of ESR:**
  - Wintrobe's method:
    - Men: 0–6.5 mm/hr
    - Women: 0–15 mm/hr
  - Westergren's method:
    - Men: 3–5 mm/hr
    - Women: 4–7mm/hr
- **Increases in:** Tuberculosis, anemia, multiple myeloma, rheumatoid arthritis, collagen vascular disease, etc.
- **Decreases in:** Polycythemia

COAGULATION TEST

- **Bleeding Time**
  - It is the duration of bleeding from a standard puncture wound on skin, after cut or injury till arrest of bleeding.
  - It is the measure of number and function of platelets as well as integrity of vessel walls.
  - Normal value: 3–5 minutes (Ivy method), 1–3 or 4 minutes (Duke's method)
  - Prolonged in: Thrombocytopenia, leukemia, aplastic anemia, severe liver disease, etc.
  - **Methods:**
    - Ivy method
    - Duke's method
    - Fingertip method
    - Template method
- **Clotting time:**
  - It is the time taken for the blood to clot spontaneously in a glass tube.
  - It tests for intrinsic and common coagulation pathway.
  - Normal value: 4 – 11 minutes at 37°C.
  - Prolonged in: Severe deficiency of clotting factors, disseminated intravascular coagulation, heparin administration, etc.
- **Activated partial thromboplastin time:**
  - The aPTT measures the time necessary to generate fibrin from initiation of the intrinsic pathway.
  - The aPTT is a good screening test for inherited or acquired factor deficiencies.
  - Normal range: 30–40 seconds
  - Prolonged in: Vitamin K deficiency, liver diseases, heparin therapy, DIC, etc.
- **Prothrombin time:**
  - The PT measures the time necessary to generate fibrin after activation of factor VII. It measures the integrity of the "extrinsic" and "common" pathways (factors VII, V, X, prothrombin, and fibrinogen).
  - Normal value, usually between 12 and 15 seconds.
  - Prolonged in: Obstructive jaundice, fibrinogen therapy, vitamin K deficiency, liver diseases, hemorrhagic disease of newborn, etc.
- **Thrombin time:**
  - This test measures the time taken for clot formation when thrombin is added to plasma.
  - It tests the conversion of fibrinogen to fibrin.
  - Normal range: 12 to 19 seconds
  - Prolonged in: Multiple myeloma, amyloidosis, etc.

BLOOD BANK

- A place where blood is collected from donors, typed, separated into components, stored, and prepared for transfusion to recipients.
- A blood bank may be a separate free-standing facility or part of a larger laboratory in a hospital.

Storage of Blood

- Each unit of whole blood is normally, separated into several components.
- Red blood cells may be stored under refrigeration for a maximum of 42 days, or they may be frozen for up to 10 years.
- Platelets are stored at room temperature and may be kept for a maximum of five days.
- Granulocytes are sometimes used to fight infections, although their efficacy is not well-established. They must be transfused within 24 hours of donation.

BLOOD GROUPING

- Karl Landsteiner discovered human blood groups in 1901.
- Blood grouping is based on the presence or the absence of inherited antigenic substance on the surface of red blood cells.

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- ABO system is the most important blood group system in human blood transfusion.
- **Importance of blood grouping:**
  - Blood transfusion
  - Organ transplantation
  - Hemolytic disorder in newborn, etc.

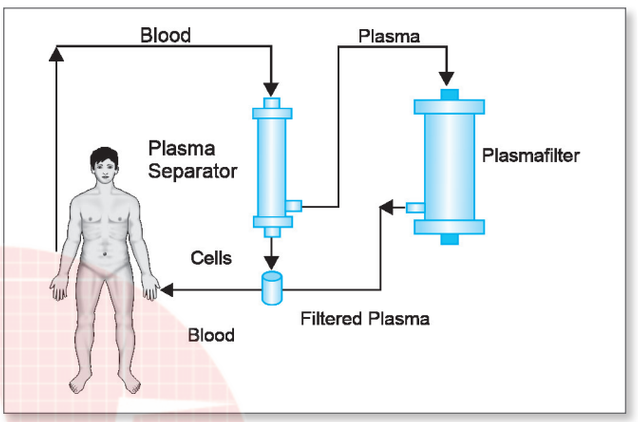
Blood group	Antigens	Antibodies	Can give blood (RBC) to	Can receive blood (RBC) from
AB	A and B	None	AB	AB, A, B, O
A	A	B	A and AB	A and O
B	B	A	B and AB	B and O
O	None	A and B	AB, A, B, O	O

CROSSMATCHING

- It is a direct test of compatibility of donor's cells with recipient serum.
- In this test, the donor RBCs are mixed with the recipient serum on the slide.
- If agglutination occurs, this means that the donor's blood is incompatible with the recipient blood.
- Crossmatching is done to prevent any transfusion reaction that may occur after or during transfusion.

PLASMAPHERESIS

- Plasmapheresis represents the automated selective removal of plasma.
- It is a therapeutic intervention that involves extracorporeal removal, return, or exchange of blood plasma or components.
- Centrifugation is done to separate the blood components.
- This is used as a method of blood purification for an effective temporary treatment of various autoimmune diseases.
- Certain diseases that are treated by plasmapheresis are as follows:
  - Myasthenia gravis
  - Thrombocytopenic purpura
  - Guillain-Barre syndrome, etc.



BLOOD TRANSFUSION

Read, Revise & Recall
HIGH YIELD Topics
For more, refer to
Nursing Next Live app

Transfer of bloodp0 or blood components from donor into the bloodstream of recipient is called "blood transfusion".

Transfusion Reaction

It is an unfavourable transfusion related event occurring in a patient during or after transfusion of blood components.

Types of Transfusion Reaction

- **Reaction due to mismatched blood transfusion:**
  - Transfusion reaction due to ABO and Rh incompatibility
- **Reaction due to faulty techniques during transfusion of blood:**
  - Thrombophlebitis, air embolism, etc.
- **Due to massive blood transfusion:**
  - Circulatory shock, hyperkalemia, hypocalcemia, etc.
- **Infection transmission:**
  - Hepatitis A and B, glandular fever, HIV, etc.

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CONCEPTUAL EXERCISES

LONG ANSWER QUESTION

1. **Write about routine hematological investigations and coagulation investigations done in hematology laboratory along with their normal values.** ***(CCS)***

Answer

Routine Hematological Investigations

- **White Blood Cell Count (WBC)**
  - A WBC count is a blood test to measure the number of white blood cells (WBCs) in the blood.
  - WBCs are also called leukocytes. They help fight infections. There are five major types of white blood cells:
    1. Basophils
    2. Eosinophils
    3. Lymphocytes (T cells, B cells, and Natural killer cells)
    4. Monocytes
    5. Neutrophils
- **Differential white blood count:** It measures the percentages of each leukocyte present.

Cell type	Normal value (percent)	Elevated levels may indicate
Neutrophil	54–62	Bacterial infections, stress
Lymphocyte	25–33	Mononucleosis, whooping cough, viral infections
Monocyte	3–9	Malaria, tuberculosis, fungal infections
Eosinophil	1–3	Allergic reactions, autoimmune diseases, parasitic worms
Basophil	<1	Cancers, chicken pox, hypothyroidism

- **Red blood cell count (RBC)**
  - RBCs carry oxygen throughout the body and remove excess carbon dioxide.
  - Reduced values of RBCs may be a sign of anemia or other diseases. In rare cases, increased numbers may cause problems with blood flow.
- **Platelet count:**
  - Platelets are the cell fragments that play a role in blood clotting.
  - Deficiency in blood platelets results in thrombocytopenia. For example: Aplastic anemia, Acute leukemia, etc.
- **Hematocrit red blood cell volume (HCT)**
  - This means the portion of red blood cells in a certain amount of whole blood.
  - The hematocrit test measures the percentage of red blood cells in blood.
  - A low hematocrit may be a sign of too much bleeding or it may indicate kidney disease, hemolytic anemia, etc.
  - A higher than normal hematocrit can be caused by dehydration or other disorders.
- **Hemoglobin concentration (Hb)**
  - This is the oxygen-carrying protein in red blood cells.
  - Abnormalities can be a sign of problems ranging from anemia to lung disease.
  - Increased hemoglobin concentration is present in Polycythemia vera, etc.
  - Conditions with decreased hemoglobin concentration is Anemia, bleeding disorders, hemorrhagic disorders, etc.
- **Red blood cell indices (measurements)**
  - Red blood cell (RBC) indices measure the size, shape, and quality of red blood cells.
  - Four types of red blood cell indices are:
    1. **Mean corpuscular volume (MCV):** Measures the average size of red blood cells.
    2. **Mean corpuscular hemoglobin (MCH):** Measures the average amount of hemoglobin in a single red blood cell.
    3. **Mean corpuscular hemoglobin concentration (MCHC):** Measures hemoglobin in red blood cells.
    4. **Red cell distribution width (RDW):** Measures differences in the volume and size of red blood cell.

Normal values of various hematological investigations

Hematological investigations	Normal values	SI units
White blood cells (WBC)	4500–11,000/mm^3	4.5–11.0 x 10^9/L
Red blood cells (RBC)	Male: 4.3–5.9 million/mm^3 Female: 3.5–5.5 million/mm^3	Male: 4.3–5.9 x 10^{12}/L Female: 3.5–5.5 x 10^{12}/L
Platelets	150,000–400,000/mm^3	150–400 x 10^9/L
Hematocrit	Male: 41%–53% Female: 36%–46%	Male: 0.41–0.53 Female: 0.36–0.46

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Hematological investigations	Normal values	SI units
Hemoglobin (Hb)	Male: 13.5–17.5 g/dL Female: 12.0–16.0 g/dL	Male: 2.09–2.71 mmol/L Female: 1.86–2.48 mmol/L
Mean corpuscular volume (MCV)	80–100 μm^3	80–100 fl
Mean corpuscular hemoglobin (MCH)	25.4–34.6 pg/cell	0.39–0.54 fmol/cell
Mean corpuscular hemoglobin concentration (MCHC)	31%–36% Hb/cell	4.81–5.58 mmol Hb/L

Routine Coagulation Investigations

For Answer Refer to Synopsis-"Coagulation Test" Pg. No. 512

SHORT NOTES

1. Write a note on iron-deficiency anemia. *(CCS, MGR)*

Answer

Iron-deficiency Anemia

Iron-deficiency anemia is the most common cause of anemia, which occurs due to either deficiency of dietary iron or decreased absorption of iron in the body. This results in microcytic and hypochromic red cells on the peripheral blood smear.

Pathophysiology

- It is the most common form of anemia.
- In case of insufficient intake or absorption, body depletes its iron stores over the time. This occurs without reducing the serum iron levels and can be assessed by serum ferritin measurements. This is the initial stage.
- In the second stage, the Hb levels decrease.
- In the third or final stage that is considered iron-deficiency anemia, the Hb levels further fall and RBC production is limited and abnormal RBCs are produced by the body.

Etiology

- Iron-deficiency anemia results from prolonged negative iron balance.
- Causes of iron-deficiency anemia include:
  - Increased iron loss
    - Internal bleeding
    - Menstruation
    - Childbirth
    - Chronic blood loss
  - Inadequate iron intake
  - Increased iron demand
    - Increased demands during childhood, pregnancy
  - Decreased iron absorption
    - Due to GI surgeries
    - Intake of drugs that impair iron absorption.

Clinical Presentation

- Fatigue and generalized weakness
- Palpitations
- Pallor
- Dizziness or light-headedness
- Tachycardia
- Headache
- Irritability
- Shortness of breath
- Brittle spoon shaped nails—koilonychia
- Angular cheilosis
- Splenomegaly
- Cold extremities
- Frequent infections
- Atrophic Glossitis
- Decreased mental acuity.

Laboratory Diagnosis of Iron-deficiency Anemia

- CBC
  - Hb—Decreased
  - Hematocrit—Decreased
  - RBC count—Decreased
  - WBC count—Decreased
  - Platelet count—Normal
  - MCV—Decreased
  - MCH—Decreased
  - MCHC—Decreased
  - RBC distribution width—Increased
  - Reticulocyte count—Normal or increased
  - Platelet count—Normal or increased in patients who had bleeding
  - ESR—Normal or slightly increased
- **Peripheral blood smear**
  - Microcytic, hypochromic red cells
  - Poikilocytosis (variation in shape).

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- Anisocytosis or variation in cell size
- Elliptically form RBC
- Target cells, pencil cells
- Polychromatic cells.

- **Bone marrow:**
  - Erythroid hyperplasia (increased cellularity)
  - M:E ratio decreased
  - Normoblastic erythropoiesis with predominance of small polychromic normoblasts
  - Dyserythropoiesis—Mild
  - Sideroblast—Reduced
  - Cytoplasmic basophilia—Present
- **Biochemical findings:**
  - **Serum iron:** Decreased
  - **Serum ferritin:** Decreased, reflecting poor iron stores in tissues
  - **Total iron binding capacity:** Raised
  - **Serum transferrin receptor protein:** Increased and indicates total red cell mass
  - **Red cell protoporphyrin:** Decreased, due to insufficient iron supply.

2. **Explain the types of anemia.** ***(CCS)***

Answer

Anemia

A condition, marked by either deficiency of red blood cells or hemoglobin in the blood, resulting in pallor, malaise and weakness.

Classification of Anemia

- Anemia is commonly classified into various types based on the following factors:
  - Based on etiology—Etiologic classification
  - Based on morphology—Physiologic classification.

Types of Anemia Based on Etiology

Anemia Due to Blood Loss

- **Acute blood loss:** Trauma (hemorrhage)
- **Chronic blood loss:** GIT bleeding, menstruation blood loss or helminthic infestation.

Anemia Due to Decreased RBC Synthesis

- **Inherited genetic defect:**
  - Defect leading to stem cell depletion: Fanconi anemia, telomerase defects.
  - Defect leading to erythroblast maturation: Thalassemia syndrome.
- **Nutritional deficiency:**
  - Deficiencies affecting DNA synthesis: Vitamin B_{12} and folate deficiency.
  - Deficiencies affecting hemoglobin synthesis: Iron-deficiency.
- **Erythropoietin deficiency:** Anemia of chronic disease, renal failure
- **Immune mediated injury of progenitors:** Aplastic anemia, pure red cell aplasia
- **Inflammation-mediated iron sequestration:** Anemia of chronic disease
- **Primary hemopoietic neoplasms:**
  - Acute leukemias, myelodysplasia, myeloproliferative disorders
- **Space occupying marrow lesions:** Metastatic neoplasms, granulomatous disease
- **Infection of red cell progenitors:** Parvovirus B19 infection
- **Unknown mechanism:** Endocrine disorders, hepatocellular liver diseases.

Increased Red Cell Destruction/Hemolytic Anemia

- **Inherited genetic defect:**
  - **Red cell membrane disorders:** Hereditary spherocytosis, hereditary elliptocytosis, enzyme deficiencies
  - **Hexose monophosphate shunt enzyme deficiencies:** G6PD deficiency, glutathione synthetase deficiency
  - **Glycolytic enzyme deficiencies:** Pyruvate kinase deficiency, hexokinase deficiency, hemoglobin abnormalities.
  - **Deficient hemoglobin synthesis:** Thalassemia syndromes
  - **Structurally abnormal globins (hemoglobinopathies):** Sickle cell anemia, unstable hemoglobin.
- **Acquired genetic defects:**
  - Deficiency of phosphatidylinositol—linked glycoproteins: PNH
  - Antibody mediated destruction
    - Hemolytic disease of newborn (Rh disease), transfusion reactions
    - Drug induced, autoimmune disorders
  - **Mechanical trauma:**
    - **Microangiopathic hemolytic anemias (MAHA):** Hemolytic uremic syndrome (HUS), DIC, TTP
    - **Cardiac traumatic hemolysis:** Defective cardiac valves
    - **Repetitive physical trauma:** Bongo drumming, marathon running, karate chopping.

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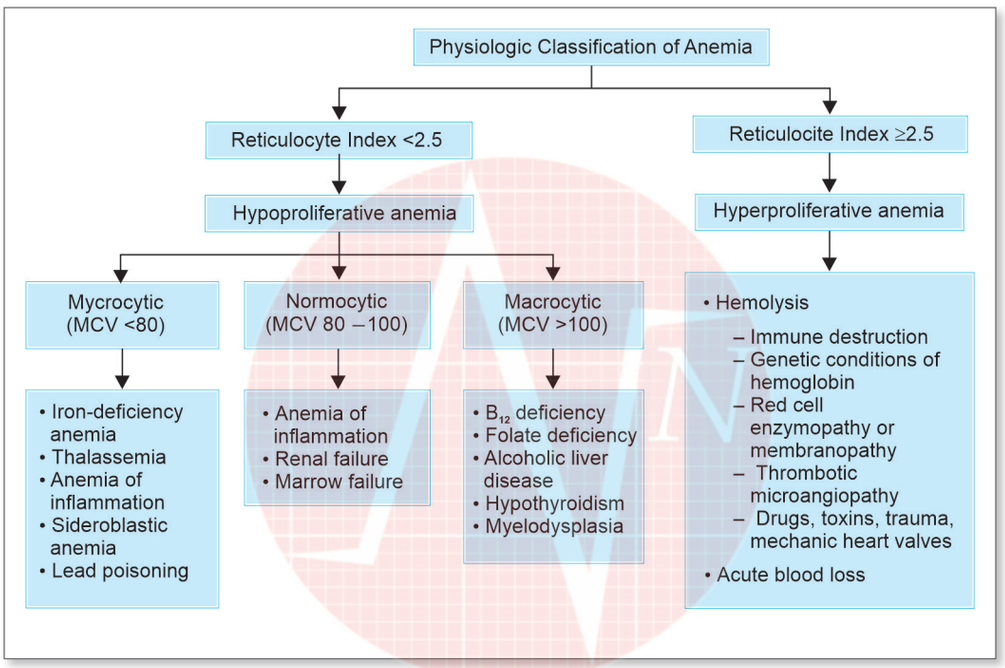
- **Infection of red cells:** Malaria, babesiosis
- **Toxic or chemical injury:** Clostridial sepsis, snake venom, lead poisoning
- **Membrane lipid abnormalities:** Abetalipoproteinemia, severe liver disease
- **Sequestration:** Hypersplenism.

Physiologic Classification of Anemia



3. Write a note on Coombs test. *(CCS)*

Answer

Coombs Test

This test is used to detect the incomplete antibodies present in serum. These antibodies coat antigens, but donot agglutinate them.

Principle of Coombs Test

- When human gamma globulin directed against such incomplete antibodies are made to react with these incomplete antibodies and agglutination takes place.
- Normal human RBC in the presence of antibody directed toward the antigen they possess, may fail to agglutinate when centrifuged and become sensitized.
- Sensitization of RBCs may be with the immunoglobulin G or complement.
- For the agglutination to occur, an additional anti-antibody or anti-complement factors that would react with the Fc portion of the Ig G or with the C3b component are required.
- This will lead to the formation of bridge between the antibodies or complement coating the red cells leading to agglutination.
- The RBC coating or sensitization can occur in viro or in vivo following incubation at 37°C with serum containing antibody.

Methods

1. Direct Coombs Test

- This method detects the incomplete antibodies coated on the surface of red cells.
- RBCs are separated from the blood of such patients, and suspension is prepared in normal saline.
- Now, antibodies against the incomplete antibodies coating RBCs are added, which bind with these incomplete antibodies and lead to agglutination of RBCs. This is positive Coombs test.
- Results
  - Positive result
    - Agglutination or clumping of blood cells occurs.

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- Negative result
  - No clumping is seen. This means you have no antibodies to RBCs.
- Indications
  - Hemolytic disease of newborn
  - Autoimmune hemolytic anemia.

2. Indirect Coombs Test

- Here we detect the incomplete antibodies present in a person's sera.
- The serum from the patient is taken and added to suspension of O positive RBCs. If the serum contains incomplete antibodies against Rh antigen, it will coat the O positive RBCs. The suspension is washed many times to remove excess unbound antibodies in the serum.
- Thereafter, Coombs serum is added. If agglutination occurs, the test is said to be positive.
- Indications
  - In crossmatching of blood to detect incomplete antibodies in donor's serum.
  - In case of Rh negative mother whose 1st child is Rh positive.

Indications of Coombs Test

- Hemolytic anemia
- Chronic lymphocytic leukemia
- Erythroblastosis fetalis
- Mycoplasmal infections
- Systemic lupus erythematosus
- Syphilis.
- Infectious mononucleosis
- Abortion in Rh negative female.

	Observation	Conclusions
Positive control (PC)	• Agglutination • No Agglutination	• Correctly performed test procedure. • Coombs serum may not be proper. • Repeat the sample.
Negative control (NC)	It should show no agglutination, because saline does not contain Anti-D or any other antibodies.	
Test (Serum) (T)	• Agglutination (and if PC results are correct) • No agglutination	• Patient's serum contains Anti-D. • Patient's serum does not contain Anti-D.

4. Write in short about blood grouping and crossmatching. *(RUHS, CCS)*

Answer

Blood Grouping

- A total of 30 blood group systems have been described. Each blood group system is a series of red cell antigens, determined by genetic loci.
- The blood group system of clinical importance is ABO and Rh.
- Minor blood group systems include MNS, Duffy, Keil, Kidd.

ABO and Rh Blood Group Systems

Properties	ABO system	Rh system
Blood groups	4 main blood groups: A, B, AB and O	Rh positive and negative
Genetic loci	On chromosome 9	On chromosome 1
Antigens and antibodies	Group / Antigen / Antibody: O / H / Anti-A and Anti-B A / A / Anti-B B / B / Anti-A AB / A and B / None	• C, c, D, E, e Antigens • 'd' indicates the absence of D • Anti-D antibody: Most important
Antigens also seen on/in	Endothelial and epithelial cell Plasma, saliva, semen (Not is CSF)	No other cells
Type of Ab	IgM; naturally occurring antibodies	IgG; do not occur naturally
Clinical importance	• Anti-A and anti-B Ab can cause severe intravascular hemolysis after incompatible transfusion • ABO-matching is required before transplantation of solid organs	Rh –ve individuals make anti-D Ab if: • Transfused with Rh +ve blood or, • Rh –ve pregnant women, is exposed to Rh +ve fetal RBCs that have crossed the placenta

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Bombay Blood Group/Bombay Phenotype

- It is characterized by the absence of A, B and H antigens on red blood cells and the presence of anti-A, anti-B and anti-H antibodies.
- It presents genetically as homozygous HH gene.
- Clinical importance of Bombay blood group:
  - These are clinically typed as O blood group, but they cannot receive blood group O blood donation.
  - They can be safely transfused with other Bombay blood group only.
  - These are very rare.

Crossmatching of Blood

- It is a procedure performed prior to the transfusion of blood or blood products to detect any serological incompatibilities in the donor's or recipient's blood.
- Crossmatching is done to prevent any transfusion reaction that may occur after or during transfusion.

Clinical Importance of Crossmatching

- To detect the most of the recipient antibodies directed against the donor's red blood cells antigens
- To the detect most of the donor antibodies directed against the recipient's red blood cell antigens
- To detect major errors in the ABO grouping, labeling and identification of donor and recipients.

Principles of Crossmatching

- Crossmatching is based on the principle of serological detection of any clinically significant irregular/unexpected antibodies in either donor or recipient's blood.
- There are two types of cross matches as follows:
  1. **Major cross match**: It involves testing the donor's red cells with recipient's serum to determine the presence of any antibody which may cause hemolysis or agglutination of donor red cells. This is more important than minor cross match.
  2. **Minor cross match**: It involves testing of donor's plasma with recipient's red cells to determine the presence of any antibody which may cause hemolysis or agglutination of recipient's red cells.

Types of Crossmatching

Types of crossmatching	Donor's	Recipient's
Major	RBCs	Serum/Plasma
Minor	Serum/plasma	RBCs

5. Write a note on Benedict's test for urine sugar. *(RUHS)*

Answer

Benedict's Test

Benedict's test is a chemical analytical test used for the detection of reducing sugar in a solution/urine.

Principle of Test

- Benedict's test: When heated, it changes to orange red/ brick red. This is due to the reducing property of simple carbohyrdrates (monosaccharides – glucose and fructose).
- The copper ions (cupric) in the Benedict's solution are reduced to (cuprous) ions resulting in color change

Benedict's Reagent

Copper sulphate	17.3 g
Sodium or potassium citrate	173.0 g
Sodium carbonate (crystallized)	200.0 g
Distilled water	1000 mL

Procedure

- 5 mL of Benedict's reagent is boiled in a test tube.
- After cooling, addition of 8 drops of protein free urine.
- Boil the mixture for 2 minutes and then cool.
- A yellow to red precipitate indicates the presence of reducing sugar. It detects 0.15%– 0.2% of glucose in the urine.

Interpretation

- **If color changes to green:** 0.1–0.5% sugar in solution
- **If color changes to yellow:** 0.5–1.0% sugar in solution
- **If color changes to orange:** 1–1.5% sugar in solution
- **If color changes to red:** 1.5–5% sugar is present
- **If colour changes to brick red:** <2% sugar is present in solution
- **Positive Benedict's test:** Formation of a green yellow to reddish precipitate within 3 minutes. Example—Glucose.

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SHORT ANSWER QUESTIONS

1. State two difference between bleeding and clotting time. ***(MGR, CCSU)***

Answer

Differences between Bleeding and Clotting Time

Criteria	Bleeding Time	Clotting Time
Purpose	Measures the ability of blood vessels to constrict and form a platelet plug.	Evaluates the efficiency of the coagulation cascade and the formation of a fibrin clot.
Clinical Significance	Abnormal bleeding time may indicate disorders related to platelet function, such as thrombocytopenia, von Willebrand disease.	Prolonged clotting time may suggest deficiencies in coagulation factors and Conditions such as hemophilia, liver disease, or vitamin K.

2. State five complications of transfusion reaction. ***(MGR)***

Answer

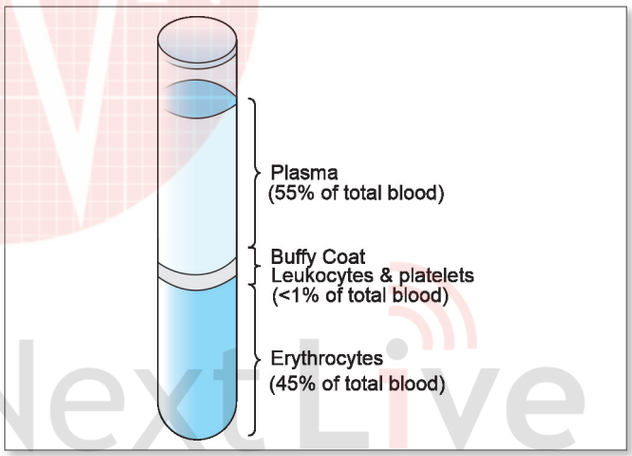
Five Complications of Transfusion Reaction

1. **Hemolytic acute reaction:**
   - **Reason:** Blood types of the donor and the receiver are incompatible.
   - Signs and symptoms include hemoglobinuria, back discomfort, fever, chills, and perhaps fatal consequences.
2. **Sensitivity response:**
   - **Reason:** Hypersensitivity to elements in the blood substitute.
   - Hives, itching, and, in extreme situations, anaphylaxis are the symptoms.
3. **Transfusion-associated circulatory overload (TACO):**
   - **Reason:** Excessive or quick transfusion volume.
   - Signs and symptoms include fluid accumulation, coughing, and dyspnea.
4. **Hemolytic reaction delay:**
   - **Reason:** Immune systems delayed reaction to a tiny incompatibility that was missed during early testing.
   - **Symptoms:** Jaundice, a progressive drop in hemoglobin levels.
5. **Graft-versus-host disease (GvHD):**
   - **Reason:** Tissues that are attacked by donor lymphocytes.
   - Symptoms include liver dysfunction, diarrhea, and rash.

3. Enlist components of blood. ***(CCS)***

Answer

- Blood is a fluid connective tissue that consists of plasma, blood cells and platelets. It circulates throughout our body delivering oxygen and nutrients to various cells and tissues.
- **Components of blood:**
  - Red blood cells (Erythrocytes)
  - White blood cells (Leukocytes)
  - Platelets
  - Plasma



4. Define blood bank. Write two uses of blood bank. ***(CCSU, MGR)***

Answer

- Blood bank is a place where blood is collected from donors, typed, separated into components, stored, and prepared for transfusion to recipients.
- A blood bank may be a separate free-standing facility or part of a larger laboratory in a hospital. Two uses of blood bank are:
  1. Collection and storage of blood before it is used for transfusion
  2. Help in determining the blood type

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5. Enumerate the mechanism of blood grouping. *(MGR)*

Answer

In blood transfusion, the two most important group systems examined are the ABO system and the Rhesus system.

1. The ABO blood group system
   - It consists of 4 types of blood groups—A, B, AB, and O
   - Mainly based on the antigens and antibodies on red blood cells and in the plasma.
2. The Rh blood group system
   - It consists of 50 defined blood group antigens.
   - In the Rh system, the most important antigens are D, C, c, E, and e.

Blood Group	Antigens	Antibodies	Can give blood (RBC) to	Can receive blood (RBC) from
AB	A and B	–	AB	AB, A, B, O
A	A	B	A and AB	A and O
B	B	A	B and AB	B and O
O	–	A and B	AB, A, B, O	O

CONCEPTUAL REVISION

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Golden Points

- Hemoglobin is made up of 'heme' means something that contains iron and 'globin' means protein.
- Photoelectric colorimeter method is the recommended method for hemoglobin estimation.
- Blood is composed of formed elements known as "blood cells" and fluid matrix called "plasma".
- The Prothrombin time measures the time necessary to generate fibrin after activation of factor VII.
- Packed cell volume is the volume (in percentage) occupied by the red blood cells obtained after the centrifugation of whole blood sample.
- ESR is performed to assess the prognosis of inflammatory activity in the body.
- Red blood cell (RBC) indices measure the size, shape, and quality of red blood cells.
- Anemia is a condition due to either deficiency of red blood cells or hemoglobin in the blood, resulting in pallor, malaise and weakness.
- Blood bank is a place where blood is collected from donors, typed, separated into components, stored, and prepared for transfusion to recipients.
- Transfusion reaction is an unfavourable transfusion related event, occurring in a patient during or after transfusion of blood components.

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MULTIPLE CHOICE QUESTIONS

1. Erythrocyte sedimentation rate:

a. Is of diagnostic value
b. Is of prognostic value
c. Shows three layers in a capillary tube
d. Is used to prepare a red cell button for smears

Ans. b. Is of prognostic value

2. Decreased ESR is seen in:

a. Sickle cell anemia
b. Increased fibrinogen
c. Anemia
d. Hypoviscosity

Ans. a. Sickle cell anemia

3. Which of the following blood components has the shortest shelf life?

a. Red Blood Cells
b. Platelets
c. Fresh frozen plasma
d. Cryoprecipitate

Ans. b. Platelets

4. Bleeding time increases in which of the following conditions?

a. Von Willebrand disease
b. Hemophilia A
c. DIC
d. Both a and c

Ans. d. Both a and c

5. Eosinophillia is found in:

a. Cryptococcus
b. HPV
c. Stronglyloides
d. Typhoid

Ans. c. Stronglyloides

6. In obstructive jaundice, which of the following enzyme is elevated?

a. GGT
b. AST
c. ALT
d. LDH

Ans. a. GGT

7. Most common malignancy of blood is:

a. ALL
b. CLL
c. AML
d. CML

Ans. a. ALL

8. Normal white cell count in an adult is:

a. 20, 000–30,000/mL
b. 4000–11,000/mL
c. 15000–20000/mL
d. <10000/mL

Ans. b. 4000–11,000/mL

9. Size of red blood cell is measured by:

a. MCHC
b. MCV
c. MCH
d. ESR

Ans. b. MCV

10. Hematocrit is the ratio of:

a. Platelets to whole blood
b. WBCs to whole blood
c. RBCs to whole blood
d. None of the above

Ans. c. RBCs to whole blood

Adult Health Nursing

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Section Outline

PART I ADULT HEALTH NURSING-I

PART II ADULT HEALTH NURSING-II

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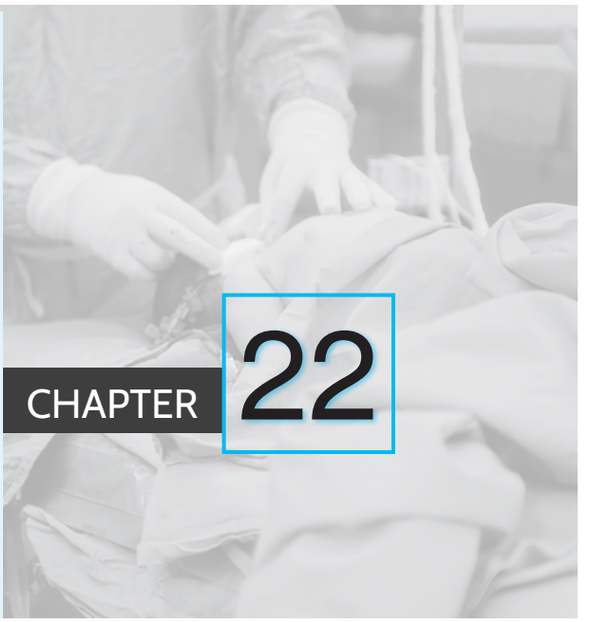
Nursing Management of Patients in Critical Care Unit



CHAPTER 22

CONCEPTUAL THEORY

Terminology

Acidosis: Excessive amount of acid production and accumulation of acid in blood.
It can respiratory and metabolic.
Central line: Intravenous line placed in a large vein that goes to the heart.
Chest tube: Tube inserted in the chest to withdraw air or fluids from the lungs.
Edema: Swelling due to large amount of fluid accumulation in tissues.
Murmur: Abnormal heart sound.
Ventilator: It is a medical equipment that mechanically ventilates a patient who is physically unable to breathe.

CRITICAL CARE NURSING

Critical care nursing is defined as care focused on utmost care of the critically ill or unstable patients following extensive injury, surgery or life-threatening disease.

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Principles of Critical Care Nursing

Principle	Rationale
Never leave the patient alone	Critically ill patients are unconscious or semiconscious usually; may remove invasive lines and tubes or self extubate quickly. Always there is the risk of life-threatening changes in the critically ill patient conditions.
Nurse patient ratio must be 1:1	Each nurse must be responsible for complete observation and care of the patient and she/he can detect changes immediately. This is done for avoiding any miscommunication and mind divert of nurse to any other patient.
Continue ECG monitoring	Intensive monitoring is must for critically ill patient. Alarms are left on ECG at all times.
Analyze and obtain ECG strip	ECG strips are analyzed and recorded every four hours to determine hemodynamic stability.
Every Hour: Vital signs	Regular vital stability is key for critically ill patient.
4 hours temperature	Changes in the temperature indicate infection in the body.
Hourly neurological assessment	Patients with neurological problems must have hourly assessment by using Glasgow Coma Scale for any improvement or deterioration signs
Change position in every 2 hours	To allow skin perfusion and relieve pressure points
Chest physiotherapy every 4 hours	Immobility can cause retention of secretions and reduced ventilations

Contd...

Principle	Rationale
Range of motion exercise	ROM exercise is recommended for critically ill patient to prevent contracture formation, frozen joints and to promote venous return.
Mouth care every four hours	To prevent mouth ulcer and in intubated patients, reduce risk of ventilator associated pneumonia.
Restrain patients	According to the hospital policy, nurse should restrain patient to ensure the tube and lines are not disconnected.
Personal care in night shift	Bathing, nail care, and hair care washing must be done in night shift as night is less hectic.
Explain the procedures	All the procedures must be explained to the patient or patient's relatives.
Provide emotional and psychological support	Critical condition causes stress to the patient and family members.
Safe environment	To reduce risk of fall, accidents to patient, visitors or staff.
Isolation technique	As per infection control policy, minimize cross infection to the patients, staff and visitors.
Labeling-medication, IV bags, any tubes and drains, hemodynamic transducers and monitors	To reduce risk of error
Medication review	All medications upon admission to the unit should be reviewed by the critical care doctor to ensure optimal treatment.
Written order	All the treatment and care must be written by critical care physician to maintain consistent management and care.
Not at bedside	Narcotics should not be kept at bedside locker with other medicines to maintain narcotic control.
Limited visitors	To prevent infection, to promote privacy and to accommodate space limitation
IV access to heparin lock	In critically ill patients, there is always a risk of rapid resuscitation with IV drugs or fluid, if needed.
Change the shift	During change of shift, reports will include a review of all physician's orders, lab reports, medication administration and complete documentation to reduce potential errors.
Wear personal protective equipment	To prevent cross infection.

INTENSIVE CARE UNIT

Physical set up of ICU

The physical set up of an ICU varies from hospital to hospital from an open cube to single room. Here, we will discuss about 200-bedded hospital ICU, the physical set up is as:

- **Size:** Factors affecting size of IU are:
  - Number of acute bed: 12% of beds are for ICU in acute hospitals, 20% of beds are for ICU in tertiary care hospitals
  - Types of bed pediatric or adult
  - Occupancy of wards
  - History of refusal
  - Number of operation theaters
  - Availability of space
  - Medical equipment
  - Location
  - Ability to transfer patient
- **Patient area:**
  - Area should be at least 215 sq ft in cubicle and 250 sq ft for single room.
  - The nonsplash handwash basin should be kept there.
  - There should be adequate separation between beds for infection control.
  - The cubicle should be rectangular for adequate space.
  - There should be 3 ft distance from wall to head in each side for appropriate examination from each side.
  - Utilities in each bed space should be:
    - 4 oxygen
    - 3 air
    - 3 suction
    - 16 to 20 power outlet
    - A bedside light
    - A telephone and data outlet
- **Central station/Nurse's station:**
  - About 100 to 150% space is required for nurse's station.
  - It is used for the following:
    - Communication
    - Monitoring
    - Drugs
    - Documentation/Recording and reporting
    - Emergency trolley/Crash cart
    - Storage

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- Nurse's office
- Consultation office
- On call/Clinical doctor's room
- Staff room
- Reception area
- Relative room
- Procedure room
- Multipurpose room
- Patient's bathroom.

Equipment and Supplies in ICU

- Ventilator
- Bag mask
- Endotracheal tube
- Laryngeal tube
- Laryngeal mask
- Tracheostomy tube
- Oropharyngeal airway
- Nasopharyngeal airway
- Combi-tube
- Cardiac monitor
- Pulse oximeter
- Nasogastric tube
- Intravenous tube
- Nasojejunal tube
- Arterial line
- Percutaneous endoscopic gastrostomy tube
- Central line
- PICC line.

NURSING MANAGEMENT OF CRITICALLY ILL PATIENT

Following parameters are monitored in critically ill patient by nurse:

Parameters	Description
Temperature Normal (96.8 F)	Body temperature is an indicator of balance between heat produced and heat loss. It may be affected by the following: • Infection • Sepsis • Skin exposure • Oral temperature taken after eating
Blood pressure Normal (120/80 mmHg)	Blood pressure measures the blood flow in the arteries. In blood pressure systole, diastole and pulse pressure is measured. Factors affecting blood pressure are as: • Sedatives • Pain • Position • Medication • Vessel wall elasticity • Cardiac output • Vascular blood volume
Respiratory rate Normal (12 -20 breaths/min)	A low and high respiration is indication of clinical deterioration. Following are common terminologies used in respiratory rate: • Tachypnea: Increased rate • Bradypnea: Decreased rate • Dyspnea: Difficulty in breathing • Hypoxia: Insufficient oxygen in cellular level • Hypoxemia: Low level of oxygen in blood • Anoxia: Lack of oxygen
Pulse monitoring Normal (60 to 100 av. 70)	Pulse is generated when blood is pushed into the vessels by contraction and relaxation of heart. The factors affecting pulse are: • Age • Medication • Hyper and hypovolemia • Existing medical condition Pulse incorporates not only heart rate but also strength of pulse, regularity and rhythm of pulse is also considered.
Oxygen saturation Normal (95% to 100%)	Oxygen saturation is one of the vital monitoring parameters to measure arterial oxygen saturation. Less than 90% indicates critical conditions.
Level of consciousness	Usually, patients in critical care unit are unconscious or sedated, therefore, level of consciousness is very important to monitor to know about cerebral function. Glasgow coma scale and AVPU (Alert, painful stimulation, verbal stimulation and unresponsiveness). Factors affecting LOC are: • Sedative • Analgesics • Opioids • Hypoxia • Hyperglycemia • Alcohol • Hypotension • Cerebral pathology
Pain monitoring	Monitoring pain is important in critically ill person as pain can increase anxiety and cause other body functions to suffer. Tools used to assess pain are as: • Numeric pain scale • Analogue scale • Behavioral pain scale • Critical care pain observation scale.

Contd...

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Parameters	Description
Urine output monitoring	Urine output is an indicator of renal perfusion and cardiac output. Terminologies associated with urine output are: • **Anuria:** Less than 50 mL urine output in 24 hours • **Oliguria:** Less than 400 mL urine output in 24 hours • **Polyuria:** Less than 3000 mL in 24 hours • **Dysuria:** Painful urination
Continuous ECG Monitoring	The ECG should be monitored continuously from cardiac monitor for patient with arrhythmias or rapidly changing heart rate.
Pulmonary Artery Catheter Monitoring	A PAC is inserted via central vein in pulmonary artery. It is used to determine cardiac output, preload and measured central venous oxygen saturation. Potential indications for pulmonary artery catheterization are: • Cardiac tamponade • Complicated heart failure • Complicated MI • Ventricular septal rupture • Hemodynamic instability • Pulmonary hypertension
Intracranial pressure monitoring	The ICP monitoring is standard for patients with: • Brain disorder • Head injury • Hydrocephalus • Intracranial hypertension • Postembolic management of arteriovenous malfunction
Central venous pressure monitoring	Through the jugular vein, catheter measures the blood pressure in central venous compartment. It is important to measure central venous pressure in patients with renal or cardiac overload.
End tidal CO_2 monitoring	End tidal CO_2 is measured through Capnography and it shows CO_2 in exhaled air which is related to CO_2 level in blood and ventilation status.
Blood test monitoring	The routine monitoring of blood includes: • Electrolytes • Complete blood count • Coagulation profile • For TPN patient- Liver enzyme • Blood culture in case of fever • ABG • Glucose monitoring • Cardiac markers

ADVANCED CARDIAC LIFE SUPPORT (ACLS)

The ACLS algorithm adds the following to the BLS algorithm: rhythm recognition in cardiac arrest, resuscitation medications, treatment of reversible causes of cardiac arrest, and advanced airway management. Maximizing high-quality CPR and early defibrillation remain the most important factors for survival and good neurological outcome

ACLS Algorithm

- Priority 1: CPR
  - Perform high-quality CPR for at least 2 minutes before the first rhythm check.
  - Avoid interrupting CPR unless it is for rhythm and pulse checks and/or shock delivery.
  - Consider an advanced airway only if necessary and feasible without major interruption of CPR.
- Priority 2: Rhythm and pulse check
  - Attach monitors and/or defibrillator pads.
  - Pause CPR for no longer than 10 seconds for rhythm recognition in cardiac arrest.
  - Shockable rhythms (Vfib or pulseless VT): Proceed to defibrillation; draw up epinephrine PLUS either amiodarone OR lidocaine.
  - Nonshockable rhythms (pulseless electrical activity or asystole): Do not defibrillate; draw up epinephrine.

Repeat rhythm and pulse check every 2 minutes, resuming CPR in between each check.

- Priority 3: Defibrillation of shockable rhythms
  - Deliver a shock (e.g., 200 J biphasic) as soon as Vfib or pulseless VT is recognized.
  - Resume CPR immediately after shock and continue for 2 minutes until next rhythm and pulse check.
  - If a second attempt at defibrillation is unsuccessful, administer resuscitation medications.
- Priority 4: Resuscitation medications
  - Obtain peripheral IV/IO access and administer medications without interrupting CPR.
  - Nonshockable rhythms: Administer epinephrine 1 mg IV/IO as soon as possible; repeat every 3–5 minutes as needed.
  - Shockable rhythms
- After 2nd unsuccessful cycle of defibrillation: administer epinephrine 1 mg IV/IO; repeat every 3–5 minutes as needed.
- After 3rd unsuccessful cycle of defibrillation, administer:
  - Amiodarone 300 mg IV/IO once, then 150 mg IV/IO once after 3–5 minutes
  - OR lidocaine 1–1.5 mg/kg IV/IO once, then 0.5–0.75 mg/kg IV/IO once after 3–5 minutes
  - Re-evaluate indications and dosage at each subsequent rhythm and pulse check.
- Priority 5: Hs and Ts
  - Address these in parallel with CPR, defibrillation, and resuscitation medications.

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5Hs:

- Hypovolemia
- Hypoxia
- Hyperkalemia/hypokalemia
- Hydrogen ions (acidosis)
- Hypothermia

5Ts:

- Tension pneumothorax
- Tamponade (cardiac)
- Toxins
- Thrombosis (pulmonary)
- Thrombosis (coronary)

CARDIOPULMONARY RESUSCITATION (CPR)

Approach

- For sudden cardiac arrest, use the CAB approach to begin chest compression as soon as possible.
  - Chest compressions
  - Airway
  - Breathing
- Prioritize airway and breathing (i.e., ABC approach) for cardiac arrest secondary to respiratory arrest.
- Minimize interruptions to CPR.
- If the diagnosis of cardiac arrest is uncertain, initiating CPR is preferable to withholding CPR.

Chest Compressions

- Chest compression technique differs in children, infants, and neonates.
- Key targets for high-quality chest compressions:
  1. Compression rate: 100–120 per minute
  2. Compression depth for adults: 5–6 cm (2–2.5 inches)
  3. Allow full chest recoil between compressions.

Chest compressions ratio			
	Adult	**Child**	**Infant**
Single rescuer	30:2	30:2	30:2
Double rescuer	30:2	15:2	15:2
Hand placement for chest compressions			
	Adult	**Child**	**Infant**
Single rescuer	2 hand technique	1 or 2 hand technique	2 finger technique
Double rescuer	2 hand technique	1 or 2 hand technique	2 thumb encircling technique

Provider Positioning and Technique (Adults and Children; Excluding Infants)

1. Kneel or stand next to the patient depending on whether they are on the ground or in a bed, respectively.
2. Place the hands (one on top of the other, fingers interlaced) over the sternum.
3. Keep the arms straight (do not bend the elbows); the shoulders should be directly above the hands.
4. Use full body weight to deliver rapid, firm compressions.
   - Patient positioning: supine on a firm surface
   - Minimizing interruptions
     - Restart CPR between rhythm analysis and shock delivery (while the defibrillator is charging).
     - Resume CPR immediately after shock delivery

Rescue Breathing

Mouth-to-mouth

- Open the airway using the head-tilt/chin-lift maneuver.
- Pinch the patient's nose closed.
- Form a tight seal over the patient's mouth.
  - Breathe slowly into the patient's mouth for ~ 1 second; check for chest rise to confirm sufficient ventilation.
  - Move away from the patient's mouth between breaths to allow air to escape, ensuring the patient's airway remains open.
    - **If equipment is available:** Ventilate with 100% O_2; select a modality based on patient factors and provider expertise.
    - **Bag-Mask ventilation(with or without basic airway adjuncts):** Administer 2 breaths after every 30 chest compressions.

Advanced Airway

- Maintain an uninterrupted rate of 10 breaths/minute.
- Do not interrupt CPR for >10 seconds to facilitate placement of an advanced airway.
- Return to BMV if an advanced airway has not been secured within 10 seconds.

USE AND CARE OF CRITICAL CARE BIOMEDICAL EQUIPMENT

Definition

Intensive care unit (ICU) equipment includes patient monitoring, respiratory and cardiac support, pain management devices, emergency resuscitation and other life support equipment.

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Life Support and Emergency Resuscitation Devices

- Mechanical Ventilator
- Laryngoscope
- Airway
- Infusion pump
- Crash cart (Resuscitation cart)
- Intra-aortic balloon pump
- Continuous positive air pressure machine (CPAP)
- Defibrillator.

Bedside Monitor

A bedside monitor is a display of major body functions on a device that looks like a television screen or computer monitor.

Role of Nurse

- Check properly each connection so as to get a desired reading.
- Any abnormality in a reading is signalled by an alarm so inform doctor immediately.

Central Venous Line or Catheter

- A central venous catheter is a special IV line that is inserted into a large vein in the body.
- Several veins are used for Central venous catheters including those located in the shoulder (subclavian vein), neck (jugular vein), and groin (femoral vein)

Role of Nurse

- Monitor the signs of complications
- Assess for patency of the CVP line.
- Sterile dressing should be done to prevent infection (CVP care per the Hospital protocol)
- The length of the indwelling catheter should be recorded and regularly monitored.

ICP Monitor

ICU patients who have sustained head trauma, brain hemorrhage, brain surgery, or conditions in which the brain may swell might require intracranial pressure monitoring.

Role of Nurse

- Optimizing cerebral tissue perfusion
- Preventing infection
- Maintaining patient's airway
- Maintaining negative fluid balance.

Infusion Pump

An intravenous infusion pump is a machine that carefully controls the rate at which IV fluids and/or medications are given.

Role of Nurse

- Using aseptic technique and universal precautions, IV infusion should be set
- Setting the flow rate as prescribed, calculating the amount of fluid.
- Observe for the signs of infiltration such as thrombophlebitis, fluid or electrolyte overload and embolism before administration.

Resuscitation Cart (Crash Cart)

The resuscitation cart contains all of the equipment and medications needed for Advanced life support and CPR (cardiopulmonary resuscitation).

Role of Nurse

- Keep the resuscitation cart ready all the time.
- Check the devices and ensure that the devices are kept in charging
- Check for the emergency (life saving) medication for their expiry date.

Defibrillator

A defibrillator is a device that is designed to pass electrical current through a patient's heart. The passing of electrical current through the heart is called defibrillation. A defibrillation is done through pads placed on the patient's chest.

Role of Nurse

- Keep the patient in comfortable position and obtain 12-lead ECG
- Give the patient 100% oxygen by inhalation.
- Apply electrode paste on the DC paddle, rub it and apply the paste at the patient's chest in the second intercostal space at the right side of breast line and at the apex of the heart.
- TURN OFF the oxygen to the patient as a spark from paddle could blow the oxygen on the fire.
- Be sure to say "ALL CLEAR". No one should touch the patient or the bed during cardioversion.
- Check the rhythm on ECG monitor.
- Keep the patient in comfortable position and give 100% oxygen by inhalation.

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- Report and record the procedure
- Clean the paddle area with spirit swab
- Keep the defibrillator on continue electrical charging.

Maintenance of ICU Equipment

- Since ICU equipment are used continuously on critically ill patients, it is essential that equipment be properly maintained, particularly devices that are used for life support and resuscitation.
- Staff in the ICU should perform daily checks on equipment and inform biomedical engineering staff when equipment needs maintenance, repair, or replacement.
- For mechanically complex devices, service and preventive maintenance contracts are available from the manufacturer or third-party servicing companies, and should be kept current at all times.

TRANSITIONAL CARE

Transitional care or care transition is defined as a set of actions designed to ensure the coordination and continuity of healthcare as follows:

- Patient's transfer between different locations or different levels of care within the same location.
- Representative locations include (but are not limited to) hospitals, subacute and postacute nursing facilities, the patient's home, primary and specialty care offices, and long-term care facilities.

Elements of Transitional Care

- Communication
- Changes in plan of care
- Medication reconciliation
- Follow-up tests and services
- Education of the patient and family
- Transfer of all information when site of care changes
- Involvement of team during hospitalization, discharge, follow-up, etc.

Role of Transitional Care Nurse

- The TCN role is very different from a traditional nursing position. It incorporates the skills of a nurse, care manager, and patient advocate and knowledge of evidence-based care, managing complexity, palliative care, active engagement of family caregivers, interdisciplinary team care, theories and strategies for individualized care and behavioral change, quality improvement, and organization, delivery and financing of services across an episode of acute care.
- Healthcare transitions ensure safe and efficient movements of patients between different sectors of care within the healthcare system.
- Transition as a concept is central to the nursing discipline as a whole. Nurses often are the primary health professionals involved in encounters with patients and their families that relate to transitional periods of instability.

ETHICAL AND LEGAL ISSUES

Informed Consent

- Informed consent implies to permission by the patient to perform an act on his body either for diagnosis or therapeutic procedure.
- The four elements of consent are:
  1. Voluntariness
  2. Capacity
  3. Knowledge
  4. Decision making.

Types of Consent

- Implied Consent
- Expressed consent (verbal written).

Points to be Considered in Consent

- Consent must be given voluntarily
- If patient is not mentally capable (critical patients), informed consent should be obtained from surrogate or legal next of kin.
- It should be given by a person of sound mind and above the age of 18 years.
- Requires the disclosure of basic information considered necessary for decision making.
- Patients providing consent should be free from pain and depression.

MEDICOLEGAL CASE

- Request of the patient or relatives or friend for not registering the case as Medicolegal should not be accepted.
- The MLC should be registered as soon as physician suspect' foul play or case brought several days after the incident.
- The MLC is received in hospital by; any case brought by police for the purpose of examination and reporting and any case referred for expert management and advice.
- Following cases should be considered as MLC and to be intimated to the police regarding such cases:
  - All cases of injuries
  - All cases of burn
  - Alleged cases of assault
  - All cases of suspected or evident of poisoning or intoxication
  - Case referred from court.

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- Cases of suspected or evident criminal abortion
- Cases of unconscious/comatose where its cause is not natural or not clear
- Cases brought dead/dead on arrival/sudden unexpected death, etc.
- Cases of suspected self inflicted injuries or tempted suicide

- The important considerations in MLC are notification to police, collection and preservation of samples, recording of dying declaration, etc.

END STAGE CARE

Definition of Loss

Loss is any situation either potential or perceived in which a valued object is changed or is no longer accessible to individual. Because change is major constant in life.

Types of Loss

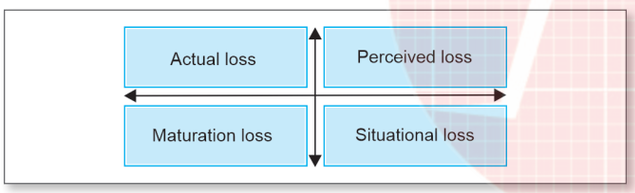

Figure 22.1: Stages of grief

Signs of Approaching Death

Cardiac dysfunctions	• Failing cardiac function is one of the first signs • The apical pulse rate may reach 100 or more per minute
Peripheral circulation change	• Reduced cardiac output compromises peripheral circulation and impairs cellular metabolism and produces less heat. • Skin become pale and cold.
Pulmonary function	• Failure of heart pumping results in less exchange of gases • Decreased O_2 saturation.
CNS function alterations	• Continuous episodes of apnea • Less sensory functions
Renal impairment	• Low cardiac output results in decreased urine volume
Gastrointestinal tract	• Peristalsis decreases • Increased nausea and vomiting.

Role of Nurse in End Stage Care

- Relief for physical symptoms
- Achieving quality of life
- Maintaining an independent patient
- Relief from mental and social isolation
- Family support
- Reduce isolation, fear and anxiety

CONCEPTUAL EXERCISES

LONG ANSWER QUESTION

1. a. **Explain principles of critical care nursing.**
   b. **Discuss physical set up of ICU in 200 bedded hospital.**
   c. **How to maintain infection control in ICU? *(RUHS)***

Answer

a. Principles of Critical Care Nursing

Definition

Critical care nursing is defined as care focused on utmost care of the critically ill or unstable patients following extensive injury, surgery or life-threatening disease.

Principles

Principles	Rationale
Never leave the patient alone	Critically ill patients are unconscious or semiconscious usually; may remove invasive lines and tubes or self extubate quickly. Always there is the risk of life-threatening changes in the critically ill patient conditions.
Nurse patient ratio must be 1:1	Each nurse must be responsible for complete observation and care of the patient and she/he can detect changes immediately. This is done for avoiding any miscommunication and mind divert of nurse to any other patient.
Continue ECG monitoring	Intensive monitoring is must for critically ill patient. Alarms are left on ECG at all times.

Contd...

Principles	Rationale
Analyze and obtain ECG strip	ECG strips are analyzed and recorded every four hours to determine hemodynamic stability.
Every hour: Vital signs	Regular vital stability is key for critically ill patient.
Every 4 hours: Temperature	Changes in the temperature indicate infection in the body.
Hourly neurological assessment	Patients with neurological problems must have hourly assessment by using Glasgow Coma Scale for any improvement or deterioration signs
Change position in every 2 hours	To allow skin perfusion and relieve pressure points
Chest physiotherapy every 4 hours	Immobility can cause retention of secretions and reduced ventilations
Range of motion exercise	ROM exercise is recommended for critically ill patient to prevent contracture formation, frozen joints and to promote venous return.
Mouth care every four hours	To prevent mouth ulcer in intubated patients, reduce risk of ventilator associated pneumonia.
Restrain patients	According to the hospital policy, nurse should restrain patient to ensure the tube and lines are not disconnected.
Personal care in night shift	Bathing, nail care, and hair care washing must be done in night shift as night is less hectic.
Explain the procedures	All the procedures must be explained to the patient or patient relatives.
Provide emotional and psychological support	Critical condition causes stress to the patient and family members.
Safe environment	To reduce risk of fall, accidents to patient, visitors or staff.
Isolation technique	As per infection control policy, minimize cross infection to the patients, staff and visitors.
Labeling-medication, IV bags, any tubes and drains, hemodynamic transducers and monitors	To reduce risk of error
Medication review	All medications upon admission to the unit should be reviewed by the critical care doctor to ensure optimal treatment.
Written order	All the treatment and care must be written by critical care physician to maintain consistent management and care.
Not at bedside	Narcotics should not be kept at bedside locker with other medicines to maintain narcotic control.
Limited visitors	To prevent infection, to promote privacy and to accommodate space limitation
IV access to heparin lock	In critically ill patients, there is always a risk of rapid resuscitation with IV drugs or fluid, if needed.
Change the shift	During change of shift, reports will include a review of all physician's orders, lab reports, medication administration and complete documentation to reduce potential errors.
Wear personal protective equipment	To prevent cross infection.

Contd...

b. Physical Setup in ICU in 200-Bedded Hospital

- The physical set up of an ICU varies from hospital to hospital from an open cube to single room.
- Here we will discuss about 200-bedded hospital ICU, the physical set up is as follows:
  - **Size:** Factors affecting size of IU are:
    - Number of acute bed: 12% of beds are for ICU in acute hospitals, 20% of beds are for ICU in tertiary care hospitals.
    - Type of bed: Pediatric or adult
    - Occupancy of wards
    - History of refusal
    - Number of operation theaters
    - Availability of space
    - Medical equipment
    - Location
    - Ability to transfer patient
  - **Patient area:**
    - Area should be at least 215 sqft in cubicle and 250 sqft for single room
    - The nonsplash handwash basin should be kept there.
    - There should be adequate separation between beds for infection control.
    - The cubicle should be rectangular for adequate space.
    - There should be 3ft distance from wall to head in each side for appropriate examination from each side.

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- **Utilities in each bed space should be:**
  - 4 oxygen
  - 3 air
  - 3 suction
  - 16 to 20 power outlet
  - A bedside light
  - A telephone and data outlet
- **Central station/nurse's station:**
  - About 100 to 150% space is required for nurse's station.
  - It is used for the following:
    - Communication
    - Monitoring
    - Drugs
    - Documentation/recording and reporting
    - Emergency trolley/crash cart
    - Storage
    - Nurse's office
    - Consultation office
    - On call/clinical doctor's room
    - Staff room
    - Reception area
    - Relative room
    - Procedure room
    - Multipurpose room
    - Patient's bathroom

c. Maintenance of Infection Control in ICU

- It is defined as measures practiced by healthcare personnel to prevent spread, transmission and acquisition of infection between clients, from healthcare providers to clients and from client to healthcare providers.
- Infection control in ICU depends on the following

Standard Precautions

- Set of infection control practice used to prevent transmission of diseases that can be acquired by contact with blood, body fluids, nonintact skin and mucus membrane.
- Standard precaution steps are as:
  - Handwashing
  - PPE (Personal protective equipment, like, gloves, gown, face mask)
  - Decontamination
  - Waste disposal

Hand washing	• Hand washing is the single most effective measure in infection control • Moments of handwashing: ■ Before touching patient ■ Before clean/aseptic procedure ■ After body fluid exposure risk ■ After touching a patient ■ After touching patient's surrounding
Personal Protective Equipment	• Gloves • Gown • Mask • Protective eye wear • Face shield • Apron
Decontamination/ Disinfection	• High level disinfectants: ■ 2% glutaraldehyde ■ 1% sodium hypochlorite • Intermediate level disinfectants: ■ 0.1% sodium hypochlorite ■ Iodophores and phenolic solutions • Low level disinfectants: ■ Quaternary ammonium compounds. • Sterilization: ■ Dry heat ■ Moist heat ■ Chemical sterilization ■ Radiation sterilization
Waste disposal	• Waste is segregated through proper color coding of bins: ■ Yellow: Human waste, expired medicine, chemical liquid waste ■ Red: Contaminated plastic waste ■ Blue/white: Sharp waste including metals

Contd...

SHORT NOTES

1. Write about infection control in ICU. *(RUHS)*

Answer

For Ans, Refer to Long Question 1, Pg. No. 1008

2. Write about monitoring critically ill patient in ICU. *(RUHS)*

Answer

Refer to Synopsis "Nursing Management of Critically Ill Patient" Pg. 1003

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3. Write about Cardiopulmonary resuscitation (CPR). *(RUHS)*

Answer

Definition

Cardiopulmonary resuscitation is an emergency lifesaving procedure performed when heartbeat or breathing has stopped. CPR is also called basic life support (BLS).

Indications

- Cardiac arrest or absence of pulse and respiration.
- Cardinal signs of cardiac arrest are:
  - Apnea, absence of femoral or carotid pulse.
  - Dilated pupil (due to cerebral hypoxia)
- Sequence of CPR is "CAB": C- Compression, A- Airway, B- Breathing, defibrillator.

General Instructions

- Recognize cardiac arrest by careful assessment of unconsciousness along with absence of pulse for maximum of 10 seconds before CPR.
- If client is not breathing or only gasping, activate the emergency response system and obtain an automated external defibrillator or monophasic or biphasic defibrillator bases on setting or availability of equipments.
- Start CPR within 3 to 4 minutes of cardiac arrest to avoid permanent brain damage.
- The patient should be placed supine on firm, flat surface with care taken to protect cervical spine if traumatic injury is suspected.

Procedure

Compression	
Check Pulse for 10 seconds	Carotid (adult), femoral (child), brachial (infant) If pulse is found to be absent start 30 chest compressions.
Compression depth	2 inches (5cm) in adults, 1/3rd the depth of chest size in child, 1.5 inches (4cm) in infants.
Compression rate	• 100 to 120/minute for adults, child and infant. • Breath rate should be 10 breaths per minute, 1 breath every 6 to 8 seconds.
Landmark of compression	• Center of chest between nipples for adult and children. • Just below nipple line for infant.
Compression to ventilation ratio	• For children and infant: 30:2 for single rescuer and 15:2 for two rescuers. • For adult: 30:2 for single and double rescuers.

Contd...

Compression	
Part of hand used	• Use palm of both hands for adult • One or both palms for children • For infants use two fingers if rescuer is single, use thumb encircling technique if rescuers are two

Airway

Breathing

- Breathing is assessed by listening for breath sounds at nose and lips, watching chest rise and fall.
- If neck is suspected to be injured, use head tilt chin maneuver or jaw thrust maneuver to provide ventilation.
- Once airway is cleared, provide two continuous breaths; give 10 to 12 ventilations per minute.
- Provide mouth to mouth ventilations; below air through mouth after pinching nostrils.
- Use resuscitation bag or bag mask if available.

Defibrillator

- Also called automated external defibrillator (AED), an electrical device that delivers an electrical shock that completely depolarizes the myocardium, producing a brief period of systole.
- NEVER use in under 8 years of children or anyone weighing below 25 kgs.

Two paddles of defibrillator	White paddle below clavicle and red paddle at apex of heart at left side.
Joules of energy	Biphasic 120 to 200 J, monophasic 360 J For one counter shock, resume CPR for 2 minutes. Repeat it until breathing is restored.

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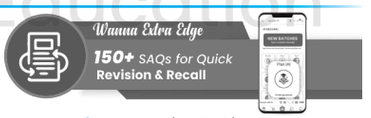
SHORT ANSWER QUESTIONS



1. List indications for oxygen therapy. *(MGR)*

Answer

Oxygen therapy is given to a patient who has low oxygen saturation that is lower than 90% on oximeter. The indications are as follows:

- Dyspnea
- Cyanosis
- Cardiac failure
- Shock
- Cyanide poisoning.

2. Enumerate drugs used in critical care unit. *(MGR)*

Answer

- Critical care unit is defined as a special department of hospital or healthcare facility that provides intensive care.
- It is also called intensive therapy unit or intensive care unit.
- **The drugs used in this unit are:**
  - **Lignocaine**: Used for acute treatment of ventricular arrhythmias from myocardial infarction, digitalis intoxication, etc.
  - **Labetalol:** For hypertensive emergencies. Used for the management of mild to severe hypertension
  - **Amiodarone:** Used for life-threatening ventricular arrhythmias
  - **Nitroglycerine:** Treatment of angina pectoris, CHF, pulmonary hypertension, control of blood pressure
  - **Morphine:** To get relief from pain of myocardial infarction, moderate to severe acute and chronic pain, etc.
  - **Propofol:** Used in the intubated patients on mechanical ventilation. For induction or maintenance of anesthesia

3. Write about standard precautions to prevent transmission of infection during patient's care. *(MGR)*

Answer

The methods of standard precaution to prevent transmission of infection during patient care are as follows:

1. Hand washing properly before and after patient care
2. Use of appropriate protective equipments before patient care.
3. Respiratory hygiene, i.e., covering mouth while cough or sneeze.
4. Safety devices should be implemented to prevent contact with needles and other sharps.

4. Why is an unconscious patient kept in lateral recovery position? *(MGR)*

Answer

an unconscious patient is kept in lateral recovery position because it keeps the airway clear and open. It also prevents aspiration of vomit or any kind of secretions which can cause choke.

5. What is VAP bundle?

Answer

VAP Bundle

- The ventilator associated pneumonia prevention bundle (VAP bundle) is a tool to improve practice to minimize risk of VAP (ventilator associated pneumonia) and reduce the mortality rate of VAP.
- **Elements of VAP bundle:**
  - Use of chlorhexidine after daily mouth care
  - Use of subglottic secretion drainage for patients ventilated for more than 48 hours.
  - Head elevation at least 30°
  - Assessment of weaning and extubation
  - Review of sedation.

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CONCEPTUAL REVISION

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Golden Points

- Critical care nursing is a defined as care focused on utmost care of the critically ill or unstable patients following extensive injury, surgery or life-threatening disease.
- Body temperature is an indicator of balance between heat produced and heat loss. It may be affected by the following: infection, sepsis.
- Usually patients in critical care unit are unconscious or sedated, therefore, level of consciousness is very important to monitor to know about cerebral function through. Glasgow coma scale and AVPU (Alert, painful stimulation, verbal stimulation and unresponsiveness).

- Electrocardiogram is a record of the electrical conduction system of the heart in the waveform to evaluate the heart's structure and function.
- The patient and nurse ratio in critical care unit is 1:1.
- Coronary care unit is a specialized intensive care unit for critically ill patients with cardiac and coronary artery disease.
- ECMO machine is mainly used to reduce the level of carbon dioxide from blood by pumping blood through an external oxygenator.
- Crash cart, also known as " Code cart", is a trolley with a set of trays/drawers/shelves that contain lifesaving equipment, drug and devices necessary to perform a code.
- Surgical site infections are the most common hospital acquired infections in the surgical patients.
- Standard precautions are set of infection control practices used to prevent transmission of diseases that can be acquired by contact with blood, body fluids, nonintact skin and mucous membrane.

MULTIPLE CHOICE QUESTIONS

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1. _____of end stage cardio sympathy patients awaiting transplantation need mechanical support.

a. 16 to 30 b. 11 to 12
c. 15 to 30 d. 18 to 29

Ans. c. 15 to 30

2. Critical care nursing is required for patients who need/have?

a. Life-threatening b. Specialized nursing
c. Intensive care d. All of them

Ans. d. All of them

3. The six chest leads (pericardial) V1, V2, V3, 18- V4, V5, V6 view the body in the horizontal Plane to the _____

a. Av node b. Val node
c. AVF node d. AVR node

Ans. a. Av node

4. In preparing a patient in the ICU for oral ET intubation, what should the nurse do?

a. Place the patient supine with the head extended and the neck flexed.
b. Tell the patient that the tongue must be extruded while the tube is inserted.
c. Position the patient supine with the head hanging over the edge of the bed to align the mouth and trachea.
d. Inform the patient that while it will not be possible to talk during insertion of the tube, speech will be possible after it is correctly placed.

Ans. a. Place the patient supine with the head extended and the neck flexed

5. What are ventricular assist devices (VADs) designed to do for the patient?

a. Provide permanent, total circulatory support when the left ventricle fails
b. Partially or totally support circulation temporarily until a donor heart can be obtained
c. Support circulation only when patients cannot be weaned from cardiopulmonary bypass
d. Reverse the effects of circulatory failure in patients with acute myocardial infarction (MI) in cardiogenic shock

Ans. b. Partially or totally support circulation temporarily until a donor heart can be obtained

6. What should the nurse do to prevent arterial trauma during the use of the IABP?

a. Reposition the patient every 2 hours.
b. Check the site for bleeding every hour.
c. Prevent hip flexion of the cannulated leg.
d. Cover the insertion site with an occlusive dressing.

Ans. c. Prevent hip flexion of the cannulated leg

7. In preparing the patient for insertion of a pulmonary artery catheter, what should the nurse do?

a. Place the patient in high Fowler's position.
b. Obtain an informed consent from the patient.
c. Perform an Allen test to confirm adequate ulnar artery perfusion.
d. Ensure that the patient has continuous electrocardiographic (ECG) monitoring.

Ans. c. Perform an Allen test to confirm adequate ulnar artery perfusion.

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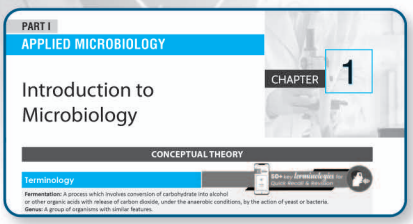

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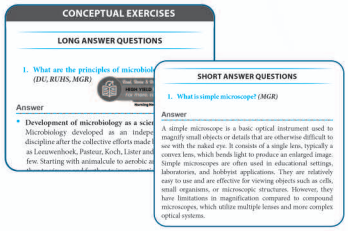

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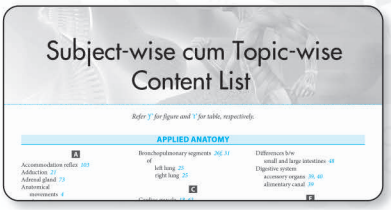

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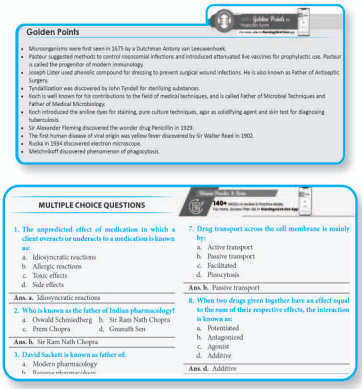

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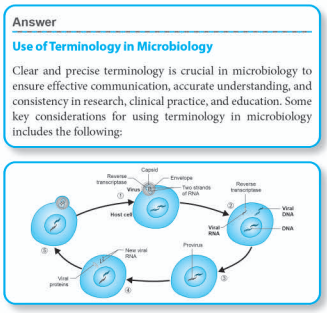

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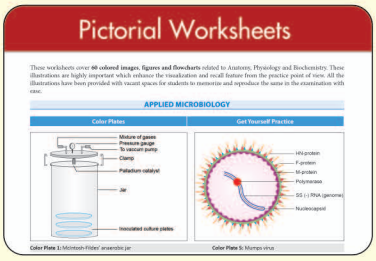

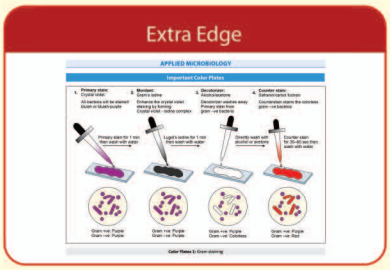

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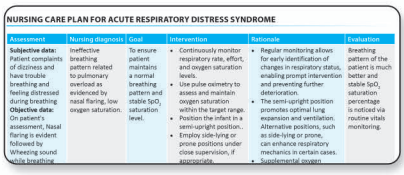

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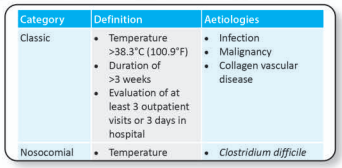

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