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Anju Dhir

Physio Brid Series

Textbook of Microbiology

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Anju Dhir

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About the Author

Anju Dhir *PhD (Microbiology)*, has served as lecturer of Microbiology at Shivalik Institute of Nursing, Shimla, Himachal Pradesh. After completing her MSc in Microbiology from Central Research Institute, Kasauli, she did PhD in microbiology from Maharaja Vinayak Global University (MVGU) Jaipur, Rajasthan. She holds gold medal in microbiology. Being a keen observer and having passion for teaching, she has dedicated herself in imparting training to the young microbiologists. She has been in teaching profession for the last 25 years. Her thesis and research paper have been published in many International Journals.

Apart from Microbiology, she is equally passionate about literature and has contributed chapters to reference book on English literature. Her online book on "Indian Common Krait – Bungarus caeruleus' has been published by Amazon on kindle. She shares knowledge throught presentations on slideshare.com by Linkedin. Knowledge of microbiology is foundation stone in health industry. The present book is one more milestone in her career which certainly is going to help the students by transforming their knowledge into practicality.

Preface

This book is an attempt to present the vast knowledge of microbiology in a simple and easy-to-understand language for degree course students in the field of physiotherapy. The book has been written keeping in view the proposed syllabus recommended by Ministry of Health, India. Not even a single topic is excluded as each topic has its unique importance.

I have tried to provide all the basic concepts of microbiology. The contents are expressed in lucid language accompanied by short and long answers. "Concept to Clinic" given in the chapters make this book more useful for students. MCQs given at the end of each chapter will help students to assess their knowledge on the specific topic. "Must Know" serves as a way of imparting extra knowledge related to the topic. The texts are supplemented by tables, and figures to make the chapters easy to be apprehended by a reader.

The book contains 18 chapters divided into A–E sections. Section A deals with General Microbiology, Section B deals with Immunology, Section C is focused on medically important bacteria, Section D discusses Virology and Section E explains Mycology. Special attention is paid to clinically relevant topics under the heading Clinical/Applied Microbiology.

Terminology is compiled at the end of the book for ease of reading.

I hope that this textbook of microbiology will serve as a standard guide for the students of Physiotherapy.

Anju Dhir

Acknowledgments

"Let difficulties know you are too difficult."
—APJ Abdul Kalam

Teachers are also learners, and in a teacher-learner relationship, knowledge is co-constructed by the two in a partnership. I have felt that my knowledge increased day by day while teaching. Creative elucidation is impossible without modest acknowledgment to one's helping hands. It is an essential part of any innovative work to fuel passion and make people feel acknowledged and cherished at the same time.

I am gratified to **"The Universe"** for giving me inspiration and energy to do such a big task. Writing a book requires a lot of patience and I found that "Patience is also a Form of Action". While doing this project, I evolved within.

My sincere thanks go to **My Mother** for her constant support, and to my son **Nityam**, who has always been a reason to live.

I owe gratitude to my students who always liked my lectures and inspired me to write this book. Therefore, thanks are due to my lovely students for their love and encouragement.

In fact, it's not money but the acknowledgment of his/her work that motivates a writer—a craving is always there in a writer for his or her work to be appreciated. I hope that my mental creation is cherished by all the readers.

I extend my special thanks to **Mr Satish Kumar Jain** (Chairman) and **Mr Varun Jain** (Managing Director), M/s CBS Publishers and Distributors Pvt Ltd for their wholehearted support in publication of this book. I have no words to describe the role, efforts, inputs and initiatives undertaken by **Mr Bhupesh Aarora** [Sr. Vice President – Publishing & Marketing (Health Sciences Division)] for helping and motivating me.

Last but not least, I sincerely thank the entire CBS team for bringing out the book with utmost care and attractive presentation. I would like to thank Dr Divya Gupta (Senior Content Strategist cum Quality Check), for her tireless efforts to provide valuable inputs, Ms Nitasha Arora (Publishing Head and Content Strategist – PGMEE and Medical) for her editorial support. I would also extend my thanks to Mr Shivendu Bhushan Pandey (Sr. Manager and Team Lead), Mr Ashutosh Pathak (Sr. Proofreader cum Team Coordinator) and all the production team members for devoting laborious hours in designing and typesetting the book.

Special Features of the Book

LEARNING OBJECTIVES

After studying the chapter, reader will be able to:

- Discuss the characteristics of mycobacteria.
- Describe the diseases such as tuberculosis, leprosy.
- Get familiar with treatment regimen for tuberculosis.

Learning Objectives indicate the competencies that a student will achieve after reading the chapter.

Every chapter begins with a **Chapter Outline** to provide a glimpse of the content discussed.

CHAPTER OUTLINE

- Significance of Normal Flora
- Normal Flora on Skin
- Normal Flora on Nails
- Normal Flora of Mouth and Respiratory Tract
  - Normal Flora of Mouth
  - Normal Flora of Upper Respiratory Tract

MUST KNOW

The strict anaerobic conditions and bacterial waste products are factors that inhibit the growth of other bacteria in the large bowel.

Facts that grossly affect a particular situation are presented in **Must Know** boxes.

Numerous **Tables** have been used to provide necessary data in compiled form.

Table 10.3: Differences between active and passive immunity

Active immunity	Passive immunity
Produced actively by host's immune system	Received passively. No active participation of host's immune system
Induced by infection or by immunogens	Readymade antibodies are induced
Long lasting and effective	Short lasting and less effective
Immunity develops only after lag period	Immunity develops immediately

Images and Flow Diagrams have been used to simplify the concepts for the students.

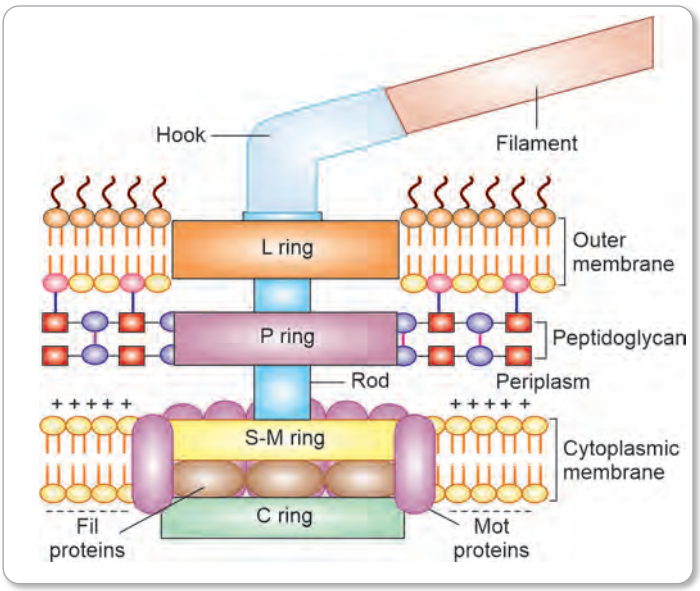


Fig. 4.2: Structure of bacterial cell wall with flagellum

Case Scenario

A 60-year-old man came with a history of persistent cough for 2 months. Since 6 months, he was feeling weakness with weight loss. Last week he had blood in sputum. He was HIV-positive too.

Microbiological Discussion/Laboratory Diagnosis

Revised National Tuberculosis Control Program (RNTCP) guidelines

- **Collection of sputum and making smear:** Sputum smear microscopic technique is quick, easy, inexpensive and simple. The results are available within a few hours. A night before the test, the patient is advised to drink lots of fluids like tea or water. It helps the body to make more sputum overnight. Morning sample is preferred and it is collected in sterile sputum collecting cup.

Case Scenarios based on real time cases have been presented for better practical overview.

Concept to Clinic box correlates the discussed topic with health care.

Concept to Clinic

History taking is very important in TB. In gauging the environmental conditions and social determinants, not only predisposition to TB can be identified but in many cases prognosis may be predicted. Having a balanced nutritious diet aids pharmacological treatment and overall recovery.

Recent Updates

The extensively drug-resistant TB is resistant to at least four of the core anti-TB drugs. It is due to the resistance to the two most powerful anti-TB drugs that are isoniazid and rifampicin in addition to resistance to any of the fluoroquinolones (moxifloxacin or levofloxacin) and to at least one of the three injectable (kanamycin, amikacin or capreomycin) second-line drugs. This type of TB takes longer to treat. Here, use of second-line anti-TB drugs is required that may be more expensive and result in more side effects.

Recent Updates are added with relevant topics for giving updated content.

Practical boxes highlight the important laboratory tests.

Practical

Dick test: It is used to know about the immune status of an individual. Positive test indicated by erythema means that the person is susceptible to scarlet fever infection.

- Dick test is a neutralization test.
- 0.2 mL of standard toxin of *streptococcus pyogenes* is injected intradermally in one forearm and the heat inactivated toxin is injected intradermally in another forearm, as control reading are taken after 24 hours.
- Positive result-erythema of 1 cm diameter which indicates susceptibility towards scarlet fever and requires immediate immunization.

Applied aspect

Beta-propiolactone

Beta-propiolactone (BPL) is a condensation product of ketone and formaldehyde. It is used in 0.2% solution for inactivation of vaccines, biological products and heat-sensitive equipment. Beta-propiolactone *is biocidal, but carcinogenic* also. It is *capable of killing all micro including viruses*. It forms sporicidal vapors in combination with UV radiations and can remove HBV from blood products.

Relevant **Applied Aspects** of the topis are given to emphasize their values in healthcare industry.

Each and every chapter ends with **Summarized one-liners** for quick revision of the chapter.

SUMMARY

- Various antimicrobials either inhibit or destroy the metabolic properties of bacteria.
- Antimicrobials are known as 'wonder drugs' used to save many lives from deadly infections.
- The antimicrobial treatment causes some side effects.
- Antimicrobial resistance occurs when infections due to bacteria, viruses, fungi and parasites are treated with the unwise use of antimicrobials.
- The replication of organisms accidentally develops mechanisms to avoid destruction by antimicrobials.
- **MRSA and MDRO** can cause infections in any part of the body, including bloodstream, urinary tract, lungs, skin, wounds or surgical site.

ASSESS YOURSELF

At the end of every chapter, **Assess Yourself** section has been included to help the students to assess their understanding of the discussed topics.

Long Answer Questions

1. How will you identify an organism in a pathological sample?
2. What are the main methods for identification of a microorganism in a lab?

Short Answer Question

1. Write notes on:
   a. Molecular techniques for identification of microorganisms
   b. Serological techniques for identification of microorganisms

Multiple Choice Questions

1. The microscopy reveals:
   a. Morphology of organism
   b. Arrangement of organism
   c. Size of organism
   d. All are correct

2. To isolate a microorganism it needs to be:
   a. Inoculated in a medium
   b. Injected in an animal
   c. None is correct
   d. Both (a) and (b) are correct

Syllabus

MICROBIOLOGY

Theory **60 Hours**

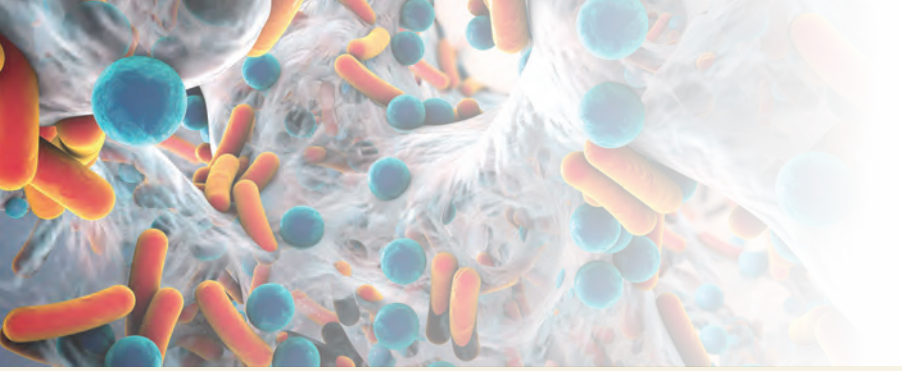
- **General Microbiology**
  - **Definitions:** Infections, parasite, host, vector, fomite, contagious disease, infectious disease, epidemic, endemic, pandemic, zoonosis, epizootic, attack rate.
  - Normal flora of the human body.
  - Routes of infection and spread; endogenous and exogenous infections; source and reservoir of infections.
  - **Bacterial cell:** Morphology limited to recognizing bacteria in clinical samples; shape, motility and arrangement; structures associated with virulence.
  - **Physiology:** Essentials of bacterial growth requirements.
  - Sterilization, disinfection and universal precautions in relation to patient care and disease prevention; definition of asepsis, sterilization, disinfection.
  - Brief description of identification of infectious diseases; principles of prevention of infectious diseases caused by common pathogens.
  - **Antimicrobials:** Mode of action, interpretation of susceptibility tests, resistance spectrum of activity.
- **Immunology**
  - Basic principles of immunity immunobiology: lymphoid organs and tissues. Antigen, Antibodies, antigen and antibody reactions with relevance to pathogenesis and serological diagnosis.
  - Humoral immunity and its role in immunity. Cell mediated immunity and its role in immunity. Immunology of hypersensitivity. Measuring immune functions. Autoimmunity.
- **Bacteriology:** To be considered under the following headings.
  - Morphology, classification according to pathogenicity, mode of transmission, methods of prevention, collection and transport of samples for laboratory diagnosis, interpretation of laboratory reports.
  - Staphylococci, Streptococci and Pneumococci.
  - **Mycobacteria:** Tuberculosis, M. leprae, atypical mycobacteria, Enterobacteriaceae.
  - **Vibrois:** V. cholerae and other medically important vibrios, Campylobacters and Helicobacters, Pseudomonas.
  - Bacillus anthracis; Sporing and non-sporing anaerobes: Clostridia, Bacteroides and Fusobacteria.
- **General Virology**
  - **General properties:** Basic structure and broad classification of viruses. Pathogenesis and pathology of viral infections. Immunity and prophylaxis of viral diseases. Principles of laboratory diagnosis of viral diseases. (HIV, Hepatitis, Polio, Measles, Rubella, Herpes). List of commonly used antiviral agents.

- **Mycology**
  - General properties of fungi. Classification based on disease: superficial, subcutaneous, deep mycosis opportunistic infections including Mycotoxins, systemic mycoses.
  - General principles of fungal diagnosis. Rapid diagnosis. Method of collection of samples. Antifungal agents.
- **Clinical/Applied Microbiology** (as relevant to diseases such as)
  - Streptococcal infections: Rheumatic fever and rheumatic heart disease, meningitis.
  - Tuberculosis.
  - Pyrexia of unknown origin, leprosy.
  - Sexually transmitted diseases, poliomyelitis.
  - Hepatitis.
  - Acute-respiratory infections, central nervous system infections, urinary tract infections.
  - Pelvic inflammatory disease, wound infection, opportunistic infections, hiv infection.
  - Malaria, filariasis, zoonotic diseases.
  - Burns.

Contents

SECTION B IMMUNOLOGY

SECTION C BACTERIOLOGY



CHAPTER 9

Antimicrobials—Resistance

LEARNING OBJECTIVES

After studying the chapter, reader will be able to:

- Discuss antimicrobial emergence.
- Discuss the antimicrobial resistance.
- Describe antimicrobial stewardship program.

CHAPTER OUTLINE

- Antibiotics
  - History
  - Definitions
  - Antibiotic Therapy
  - Precautions During Antibiotic Therapy
  - Misuse of Antimicrobials
  - Adverse Events During Treatment with Antimicrobials
- Antimicrobial Resistance
  - Present Scenario of Antimicrobial Resistance (WHO)
- Antimicrobial Sensitivity Testing
  - Disk Diffusion Method
  - Dilution Method
  - Automated Method for Antibiotic Sensitivity
- Antimicrobial Stewardship

INTRODUCTION

Nearly half of hospitalized patients receive antimicrobial agents. Antimicrobial therapy is based on the *theory of selective toxicity* that is antimicrobials can kill microorganisms without causing harm to the body of a patient.

For an antimicrobial to be effective, a fixed dose has to be given to a patient otherwise it could harm him/her.

MUST KNOW

Difference between a dose necessary for the treatment of disease and the one that may harm a person is large and is called the *therapeutic index*.

Mostly antimicrobial drugs have uninvited side effects but fortunately, these effects are not very regular in occurrence.

ANTIBIOTICS

Various antimicrobials either *inhibit or destroy the metabolic properties of bacteria*. For example, penicillin inhibits the peptidoglycan in the cell wall of bacteria.

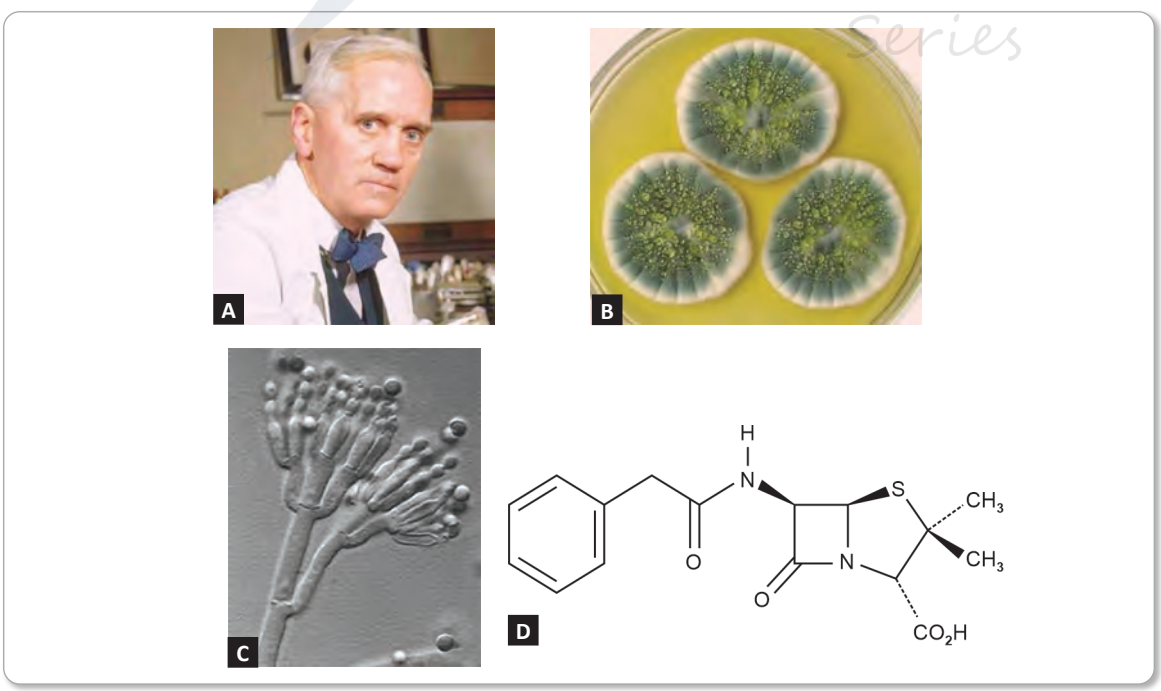
History

Antibiotics were known by their activities long before they were given this specific name that means *"against life"*. Many years ago, Chinese used moldy curd to treat boils and controlled foot infections by wearing sandals with layer of mold. Pasteur and Joubert realized that growth of anthrax bacillus was inhibited by certain other microorganisms growing in the culture plate. In 1929, Alexander Fleming observed that *Staphylococcus aureus* growth was inhibited when a mold accidently grew in it.

Later on this accidental drug was known as wonder drug—Penicillin and was found to be produced by *Penicillium notatum* (Figs 9.1A to D). Streptomycin produced by *Streptomyces griseus* was the second antibiotic invented by Dr Selman Waksman in 1948. Antibiotics belong to the broader group of *antimicrobial compounds* that are used to treat infections caused by microorganisms including fungi and protozoa. Antibiotics were originally produced by *natural* living organisms like aminoglycosides produced by *Streptomyces* genus, but some are *semisynthetic* like cephalosporins, carbapenems or *synthetic* like the *sulfonamides*, quinolone and oxazolidinones

Definitions

Selectivity: It is a property by which a drug toxicity works selectively toward the bacterium rather than the host. Based on this property antibiotics from disinfectants can be distinguished.



Figs 9.1A to D: A. Alexander fleming; B. Colony of *Penicillium notatum*; C. Hyphae of *P. notatum*; D. Structure of penicillin

Therapeutic index: It is the ratio of the "dose toxic to the host" to the "effective therapeutic dose". More is the therapeutic index the better is the antibiotic.

Categories of antibiotics: Antibiotics are categorized as bactericidal—kill the susceptible bacteria and bacteriostatic—reversibly inhibit the growth of bacteria.

Antibiotic susceptibility testing: The quantitative measure of the *in vitro* activity of antibiotics is the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC).

MIC: It is the lowest concentration of the antibiotic inhibiting visible growth under standard conditions.

MBC: It is the lowest concentration of the antibiotic that kills 99.9% of the original inoculum in a given time.

Antibiotic Therapy

Principles

The antibiotic therapy is based on *theory of selective toxicity* that is antibiotic can kill microorganism without causing harm to body of patient. Various antibiotics either *inhibit or destroy the metabolic properties of bacteria*. For example, penicillin inhibits the peptidoglycan in the cell wall of bacteria.

For an antibiotic to be effective, a fixed dose has to be given to a patient otherwise it could harm him/her. This difference between a dose necessary for treatment of a disease and the one that may harm a person is large and is called *therapeutic index*. Mostly antimicrobial drugs have uninvited side effects but fortunately these effects are not very regular in occurrence.

Classification

Antibiotics may be divided into *two broad categories* according to their effect on microorganisms: *bactericidal agents*, those that kill bacteria and *bacteriostatic agents*, those that inhibit bacterial growth.

Broad spectrum: Antimicrobial agents are called *broad spectrum* when they act against a wide range of Gram-positive and Gram-negative bacteria like tetracycline, erythromycin and cephalosporin.

Narrow spectrum: They can be *narrow spectrum* with limited action like penicillin to Gram-positive bacteria. Metronidazole is also a narrow spectrum antibiotic because of its activity against strict anaerobes and some protozoa.

Concept to Clinic

Narrow-spectrum versus broad-spectrum antibiotics

Broad spectrum antibiotics

Antibiotics can be grouped as "broad-spectrum" and "narrow-spectrum" depending on the range of bacteria it affects.

Broad-spectrum antibiotics are active against a wider number of bacterial types. They can be used for the treatment of a variety of infections. Broad-spectrum antibiotics are very useful when the infecting agent is not known.

Examples of broad-spectrum antibiotics are the aminoglycosides, quinolones, 2nd and 3rd generation cephalosporins, and some synthetic penicillins.

Narrow spectrum antibiotics

Narrow-spectrum antibiotic **allow to kill or inhibit only those bacteria species that are unwanted** (i.e., causing disease).

These antibiotics target a selected type of bacteria whereas the broad-spectrum antibiotics target wide range of bacteria. Although both types treat infections but using broad-spectrum antibiotics when they are not required may let develop antibiotic-resistance in microorganisms. This makes them hard to treat. Broad-spectrum antibiotics may have side effects, such as rashes on skin and diarrhea, etc.

Contd...

The research has proved that the narrow spectrum antibiotics have fewer side effects. Both broad and narrow spectrum antibiotics improved the symptoms in same amount of time.

- It does less collateral damage on the microbiota.
- Low inclination for the development of bacterial resistance.

Examples. Fidaxomicin, sarecycline, older penicillins (penG), macrolides and vancomycin

Mechanism of Antibiotic Action

- *Competition with a natural substance for the active site of the enzyme*, e.g., action of sulfonamides to interfere competitively with the utilization of Para Amino Benzoic Acid (PABA) or action of PABA with para-aminosalicylic acid.
- *Combination with an enzyme at a site* sufficiently close to the active site so as to *interfere with its enzymatic function*, like vancomycin, ristocetin and bacitracin.
- *Combination with nonenzymatic structural components* like drugs, which *inhibit protein synthesis* and which act by damaging cytoplasmic membranes.

Choice of Antibiotic Therapy

The antibiotic chosen for treatment of a disease depends on following factors:

- **Location of infection:** The site or location of infection is important in choosing an antibiotic because to treat an infection, *antibiotic must be in sufficient concentration* at that particular site. For example, the sites with insufficient supply of blood. Some sites with low pH inhibit certain antibiotics.
- **Organism:** Identification of the specific organism predicts the natural history of the infection and allows treatment strategy and choice of drug to be given.
- **Pattern of susceptibility:** Some organisms may show good susceptibility towards an antibiotic, but other bacteria may not. For example, penicillin is effective for treating infection of *Streptococcus pyogenes,* although Acinetobacter and Pseudomonas show resistance. Antibiotics should be chosen to cover the resistance pattern of all the potential pathogens.
- **Severity of infection:** In general, oral therapy is used when it is well-tolerated and provides an adequate therapeutic effect, the parenteral route being reserved for patients who have difficulty taking oral medications or when it is desired to provide prompter or greater antimicrobial activity. In case of severe infections, antibiotics are given by parenteral route.
- **History of allergy:** If a person has previous allergic history, the choice for antibiotics to be selected for treatment is limited.
- **Side effects:** Some antibiotics may be associated with harmful side effects and must be given carefully to a patient. For example, in patients who are already suffering from renal disease, antibiotic like amino-glycoside should be given carefully.
- **Likelihood of unwanted effects:** For example, aminoglycosides should be used with care in patients with pre-existing renal disease.
- The cost of therapy also affects the choice of antibiotic to be used for treatment.

MUST KNOW

Routes of Administration

Route of antibiotic administration is *important in treatment*. Mostly the antibiotics are prescribed for *oral* ingestion; although in case of severe infections, *intravenous* therapy is needed like in case of septicemia. As the required concentration of antibiotic is achieved at the site of infection quickly. Sometimes a person may not be able to take antibiotic orally or one may not tolerate oral therapy, in this case also intravenous route is chosen for treatment. Rarely the antibiotic is given by rectal route like metronidazole administration as surgical prophylaxis. *Intravaginal* route is chosen in treatment of vaginal infections as pessaries (solid block of antibiotic to be inserted into vagina). Infants and children are given palatable antibiotics by oral route as liquids.

Precautions During Antibiotic Therapy

The antibiotics may be given for prolonged period of time so that its concentration in body fluids may be monitored. Very high concentration of antibiotic in blood or body fluids may be harmful.

- Adequate concentration of antibiotic must be present at particular location of infection.
- Toxic level of antibiotic must not reach in blood. It should remain below therapeutic index.
- It assists in the management of an infection with intermediate susceptibility.
- While studying the pharmacokinetics of any drug, a check is kept on the absorption, distribution and protein-binding characteristics of drugs.

Misuse of Antimicrobials

Treating trivial infections/viral infections with antimicrobials has become a routine affair. People use antimicrobials without knowing the basic principles of antimicrobial therapy. Misuse of antimicrobials can be due to:

- Unnecessarily prescribing antimicrobials.
- Delayed antimicrobials administration in critically ill patients.
- When broad-spectrum antimicrobials are too generously used, or incorrect use of narrow-spectrum antimicrobials.
- When the dose of antimicrobials is not correct.
- When the duration of antimicrobials treatment is too short or too long.
- When antimicrobial treatment is not streamlined as per culture reports.

Adverse Events During Treatment with Antimicrobials

Antimicrobials known as 'wonder drugs' are used to save many lives from deadly infections. The antimicrobial treatment can cause some side effects:

- **Gastrointestinal tract:** Antimicrobial activity can upset the balance of the normal flora within the gut, e.g., beta-lactam drugs. The commensal bacteria like *Candida* species overgrow and may lead to pseudomembranous colitis.
- **Skin:** Skin may be affected by an adverse range of manifestations like mild urticarial to erythematous lesions Stevens-Johnson syndrome, which could be life threatening. Generally, discontinuation of antimicrobials therapy resolves issues.
- **Hemopoietic system:** Chloramphenicol produces dose-dependent suppression of bone marrow, granulocytopenia, thrombocytopenia and sometimes hemolytic anemia.
- **Renal system:** Tetracycline and aminoglycoside antimicrobials may be the cause of renal toxicity and damage to the convoluted tubules. These antimicrobials are given under medical guidance in patients already suffering from renal diseases.

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance (AMR) occurs when infections due to bacteria, viruses, fungi and parasites are treated with the unwise use of antimicrobials. This changes the microorganisms over time which no longer respond to medicines making infections harder to treat and it further increases the risk of severe illness, disease spread and death.

MUST KNOW

Inappropriate drug usage → Drug resistance

Resistance occurs when a previously susceptible organism is no longer inhibited by an antimicrobial at a concentration that can be safely achieved in clinical practice.

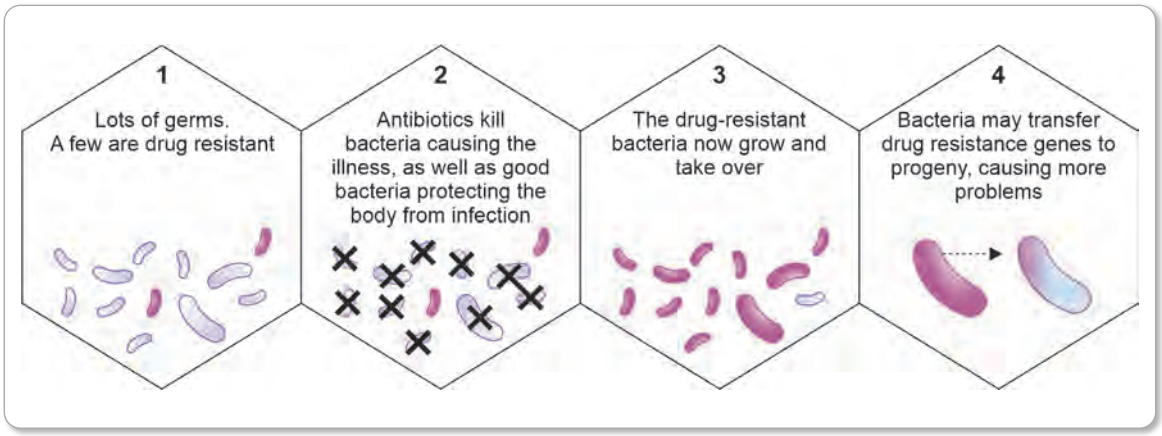


Fig. 9.2: Multidrug resistant microorganisms

A common example of antibiotic abuse is *the use of antimicrobials to treat sore throat in a viral infection*, where antimicrobials have no effect. Due to these factors, the therapeutic use of antimicrobials in hospitals is associated with an increase in *multidrug resistant* microorganisms (Fig. 9.2).

Present Scenario of Antimicrobial Resistance (WHO)

Drug Resistance in Bacteria

The replication of organisms accidentally develops mechanisms to avoid destruction with antimicrobials. This can pose a serious threat to the successful treatment of infections. The basis of drug resistant may be *genetic* or *nongenetic*. The transmission of resistance could be by transformation. For example, *Staph aureus*, *Streptococcus pneumoniae* and *Neisseria gonorrheae* incorporate penicillin resistant genes with the help of mutation, so they become resistant. Such organisms are able to synthesize peptidoglycan and maintain their cell walls in the presence of penicillin. Conjugation allows resistance genes to be transferred with the help of plasmids and this results in multi-drug resistant population of microorganisms.

- **Resistance to ciprofloxacin:** Ciprofloxacin is used to treat urinary tract infections. The rate of resistance in:
  - *Escherichia coli* varies from 8.4% to 92.9%.
  - *Klebsiella pneumoniae* varies from 4.1% to 79.4%.
- **Resistance to fluoroquinolone:** This antimicrobial is used for the treatment of urinary tract infections due to *E. coli and is* reported as ineffective in more than half of patients who used.
- **Resistance to carbapenem:** Carbapenem is last resort treatment in life threatening infections due to *Klebsiella pneumoniae.* The organism is reported to now have resistance to carbapenem.
- **Resistance to methicillin:** *Staphylococcus aureus* is commensal of skin flora and commonly causes nosocomial infections. Methicillin-resistant *Staphylococcus aureus (MRSA)* infections are reported in many people.
- **Resistance to colistin:** It is the only last resort treatment for life-threatening infections caused by carbapenem resistance due to *E. coli, Klebsiella*, etc. Resistance to colistin has been reported in many countries.
- **Resistance to rifampicin and multi-drug resistance:** Antimicrobial resistance is increasing in *Mycobacterium tuberculosis* infections and it can become source of the tuberculosis epidemic. In 2018, WHO reported half a million new cases of rifampicin-resistant TB (RR-TB) and among these, majority was multi-drug resistant TB (MDR-TB).

- **Resistance to penicillins, sulphonamides, macrolides, tetracyclines, fluoroquinolones, and early generation cephalosporins:** Highly variable strains of *N. gonorrheae* have developed resistance to penicillins, sulphonamides, macrolides, tetracyclines, fluoroquinolones, and early generation cephalosporins. Recently, the injectable extended-spectrum cephalosporin (ESC) ceftriaxone is the only drug of choice for gonorrhea.

MUST KNOW

MRSA and MDRO infections

They can cause infections in any part of the body, including bloodstream, urinary tract, lungs, skin, wounds or surgical site.

Risk factors

As compared with a healthy person, the risk is increased if a person has:

- Previous prolonged use of antimicrobials.
- An underlying disease or condition such as chronic kidney disease, diabetes, or skin lesions.
- Repeated hospitalization or regular dialysis visits.
- An existing acute illness.
- Prolonged stay in the hospital.
- Existing colonization with an MDRO.
- Patient has experienced invasive procedures, such as dialysis, use of medical devices, urinary catheters, or nasogastric tubes used to give medicines, fluids, or nutrients.
- Elderly or a patient on immune-suppressing medicine.

Drug Resistance in Viruses

Antiviral drug resistance is on the rise in immunocompromised patients because of ongoing viral replication and prolonged drug exposure. According to WHO, all antiretroviral (ARV) drugs, including newer ones, are either becoming partly or fully inactive due to the emergence of drug-resistant HIV (HIVDR).

- People receiving antiretroviral drugs may acquire HIVDR.
- People can get infected with HIV which is already drug resistant.

Concept to Clinic

The latest WHO ARV guidelines recommend the adoption of a new drug, dolutegravir as the preferred drug of choice for adults and children.

Drug Resistance in Malaria Parasites

Artemisinin-based combination therapies (ACTs) are applied as first-line treatment for uncomplicated *P. falciparum* malaria. In 2019, WHO reported partial resistance to artemisinin and resistance to a number of the ACT partner drugs in Western Pacific in the South-East Asia. Resistance to sulfadoxine-pyrimethamine is followed by artesunate-sulfadoxine-pyrimethamine failures in Africa.

Drug Resistance in Fungi

Drug-resistant fungal infections are increasing. Drug-resistant *Candida auris*, causing common invasive fungal infections, has enhanced resistance to amphotericin B, voriconazole, fluconazole, and caspofungin.

ANTIMICROBIAL SENSITIVITY TESTING

This test helps in deciding the antimicrobial drug to be given for treatment. The test also helps in identification of bacteria such as bacitracin sensitivity is shown by *Streptococcus pyogenes* and optochin sensitivity is shown by *Streptococcus pneumoniae.*

Disk Diffusion Method

Kirby-Bauer's disk diffusion is suitable for most of the microorganisms. The broth culture is inoculated on the Mueller Hinton agar (5% sheep blood is added to the media for S. *pneumoniae* and *S. pyogenes*), to make a lawn culture. After drying MHA plate antibiotic disks (6 mm in diameter) are placed at a distance of 24 mm and pressed a gently on the surface. The plates are incubated at 37°C for 16–18 hours. Susceptibility to the drug is noted by the zone of inhibition of bacterial growth around the disk, which is measured by Vernier caliper. The results are interpreted by comparing with standardized Clinical and Lab standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (Fig. 9.3).

Dilution Method

Serial dilutions of the antimicrobial is inoculated with test microbe. MIC is noted as the highest dilution of antimicrobial that inhibits the growth of microbes.

Agar Dilution

Serial dilutions of drug are prepared in molten agar and poured in petri dishes. The microorganism is inoculated on these plates. Several strains of microbes can be tested on one plate.

Broth Dilution

It can be performed in tubes (macro) or in titration plates (micro).

Epsilometer Test

It is an 'exponential gradient' method of determination of antimicrobial resistance. The E-test has been developed to provide a direct quantification of antimicrobial susceptibility of microorganisms. This is a

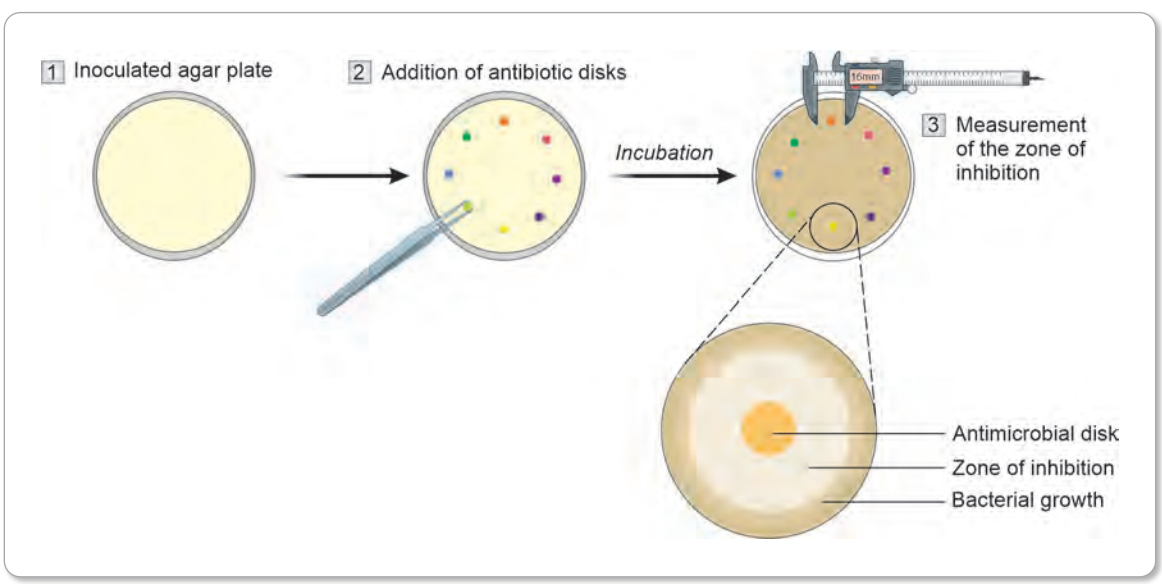


Fig. 9.3: Kirby-Bauer's disk diffusion

quantitative method that applies both the dilution of antibiotics and diffusion of antibiotics into the medium. The device consists of a predefined, continuous, and exponential gradient of antibiotic concentrations immobilized along a rectangular plastic test strip. After 48 hours of incubation, a drop-shaped inhibition zone intersects the graded test strip at the inhibitory concentration (IC) of the antibiotic. MIC at the point where the ellipse intersects the scale is noted. Round up to the highest value if MIC value is between two twofold dilutions (Fig. 9.4). MIC values of the bacteria should be interpreted as S (Susceptible), I (Intermediate), or R (Resistant) by comparing the breakpoint values of each antibiotic with the criteria recommended by CLSI.

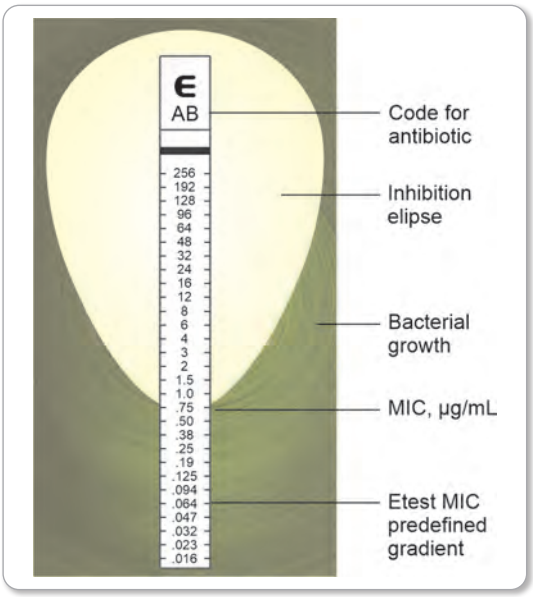


Fig. 9.4: E-test inhibition ellipse showing the MIC at the intersection of the growth of the organism and the calibrated strip

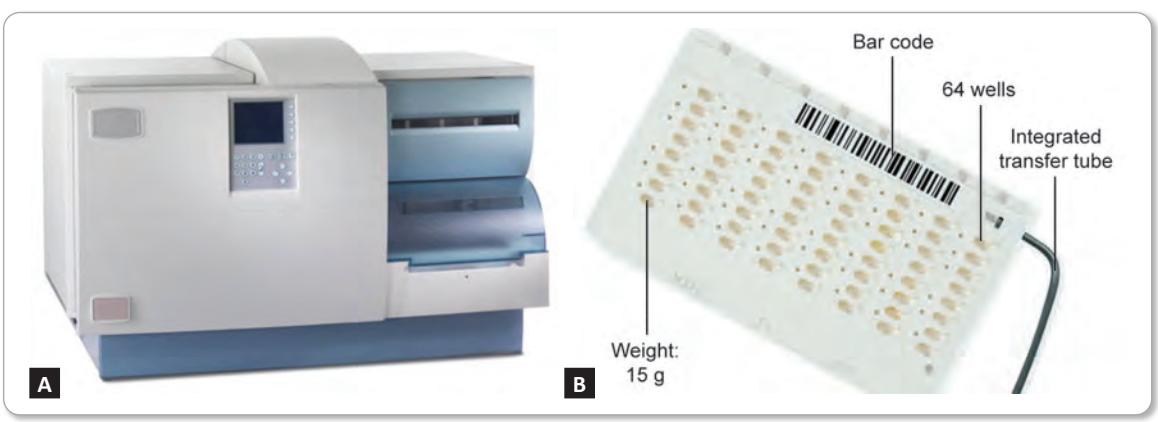
Automated Method for Antibiotic Sensitivity

VITEK 2

It can perform antibiotic sensitivity test of both bacteria and yeasts. The principle is micro broth dilution. The suspension of microbes (doubling dilution) is added to the 64 wells on a reagent card and incubated at 35.5°C for 15 minutes. The readings are noted by optical system of the equipment — nephelometry to check any turbidity, which indicates that the organism has grown in that antibiotic well. The MIC is determined at the highest dilution of antimicrobial that inhibits the growth of microbes. Within 10–18 hours, the results are available (Figs 9.5A to C).

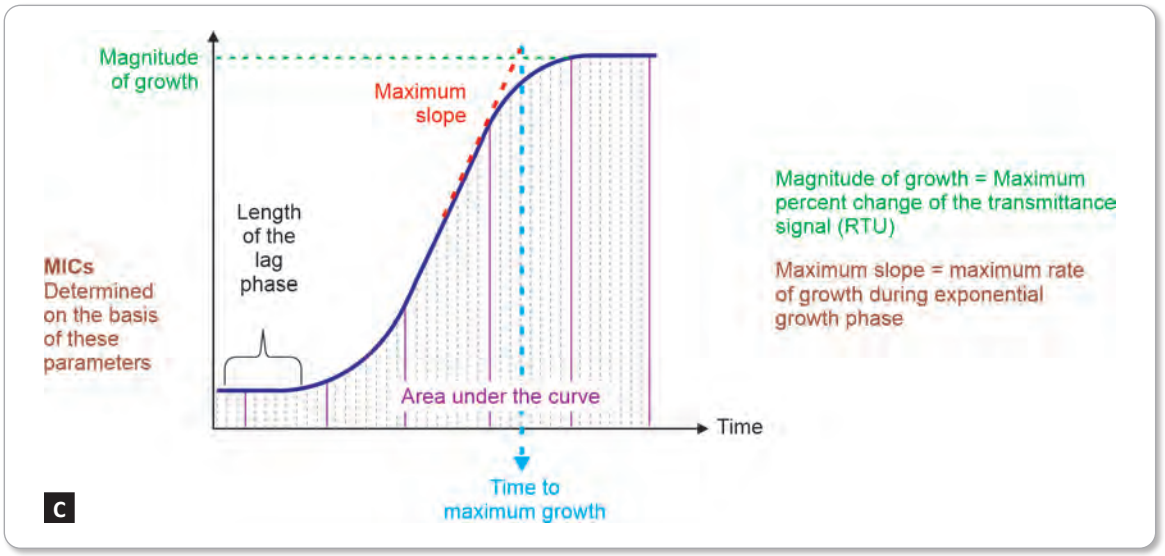
ANTIMICROBIAL STEWARDSHIP

The antimicrobial stewardship program or ASP can help in judicious use of antimicrobials and give beneficial results. The Tripartite Executive Committee decided to set all future World Antimicrobial Awareness Week (WAAW) dates as 18–24 November. The overarching slogan used for the last 5 years was "Antimicrobials: Handle with Care." This was changed to "United to preserve Antimicrobials" in 2020.



Figs 9.5A and B

Contd...



Figs 9.5A to C: VITEK 2 – A. Equipment; B. VITEK 2 AST card; C. MIC determination

SUMMARY

- Various antimicrobials either inhibit or destroy the metabolic properties of bacteria.
- Antimicrobials are known as 'wonder drugs' used to save many lives from deadly infections.
- The antimicrobial treatment causes some side effects.
- Antimicrobial resistance occurs when infections due to bacteria, viruses, fungi and parasites are treated with the unwise use of antimicrobials.
- The replication of organisms accidentally develops mechanisms to avoid destruction by antimicrobials.
- **MRSA and MDRO** can cause infections in any part of the body, including bloodstream, urinary tract, lungs, skin, wounds or surgical site.

ASSESS YOURSELF

Long Answer Questions

1. Discuss susceptibility tests.
2. What are antibiotics? What are its types and explain the drug resistance in bacteria?

Short Answer Question

1. Write notes on:
   a. Drug resistance
   b. R plasmid transfer

Multiple Choice Questions

1. Drug resistance develops because:
   a. Alternative metabolic pathway is developed
   b. Enzymes to change structure of cell wall develops
   c. Competitive inhibition and cell membrane permeability is altered
   d. All of the above

2. Resistance develops among bacteria because:
   a. Bacteria multiply quickly
   b. Mutation occurs
   c. Both a and b
   d. None of the above

3. Metronidazole is:
   a. Active against all anaerobic organisms
   b. Widely distributed in the tissues
   c. Metabolized in the liver and excreted in the urine
   d. All of the above

4. Chemotherapy is the use of:
   a. Chemical substances having property to inhibit the growth of microorganism
   b. Chemicals used in treatment
   c. Antiseptics used in treatment
   d. All of the above

5. The antibiotic therapy is based on:
   a. Theory of selective toxicity
   b. Theory of selective inhibition
   c. Both (a) and (b) are correct
   d. None is correct

6. Which antibiotic has a beta-lactam ring?
   a. Cephalosporin b. Penicillin
   c. Tetracycline d. Streptomycin

7. Which of the following methods would be most appropriate for sterilizing an antibiotic solution?
   a. Dry heat sterilization b. Microfiltration
   c. Autoclaving d. Desiccation

8. Which of the following is used only in life-threatening situations when no other drug is adequate?
   a. Penicillin b. Tetracycline
   c. Chloramphenicol d. Streptomycin

9. Most antibiotics are isolated from:
   a. Viruses
   b. Aquatic microorganisms
   c. Soil microorganisms
   d. Plants

10. Which of the following drugs may show plasmid-mediated resistance?
   a. Nalidixic acid b. Ampicillin
   c. Rifampicin d. Methicillin

11. The larger the ..... better is the chemotherapeutic agent.
   a. Therapeutic index b. Therapeutic dose
   c. Selective toxicity d. Spectrum

Answer Key

Multiple Choice Questions

1. d	**2.** c	**3.** d	**4.** a	**5.** a	**6.** d
7. c	**8.** b	**9.** b	**10.** c	**11.** d	

Textbook of

Microbiology for Physiotherapy Students

Learning Objectives indicate the competencies that a student will achieve after reading the chapter.

LEARNING OBJECTIVES

After studying the chapter, reader will be able to:

- Discuss the characteristics of mycobacteria.
- Describe the diseases such as tuberculosis, leprosy.
- Get familiar with treatment regimen for tuberculosis.

Chapter Outline provides a glimpse of the content discussed.

CHAPTER OUTLINE

- Significance of Normal Flora
- Normal Flora on Skin
- Normal Flora on Nails
- Normal Flora of Mouth and Respiratory Tract
  - Normal Flora of Mouth
  - Normal Flora of Upper Respiratory Tract

Concept to Clinic box correlates the discussed topic with health care.

Concept to Clinic

History taking is very important in TB. In gauging the environmental conditions and social determinants, not only predisposition to TB can be identified but in many cases prognosis may be predicted. Having a balanced nutritious diet aids pharmacological treatment and overall recovery.

Case Scenarios based on real-time cases have been summarized for better practical overview.

Case Scenario

A 60-year-old man came with a history of persistent cough for 2 months. Since 6 months, he was feeling weakness with weight loss. Last week he had blood in sputum. He was HIV-positive too.

Microbiological Discussion/Laboratory Diagnosis

Revised National Tuberculosis Control Program (RNTCP) guidelines

- **Collection of sputum and making smear:** Sputum smear microscopic technique is quick, easy, inexpensive and simple. The results are available within a few hours. A night before the test, the patient is advised to drink lots of fluids like tea or water. It helps the body to make more sputum overnight. Morning sample is preferred and it is collected in sterile sputum collecting cup.

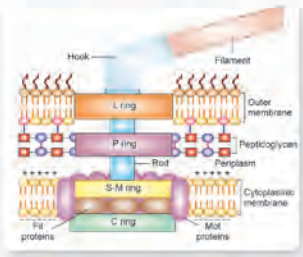
Applied Aspect of the topic is given to emphasize its value in health care industry.

Applied aspect

Beta-propiolactone

Beta-propiolactone (BPL) is a condensation product of ketone and formaldehyde. It is used in 0.2% solution for inactivation of vaccines, biological products and heat-sensitive equipment. Beta-propiolactone *is biocidal, but carcinogenic* also. It is *capable of killing all micro including viruses*. It forms sporicidal vapors in combination with UV radiations and can remove HBV from blood products.

Images and Flow Diagrams have been used to simplify the concepts for the students.



Summarized one-liners at the end of every chapter for quick revision.

SUMMARY

- Various antimicrobials either inhibit or destroy the metabolic properties of bacteria.
- Antimicrobials are known as 'wonder drugs' used to save many lives from deadly infections.
- The antimicrobial treatment causes some side effects.
- Antimicrobial resistance occurs when infections due to bacteria, viruses, fungi and parasites are treated with the unwise use of antimicrobials.
- The replication of organisms accidentally develops mechanisms to avoid destruction by antimicrobials.
- **MRSA and MDRO** can cause infections in any part of the body, including bloodstream, urinary tract, lungs, skin, wounds or surgical site.

ASSESS YOURSELF

Long Answer Questions

1. How will you identify an organism in a pathological sample?
2. What are the main methods for identification of a microorganism in a lab?

Short Answer Question

1. Write notes on:
   a. Molecular techniques for identification of microorganisms
   b. Serological techniques for identification of microorganisms

Multiple Choice Questions

1. The microscopy reveals:

Assess Yourself section has been included to help the students in assessing their understanding of the discussed topics.

About the Author

Anju Dhir *PhD (Microbiology)* is former Lecturer, Department of Microbiology at Shivalik Institute of Nursing, Shimla, Himachal Pradesh. She is gold medalist in Microbiology. She has been in teaching profession for the last 25 years. Her thesis and research papers have been published in many national and international journals.

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