1. GUIDELINES FOR THE RATIONAL USE OF ANTIBIOTICS

INTRODUCTION

Rational use of antibiotics is extremely important as injudicious use can adversely affect the patient , cause emergence of antibiotic resistance and increase the cost of health care.

TYPES OF ANTIBIOTICS

There are various antibiotics available and they come in various different brand names. Antibiotics are usually grouped together based on how they work. Each type of antibiotic only works against certain types of bacteria or parasites. This is why different antibiotics are used to treat different types of infection.

The main types of antibiotics include:

- ➢ Penicillin's phenoxymethylpenicillin, flucloxacillin and amoxicillin.
- ➢ **Cephalosporin's** Cefaclor,cefadroxil and cefalexin.
- ➢ Tetracycline's doxycycline and lymecycline
- ➢ **Aminoglycosides** gentamicin and tobramycin.
- ➢ **Macrolides** erythromycin,azithromycin and Clarithromycin
- ➢ Clindamycin.
- ➢ **Sulfonamides and trimethoprin** Co-trimoxazole
- ➢ Metronidazole and **tinidazole**.
- ➢ Quinolones ciprofloxacin, levofloxacin and norfloxacin.
- ➢ Nitrofurantoin - used for urinary infection

NEED OF ANTIBIOTICS

❖Antibiotics are generally only useful for the treatment of bacterial infections. The majority of infection seen in general practice are of viral origin and antibiotics can neither treat viral infection nor prevent secondary bacterial infections in these patients.

❖Even where a bacterial a etiology is established, an antibiotics may not be always necessary .

❖Collection of pus should be drained surgically and if drainage is adequate, antibiotics are often not required . Many bacterial infections resolve spontaneously.

USES OF ANTIBIOTICS

Antibiotics are used to treat or prevent some types of bacterial infections. They are not effective against viral infections, such as the common cold or flu.

Antibiotics should only be prescribed to treat health problems:

- ➢ that are not serious but are unlikely to clear up without antibiotics **– such as acne**

➢ that are not serious but could spread to other people if not promptly treated **– such** as the skin infection impetigo or the sexually transmitted infection Chlamydia.

➢ where evidence suggests that antibiotics could significantly speed up recovery **– such as a kidney infection**

➢ that carry a risk of more serious complications **– such as cellulitisor pneumonia**

SELECTION OF ANTIBIOTICS

In the process of selecting an antibiotics, three main factors need to be considered ;

➢ Based on the etiology agent .

➢ Based on the patient.

➢ Based on the pharmacokinetic properties & dose of antibiotic.

➢ Based on efficacy of therapy.

INCONSISTENT MICROBIOLOGY REPORTS:

• If the patient is responding there is no necessity to change antibiotic even when the laboratory reports a resistant organism. The isolate in question could have been a colonizer or a contaminant.

• Infection may resolve spontaneously and the antibiotic could have affected the bacteria in a way that makes susceptible to the host's immune defenses .

• If the patient's condition fails to improve , a change in antibiotic may be necessary even when the laboratory reports a sensitive organism.

CAUSE OF NON RESPONSE TO ANTIBIOTIC

A patient may fail to respond to an antibiotics for a number of reason which include:

➢ The aetiology agent is resistant to the antibiotic

➢ The diagnosis is incorrect

➢ The choice of antibiotic is correct bit the dose and / or route of administration is wrong

➢ The antibiotic cannot reach the site of infection

There is a collection of pus that should be drained surgically or a foreign body/ devitalized tissue that should be removed

o There is secondary infection

o Antibiotics fever

o Non compliance of the host

CHANGING FROM INTRAVENOUCS TO ORAL:

✓ Wherever feasible intravenous therapy should be changed to oral therapy.

✓ The oral antibiotic (not necessarily the oral preparation of the intravenous

antibiotics) should be selected based on clinical and laboratory finding.

✓ Similarly not hesitate to revert to intravenous therapy if the patient's condition warrants it.

REGULATIONS TO REDUCE INAPPROPRIATE USE

Enforcing regulations to control the distribution and use of antibiotics will be necessary to minimize the development of resistance and conserve antibiotic effectiveness for as long as possible. Which type of legislations that are most appropriate will differ between countries.
Regulations must take into account the financial, structural and geographical obstacles to finding a balance between access and excess, particularly in low-income countries.

POOR PROVIDER KNOWLEDGE AND LACK OF GUIDELINES

➢ Poor provider knowledge and lack of treatment guidelines are important contributors to inappropriate use of antibiotics.

➢ Providing quality education for health care professionals, farmers, veterinarians and other animal health professionals is key (see Elements of a national action plan – Awareness and understanding).

➢ Creating or updating guidelines and making sure there is access to good quality essential antibiotics and diagnostics are other key areas.

GUIGELINES ON ANTIBIOTIC THERAPY

The following guidelines are issued for the more common infection only. However even for common infections they may not apply to certain patients. When in doubt always seek a second opinion. The recommendation for first and second choice regimens are based on a global assessment of efficacy, adverse effects, prevailing sensitivity patterns and cost. It should also be noted that guidelines such as these have to be reviewed and updated from time to time.

NOTES:

➢ Erythromycin may be substituted for by a newer macrolide.

➢ Gentamicin may be substituted for by another aminoglycoside depending on the local prevailing sensitivity pattern.

➢ Where ampicillin is recommended amoxicillin may also be used.

➢ Ampicillin/amoxicillin may be substituted for by a beta lactam/beta lactamase inhibitor combination depending on the local prevailing sensitivity pattern.

➢ Cloxacillin is the drug of choice for severe methicillin-sensitive *Staphylococcus aureus.* For oral therapy flucloxacillin is preferred to cloxacillin as the former is more reliably absorbed and achieves higher tissue levels. In some children who cannot tolerate cloxacillin a first or second generation cephalosporin may be used.

➢ Quinolones are not recommended in children.

Guidelines for the rational use of antibiotics

Rational use of drugs:

Rational use of drugs may be defined as: Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and the lowest cost to them and their community.

Prophylaxis refers to the prevention of an infection and can be characterized as primary prophylaxis, secondary prophylaxis, or eradication. Primary prophylaxis refers to the prevention of an initial infection. Secondary prophylaxis refers to the prevention of recurrence or reactivation of a preexisting infection. Eradication refers to the elimination of a colonized organism to prevent the development of an infection. These guidelines focus on primary perioperative
prophylaxis.

Surgical prophylaxis:

Surgical antibiotic prophylaxis is defined as the use of antibiotics to prevent infections at the surgical site. Prophylaxis has become the standard of care for contaminated and clean-contaminated surgery and for surgery involving insertion of artificial devices.

- Surgical prophylaxis or Chemoprophylaxis is used to prevent wound infections after various surgical procedures. Wound infections results when a number of bacteria are present in the wound at the time of closure.
- Antimicrobial agents directed against the invading microorganisms may reduce the number of viable bacteria below the critical level and thus prevent infection.
- Several factors are important for the effective and judicious use of antibiotics for surgical prophylaxis**.**
- When the surgery involves insertion of a prosthetic implant (e.g., prosthetic valve, vascular graft, prosthetic joint), cardiac surgery or neurosurgical procedures, the complications of infections are so drastic that most authorities currently agree to surgical prophylaxis for these indications .

Guidelines for Antimicrobial Prophylaxis in Surgery:

These guidelines were developed jointly by the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS),and the Society for Healthcare Epidemiology of America (SHEA). This work represents an

update to the previously published ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery,
as well as guidelines from IDSA and SIS.The guidelines are intended to provide practitioners with a standardized approach to the rational, safe, and effective use of antimicrobial agents for the prevention of surgical-site infections (SSIs) based on currently available clinical evidence and emerging issues.

Classification of Surgical Wound

Class	Category	Definition	Wound Infection Rate (%)
I	Clean	Wound made under ideal operating condition. No entry is made into the oropharyngeal cavity or lumen of the respiratory, alimentary, or genitourinary tract. Inflammation is not encountered and no break in sterile technique occurs.	<5
II	Clean-contaminated	Wound include entry into the oropharyngeal cavity, respiratory, alimentary, or genitourinary tract without significant spillage. Clean wounds included when minor break in sterile technique.	2–10
III	Contaminated	Includes open, fresh, and traumatic wounds; operations with major break in sterile technique; incisions encountering acute, nonpurulent inflammation, such as in cholecystitis, or cystitis	15–20
IV	Dirty	Traumatic wounds (greater than 4 hours old), perforated viscera, or operations involving clinically evident infections. Wounds containing foreign bodies or devitalized tissue are also included.	>30

Key principles of surgical prophylaxis

- Only use antibiotic prophylaxis if there is a significant risk of infection
- Surgical antibiotic prophylaxis should not be the only strategy used to reduce the risk of postoperative infection.
- Minimising the risk requires a comprehensive approach to patient management, including optimal perioperative medical management (e.g. perioperative glycaemic control in patients with diabetes), adequate debridement, and good surgical technique.
- Preoperative intravenous (IV) antibiotic administration should occur up to 60 minutes before surgical incision; however 15 to 30 minutes before surgical incision is optimal.
- Antibiotic selection may need to be modified according to patient risk factors.

- Vancomycin is not as effective as cefazolin for preventing postoperative infections caused by methicillin-susceptible Staphylococcus aureus (MSSA).
- Antibiotic pharmacokinetics are altered in obese patients, so dosage adjustment may be necessary. Seek pharmacist/infectious disease physician input in patients with BMI >30.
- Antibiotic prophylaxis with urinary catheter insertion or removal is not recommended with the exception of some high-risk patients following urological procedures.
- A single dose of antibiotic(s) is sufficient for the majority of procedures.
- Prophylaxis should not extend beyond 24 hours. Postoperative doses of IV antibiotics of up to 24 hours are only required in defined circumstances, such as some cardiac and vascular surgeries or a lower limb amputation, for which a benefit for up to 24 hours of prophylaxis has been demonstrated in clinical trials.
- Urinary or intravascular catheters or indwelling surgical drains that remain in situ are not a justification to extend the duration of antibiotic prophylaxis.
- Antibiotics for infective endocarditis prophylaxis may be needed for patients with specific cardiac conditions (see fact sheet Prophylaxis for Endocarditis).
- Extemporaneous or novel use of antimicrobials, such as topical, intracavitary, intra-tissue or in prosthetic materials, should be avoided
- Some antibiotics may be subject to restricted use or requiring approval from a clinical microbiologist or infectious disease physician. Please refer to the WA State Medicine.

The antibiotics used for surgical prophylaxis can be categorized as follows:

- Pre operative (or) pre surgical: which are used before the surgery
  E.g., vancomycin, clidamycin, gentamycin
- Post operative (or) post surgical: which are used after the surgery
  E.g., amoxicillin, ampicillin, amphotericin B

Antibiotic Prophylaxis to Prevent Surgical Site Infections

SURGERY	COMMON PATHOGENS	RECOMMENDED ANTIMICROBIALS*
Cardiothoracic	Staphylococcus aureus, coagulase-negative staphylococci	Cefazolin, cefuroxime sodium (Zinacef), or vancomycin
Gastrointestinal	Enteric gram-negative bacteria, anaerobes, enterococci	Cefoxitin (Mefoxin), cefotetan (Cefotan), ampicillin/sulbactam (Unasyn), or cefazolin plus

SURGERY	COMMON PATHOGENS	RECOMMENDED ANTIMICROBIALS*
		metronidazole
Gynecologic (vaginal, abdominal, or laparoscopic hysterectomy)	Enteric gram-negative bacteria, group B streptococci, enterococci, anaerobes	Cefoxitin, cefotetan, cefazolin, or ampicillin/sulbactam
Orthopedic	S. aureus, coagulase-negative staphylococci	Cefazolin, cefuroxime sodium, or vancomycin
Vascular	S. aureus, coagulase-negative staphylococci, enteric gram-negative bacilli	Cefazolin or vancomycin

INDICATIONS OF SURGICAL ANTIBIOTIC PROPHYLAXIS:

A classification system which ranks procedures according to their potential risk for infectious complications has greatly facilitated the study of surgical antibiotic prophylaxis. This system ranks procedures as:

- clean
- clean-contaminated
- contaminated.

Widely accepted indications for antibiotic prophylaxis are contaminated and clean-contaminated surgery and operations involving the insertion of an artificial device or prosthetic material. Less well-accepted indications for prophylaxis include clean operations in patients with impaired host defences or patients in whom the consequences of infection may be catastrophic, for example neurosurgery, open heart surgery and ophthalmic surgery.

The experts agreed that the following factors need to be considered for appropriate SAP(Box 2). Cost and availability of antibiotics were discussed as additional considerations to improve access but not as selection criteria.

1. Antibiotic

- According to the surgical procedure, including considerations about reported or probable microorganisms involved and their local antibiotic resistance patterns
- Route of administration
- Dosing
- Consideration of patient allergies

2. Timing: for SAP start and re-dosing prior to wound closure

3. Duration

The final agreed list of surgical procedures is shown in the following Participants also emphasized the fact that a procedure is not on the list does not necessarily mean that SAP is not indicated as the purpose of the list is to cover only the most frequently-encountered surgical procedures worldwide, including in LMICs.

- Neck surgery
- Clean
- Clean-contaminated
- Cardiac surgery (involving sternotomy or valve insertion)
- Thoracic surgery (non-cardiac)
- Breast surgery
- Upper gastrointestinal tract surgery (for example, surgery of the oesophagus and stomach)
- Hepato-pancreato-biliary surgery
- Cholecystectomy
- Hernia surgery
- Appendectomy
- Colorectal surgery
- Hysterectomy
- Caesarian section
- Central vascular surgery
- Peripheral vascular surgery
- Orthopaedic surgery (excluding arthroscopy)
- Bone fracture surgery
- Urologic surgery
- Prostate surgery
- Nephrectomy
- Neurosurgery
- Cranium
- Spine

Recommendations:

Antimicrobial prophylaxis is not rec-ommended for most clean procedures in patients without additional postoperative infection risk factors as listed in the Common Principles section of theseguidelines and the background discussion of this section. Although no studies have demonstrated antimicrobial efficacy in these proce-dures, expert opinion recommends that patientswith risk factors undergoing clean plastic procedures receive antimicrobial prophylaxis. The recommendation for clean-contaminated procedures, breast cancer procedures, and clean procedures with other risk factors is a single dose of **cefazolin(or)ampicillin–sulbactam** (Strength of evidence for
prophylaxis = C.) Alternative agents for patients with b-lactam allergy include **clindamycin and vancomycin**. If there are surveillance data showing that gram-negative organisms cause SSIs for the procedure, the practitioner may consider combining **clindamycin or vancomycin with another agent (cefazolin if the patient is not b-lactam allergic; aztreonam, gentamicin, or single-dose fluoroquinolone if the patient is b-lactam allergic).** Postoperative duration of antimicrobial prophylaxis should be limited to less than 24 hours, regard-less of the presence of indwelling catheters or drains.

Conclusion: Surgical antibiotic prophylaxis is an effective management strategy for reducing postoperative infections, provided that appropriate antibiotics are given at the correct time for appropriate durations and for appropriate surgical procedures. In most cases, surgical antibiotic prophylaxis is given as a single intravenous dose as soon as the patient is stabilised under anaesthetic, prior to skin incision. It is important to use a narrow spectrum antibiotic appropriate to the site of surgery. Hospital surgical antibiotic prophylaxis protocols should be regularly reviewed, as both the cost of individual antibiotics and the endemicity of multi-resistant bacteria in certain units or hospitals are subject to frequent change**.**

2. TUBERCULOSIS

Definition:

Tuberculosis (TB) is a communicable infectious disease caused by Mycobacterium tuberculosis. It can produce silent, latent infection as well as progressive, active disease.

• Globally, 2 billion people are infected and 2 million to 3 million people die from TB each year.

• M. tuberculosis is transmitted from person to person by coughing or sneezing. Close contacts of TB patients are most likely to become infected.

• Fifty-four percent of TB patients in the United States are foreign born,most often from Mexico, the Philippines, Vietnam, India, and China. In the United States, TB disproportionately affects ethnic minorities (African Americans, Hispanics, and Asians).

• Human immunodeficiency virus (HIV) is the most important risk factor for active TB, especially among people 25 to 44 years of age. An HIVinfected individual with TB infection is over 100-fold more likely to develop active disease than an HIV-seronegative patient.

Pathophysiology

• Primary infection is initiated by the alveolar implantation of organisms in droplet nuclei that are small enough (1 to 5 mm) to escape the ciliary epithelial cells of the upper respiratory tract

and reach the alveolar surface. Once implanted, the organisms multiply and are ingested by pulmonary macrophages, where they are killed, or, they continue to multiply. With bacterial multiplication, the macrophages eventually rupture, releasing many bacilli.

• Large numbers of activated macrophages surround the solid caseous (cheese-like) TB foci (the necrotic area) as a part of cell-mediated immunity. Delayed-type hypersensitivity also develops through activation and multiplication of T lymphocytes. Macrophages form granulomas to contain the organisms.

• Successful containment of M. tuberculosis requires activation of a subset of CD4 lymphocytes, referred to as Th-1 cells, which activate macrophages through secretion of interferon γ.

• Approximately 90% of patients who experience primary disease have no further clinical manifestations other than a positive skin test either alone or in combination with radiographic evidence of stable granulomas. Tissue necrosis and calcification of the originally infected site and regional lymph nodes may occur, resulting in the formation of a radiodense area referred to as a Ghon complex.

• Approximately 5% of patients (usually children, the elderly, or the immunocompromised) experience progressive primary disease at the site of the primary infection (usually the lower lobes) and frequently by dissemination leading to meningitis and often to involvement of the upper lobes of the lung as well.

• Approximately 10% of patients develop reactivation disease, which arises subsequent to the hematogenous spread of the organism. In the United States, most cases of TB are believed to result from reactivation.

• Occasionally, a massive inoculum of organisms may be introduced into the bloodstream, causing widely disseminated disease and granuloma formation known as miliary TB.

Clinical Manifestation:

• The classic presentation of pulmonary TB is nonspecific, indicative only of a slowly evolving infectious process. The onset of TB may be gradual.

• Physical examination is nonspecific, but suggestive of progressive pulmonary disease.

• Clinical features associated with extrapulmonary TB vary depending on the organ system(s) involved but typically consist of slowly progressive decline of organ function with low-grade fever and other constitutional symptoms.

• Patients with HIV may have atypical presentation. HIV-positive patients are less likely to have positive skin tests, cavitary lesions, or fever. HIVpositive patients have a higher incidence of extra pulmonary TB and are more likely to present with progressive primary disease.

• TB in the elderly is easily confused with other respiratory diseases. TB in the elderly is far less likely to present with positive skin tests, fevers, night sweats, sputum production, or hemoptysis.

Sings and symptoms:

Patients typically present with weight loss, fatigue, a productive cough, fever, and night sweats,Frank hemoptysis.

Physical examination:

Dullness to chest percussion, rales, and increased vocal fremitus are observed frequently on auscultation.

Laboratory tests:

Moderate elevations in the white blood cell count with a lymphocyte predominance.

Chest radiograph:

Patchy or nodular infiltrates in the apical area of the upper lobes or the superior segment of the lower lobes.Cavitation that may show air-fluid levels as the infection progresses.

DIAGNOSIS:

• The most widely used screening method for tuberculous infection is the tuberculin skin test, which uses purified protein derivative (PPD). Populations most likely to benefit from skin testing are listed in Table 49-2.

• The Mantoux method of PPD administration, which is the most reliable technique, consists of the intracutaneous injection of PPD containing 5 tuberculin units. The test is read 48 to 72 hours after injection by measuring the diameter of the zone of induration.

• Some patients may exhibit a positive test after an initial negative test, and this is referred to as a booster effect.

• Confirmatory diagnosis of a clinical suspicion of TB must be made via chest x-ray and microbiologic examination of sputum or other infected material to rule out active disease.

• When active TB is suspected, attempts should be made to isolate M. tuberculosis from the infected site. Daily sputum collection over 3 consecutive days is recommended.

Montaux Tuberculin Test For Tb:

The Mantoux test or Mendel–Mantoux test(also known as the Mantoux screening test,tuberculin sensitivity test, Pirquet test, or PPD test for purified protein derivative) is a tool for screening for tuberculosis (TB) and for tuberculosis diagnosis. It is one of the major tuberculin skin tests.

Criteria for Tuberculin Positivity, by Risk Group .

A) For persons who are otherwise at low risk and are tested at the start of employment, a reaction of ≥15 mm induration is considered positive.

B) Risk of TB in patients treated with corticosteroids increases with higher dose and longer duration (adapted from Centers for Disease Control and Prevention). Screening for tuberculosis and tuberculosis infection in high-risk populations: recommendations of the Advisory Council for the Elimination of Tuberculosis.

Desired Outcome:

Rapid identification of new cases of TB

• Isolation of the patient with active disease to prevent spread
• Collection of appropriate samples for smears and cultures
• Prompt resolution of signs and symptoms of disease after initiation of treatment
• Achievement of a non-infectious state, thus ending isolation
• Adherence to the treatment regimen

• Cure as quickly as possible (generally with at least 6 months of treatment).

TREATMENT

General Principles

• Drug treatment is the cornerstone of TB management. A minimum of two drugs, and generally three or four drugs, must be used simultaneously.
• Drug treatment is continued for at least 6 months and up to 2 to 3 years for some cases of multidrug-resistant TB (MDR-TB).
• Measures to assure adherence, such as directly observed therapy, are important.
• Patients with active disease should be isolated to prevent spread of the disease.
• Public health departments are responsible for preventing the spread of TB, finding where TB has already spread using contact investigation.
• Debilitated patients may require therapy for other medical conditions, including substance abuse and HIV infection, and some may need nutritional support.
• Surgery may be needed to remove destroyed lung tissue, space-occupying lesions, and some extra-pulmonary lesions.

Pharmacologic Treatment

Latent Infection

• chemoprophylaxis should be initiated in patients to reduce the risk of progression to active disease.
• Isoniazid (INH) 300 mg daily in adults is the preferred treatment for latent TB in the United States, generally given for 9 months.
• Individuals likely to be noncompliant may be treated with a regimen of 15 mg/kg (to a maximum of 900 mg) twice weekly with observation.
• Rifampin (RIF) 600 mg daily for 4 months can be used when INH resistance is suspected or when the patient cannot tolerate INH. Rifabutin 300 mg daily may be substituted for RIF for patients at high risk of drug interactions.
• Pregnant women, alcoholics, and patients with poor diets who are treated with INH should receive pyridoxine, 10 to 50 mg daily, to reduce the incidence of CNS effects or peripheral neuropathies.

Treating Active Disease

• The treatment of culture-positive pulmonary TB caused by drug-susceptible organisms. Doses of antituberculosis drugs are given.The standard TB treatment regimen INH, RIF, pyrazinamide, and ethambutol for 2 months followed by INH and RIF for 4 months.
• Appropriate samples should be sent for culture and susceptibility testing prior to initiating therapy for all patients with active TB. This data should guide the initial drug selection for the new patient. If susceptibility data are not available, the drug resistance pattern in the area where the patient likely acquired TB should be used.
• If the patient is being evaluated for the retreatment of TB, it is imperative to know what drugs were used previously and for how long. Patients must complete 6 months or more of treatment. HIV-positive patients should be treated for an additional 3 months and at least 6

months from the time that they convert to smear and culture negativity. When INH and RIF cannot be used, treatment duration becomes 2 years or more, regardless of immune status.

• Patients who are slow to respond, those who remain culture positive at 2 months of treatment, those with cavitary lesions on chest radiograph, and HIV-positive patients should be treated for 9 months and for at least 6 months from the time they convert to smear and culture negativity.

Drug Resistance

• If the organism is drug resistant, the aim is to introduce two or more active agents that the patient has not received previously. With MDR-TB, no standard regimen can be proposed. It is critical to avoid monotherapy or adding only a single drug to a failing regimen.

• Drug resistance should be suspected in the following situations:

✓ Patients who have received prior therapy for TB

✓ Patients from geographic areas with a prevalence of resistance (New York City, Mexico, Southeast Asia, the Baltic countries, and the former Soviet states)

Patients who are homeless, institutionalized, IV drug abusers, and/or infected with HIV

✓ Patients who still have acid-fast bacilli–positive sputum smears after 2 months of therapy

✓ Patients who still have positive cultures after 2 to 4 months of therapy

✓ Patients who fail therapy or relapse after retreatment

✓ Patients known to be exposed to MDR-TB cases

Special Populations

Tuberculous Meningitis and Extrapulmonary Disease

• In general, INH, pyrazinamide, ethionamide, and cycloserine penetrate the cerebrospinal fluid readily. Patients with CNS TB are often treated for

longer periods (9 to 12 months). Extrapulmonary TB of the soft tissues can be treated with conventional regimens. TB of the bone is typically treated for 9 months, occasionally with surgical debridement.

Children

• TB in children may be treated with regimens similar to those used in adults, although some physicians still prefer to extend treatment to 9

months. Paediatric doses of drugs should be used.

Pregnant Women

• The usual treatment of pregnant women is INH, RIF, and ethambutol for 9 months.

• Women with TB should be cautioned against becoming pregnant, as the disease poses a risk to the foetus as well as to the mother. INH or ethambutol are relatively safe when used during pregnancy. Supplementations with B vitamins is particularly important during pregnancy. RIF has been rarely associated with birth defects, but those seen are occasionally severe, including limb reduction and CNS lesions. Pyrazinamide has not been studied in a large number of pregnant women, but anecdotal information suggests that it may be safe. Ethionamide may be associated with premature delivery, congenital deformities and Down's syndrome when used during pregnancy. Streptomycin has been associated with hearing impairment in the new-borns, including complete deafness. Cycloserine is not recommended during pregnancy.

Renal Failure

• In nearly all patients, INH and RIF do not require dose modifications in renal failure. Pyrazinamide and ethambutol typically require a reduction in dosing frequency from daily to three times weekly.

DRUGS AND THEIR MECHANISM OF ACTION:

1.RIFAMPICIN:

Dose:10mg/kg and 600mg-1200mgIV

It is a semi synthetic antibiotic produced from Streptomyces Mediterranean. It inhibit bacterial DNA directed RNA polymerase alpha chain and thereby reduced protein synthesis and causes cell death.

2.ETHAMBUTOL:

Dose:15mg/kg/day or 30mg/kg/thrice a week

It inhibits bacterial arabinosyl transerferase and thereby disrupts the cell wall production

3.ISONIAZID:

Dose:5mg/kg and is increased up-to 300mg

It inhibit the synthesis of mycolic acid essential for bacterial cell wall synthesis after converted into active drug via bacterial catalase.It addicts with enoyl(acyl carrier protein) reductase(NADH)which results in competitive inhibitions of InhA(mycobacterium tuberculosis) enoyl reductase.

4.PYRAZINAMIDE:

Dose:20-25 mg/kg

Pyrazinamidase is produced by M.tuberculosis which deaminate Pyrazinamidase to pyrazonic acid and thus result in pyrazonic acid accumulation leading to reduced PH which inactivated fatty acid synthetase enzyme.

EVALUATION OF THERAPEUTIC OUTCOMES AND PATIENTS MONITORING:

The most serious problem with TB therapy is nonadherence to the prescribed regimen. The most effective way to ensure adherence is with directly observed therapy.

• Symptomatic patients should be isolated and have sputum samples sent for acid-fast bacilli stains every 1 to 2 weeks until two consecutive smears are negative. Once on maintenance therapy, patients should have sputum cultures performed monthly until negative, which generally occurs over 2 to 3 months. If sputum cultures continue to be positive after 2 months,drug susceptibility testing should be repeated, and serum drug concentrations should be checked.

• Patients should have blood urea nitrogen, serum creatinine, aspartate transaminase or alanine transaminase, and a complete blood count determined at baseline and periodically, depending on the presence of other factors that may increase the likelihood of toxicity (advanced age, alcohol abuse, and possibly pregnancy). Hepatotoxicity should be suspected in patients whose transaminases exceed five times the upper limit of normal or whose total bilirubin exceeds 3 mg/dL. At this point, the offending agent(s) should be discontinued, and alternatives selected.

• Therapy with INH results in a transient elevation in serum transaminases in 12% to 15% of patients and usually occurs within the first 8 to 12 weeks of therapy. Risk factors for hepatotoxicity include patient age, preexisting liver disease, and pregnancy or postpartum state. INH also may result in neurotoxicity, most frequently presenting as peripheral neuropathy or, in overdose, seizures, and coma. Patients with pyridoxine deficiency, such as alcoholics, children, and the malnourished, are at increased risk, as are patients who are slow acetylators of INH and those predisposed to neuropathy, such as those with diabetes.
• Elevations in hepatic enzymes have been attributed to RIF in 10% to 15% of patients, with overt hepatotoxicity occurring in less than 1%. More frequent adverse effects of RIF include rash, fever, and GI distress
• RIF's induction of hepatic enzymes may enhance the elimination of a number of drugs, most notably protease inhibitors. Women who use oral contraceptives should be advised to use another form of contraception during therapy.
• The red colorizing effects of RIF on urine, other secretions, and contact lenses should be discussed with the patient.
• Retrobulbar neuritis is the major adverse effect noted in patients treated with ethambutol. Patients usually complain of a change in visual acuity and/or inability to see the colour green. Vision testing should be performed on all patients who must receive ethambutol for more than 2 months.
• Impairment of eighth cranial nerve function is the most important adverse effect of streptomycin. Vestibular function is most frequently affected, but hearing may also be impaired. Audiometric testing should be performed in patients who must receive streptomycin for more than 2 months. Streptomycin occasionally causes nephrotoxicity.

3. MENINGITIS

Meningitis is an infection of the membranes (meninges) that cover the brain and the spinal cord. In meningitis, there occurs swelling and inflammation of the membranes and the characteristic presenting features of the infection are fever, headache and stiff neck.
While the most common types of meningitis may get better on their own, some types need special attention. The severity of the infection as well as the treatment varies greatly with the types of meningitis.

Meningitis: Causes, Types And Transmission
Meningitis is primarily of five types and is based on their causes. These are:
Bacterial Meningitis – It is caused by a bacterial infection and needs immediate attention or else it can be life-threatening. Vaccines may help to prevent some types of bacterial meningitis. This is often contagious and spreads through nasal and oral discharges from affected person to another.
Viral Meningitis – This is caused by viruses and the infection is serious but not commonly fatal depending on the patient status and the causative virus. Some vaccines may help to prevent some types of viral meningitis. The most common causes are enteroviruses, which often spread by the fecal-oral route from person to person.

Parasitic Meningitis – This type is caused by parasitic infections, which mainly spread through contaminated water, food and soil. These types are comparatively less prevalent in developed countries.

Fungal Meningitis – It is caused by fungi and usually spreads due to inhalation of fungal spores. Also, those having illnesses like cancer, HIV or diabetes are at an increased risk of fungal type of meningitis.

Non-Infectious Meningitis – This type of meningitis is non-infectious and does not spread via persons. It may be caused by lupus, head injury, cancers or certain drugs.

Pathophysiology of meningitis

Most cases of bacterial meningitis are preceded by nasopharyngeal colonisation by the causative organism. In most colonised individuals, infection will progress no further, but in susceptible individuals the organism invades the submucosa by circumventing host defences (e.g. physical barriers, local immunity, phagocytes) and gains access to the CNS by invasion of the bloodstream and subsequent haematogenous seeding of the CNS.

Other less common routes by which micro-organisms can reach the meninges include:

• direct spread from the nasopharynx

• blood-borne spread from other foci of colonisation or infection

• abnormal communications with the skin or mucous membranes, for example skull fractures, anatomical defects or a meningocoele

• spread from an infected adjacent focus, for example brain abscess, tuberculoma, infected paranasal air sinus or infection of the middle ear.

Once in the subarachnoid space, the infection spreads widely and incites a cascade of meningeal inflammation. The cerebral tissue is not usually directly involved although cerebral abscess may complicate some types of meningitis. The micro-organisms that most frequently cause meningitis are capable of doing so because they have a variety of virulence factors, including mechanisms for:

- attachment to host mucosal surfaces
- evasion of phagocytosis and other host defences
- meningeal invasion
- disruption of the blood–brain barrier
- induction of pathophysiological changes in the CSF space
- secondary brain damage.

Overall, the net result of infection is vascular endothelial injury and increased blood–brain barrier permeability leading to the entry of many blood components into the subarachnoid space. This contributes to cerebral oedema and elevated CSF protein levels. In response to the cytokine response, neutrophils migrate from the bloodstream into the CSF. Cerebral oedema contributes to intracranial hypertension and a consequent decrease in cerebral blood flow. Anaerobic metabolism ensues, which contributes to increased lactate and decreases glucose concentrations. If this uncontrolled process is not modulated by effective treatment, transient neuronal dysfunction or permanent neuronal injury results.

Risk Factors Of Meningitis

Some Risk Factors May Increase The Chances Of Meningitis. These Include:

Younger children
Persons living in communities like hostels, child care centers, camps, etc. where chances of infection spread are more.
Persons with compromised immune system like those with other infections or those taking immunosuppressive drugs and pregnant women.
Missing out the recommended vaccinations for he particular age group can also increase the risk.

Clinical Features Of Meningitis

Meningitis signs and symptoms may take some time to develop or may even show up in few hours. The most commonly observed symptoms include:
Very severe headache
Sudden high fever
Neck stiffness
Headache may be associated with nausea, vomiting, confusion and increased sensitivity to light.
There may be seizures, confusion, difficulty in concentrating and reduced alertness.
Unusual postures with arching of head and neck backwards may be seen.
Sometimes drowsiness, difficulty in waking up or less interest in eating and drinking, may be noted. In newborns, along with high fever, excessive irritability, poor feeding and crying may be seen. Also, a bulge may be noted in the fontanel.

Diagnosis Of Meningitis

While the physician examines the patient and takes a detailed history of the illness, certain diagnostic investigations may also be ordered.
Laboratory Tests – Blood tests to find the causative organism and other infection related parameters.
Imaging Tests – X-rays, CT scans can help in detecting location and extent of inflammation and examine head and other related areas.
Lumbar Puncture – When meningitis is suspected, the cerebrospinal fluid (CSF) is collected by lumbar puncture or spinal tap and CSF analysis is done.

Treatment Of Meningitis

Treatment of meningitis depends on the cause and type of infection. Antibiotics are given in case of bacterial meningitis, but these may not be useful for viral meningitis. However, till the cause is unclear, a broad spectrum antibiotic may be prescribed. In some viral infections like herpes meningitis, anti-viral treatment may be given. In addition, symptomatic treatment is given. These include treating fever, seizures, inflammation, headache and shock. Intravenous fluids may also be given. For some cases, corticosteroid medications may be helpful in recovery and to reduce the chances of complications. Drainage of accumulated fluid may be required in certain cases.

Vaccination For Meningitis

For some types of meningitis, vaccines are available; so it is important to follow the recommended immunization schedule for children, pregnant women and other adults. Some vaccinations are now a regular part of the childhood immunization schedule and those specified for older children and adults should be accordingly taken at the physician’s advice.

Some Of The Vaccines Available For Meningitis Are:

Haemophilus influenzae (HiB) vaccine
Pneumococcal conjugate vaccination
Meningococcal vaccination– for older children and later booster doses.

Prevention Of Meningitis

Meningitis can be contagious and can spread through the commonest means, by which other bacterial and viral infections spread. Preventive measures, if adopted can be helpful in controlling the spread of many types of meningitis. Some suggested measures include

Hand Washing – Proper hand washing methods should be practiced and the entire family, particularly children should be trained. Washing hands with soap and running water before eating, in crowded places, after handling pets and animals, before and after using toilet should be practiced.

Personal Hygiene – Measures like covering nose and mouth while sneezing or coughing, wearing masks, avoiding sharing of personal items, keeping surroundings clean should be followed.

In general, staying healthy, consuming fresh food and exercising can help in boosting the immune system. Pregnant women can be more cautious about their food and drink and follow their physician's advice.

4. Respiratory tract infections

Definition

A respiratory tract infection(RTI) is any of a number of infectious disease involving the respiratory tract. An infection of this type is normally further classified as an upper respiratory tract infection(URI or URTI) or a lower respiratory tract infection(LRI or LRTI). Lower respiratory infections, such as pneumonia tend to be far more serious conditions than upper respiratory infections, such as the common cold.

Two types of respiratory tract infections are as follows:

1. Upper Respiratory Tract Infection (URI or URTI):

The upper respiratory tract is generally considered to be the airway above the glottis or vocal cords; sometimes it is taken as the tract above the cricoids cartilage. This part of the tract includes the nose, sinuses, pharynx, and larynx.

Typical infections of the upper respiratory tract include

Tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, certain types of influenza, and the common cold.Symptoms of URIs can include cough, sore throat, runny nose, nasal congestion, headache, low grade fever, facial pressure and sneezing.

2. Lower Respiratory Tract Infection (LRI or LRTI):

The lower respiratory tract infections consists of the

Trachea (windpipe), bronchial tubes, the bronchioles, and the lungs. Lower respiratory tract infections are generally more serious than upper respiratory infections. LRIs are the leading cause of death among all infectious diseases. The two most common LRIs are bronchitis and pneumonia. Influenza affects both the upper and lower respiratory tracts, but more dangerous strains such as the highly pernicious H5N1 tend to bind to receptors deep in the lungs.

PATHOPHYSIOLOGY:

Upper Respiratory Tract Infection:

Organisms gain entry to the respiratory tract by inhalation of droplets and invade the mucosa. Epithelial destruction may ensue, along with redness, edema, hemorrhage and sometimes an exudate. Most upper respiratory infections are of viral etiology. Epiglottitis and laryngotracheitis are exceptions with severe cases likely caused by Haemophilus influenzae type b.

Bacterial pharyngitis is often caused by Streptococcus pyogenes.

Diseases includes URTI are as follows:

- ➢ Common cold
- ➢ Sinusitis
- ➢ Otitis
- ➢ Pharyngitis
- ➢ Epiglottis
- ➢ Laryngotrachitis.

Lower Respiratory Tract Infection:

Organisms enter the distal airway by inhalation, aspiration or by hematogenous seeding. The pathogen multiplies in or on the epithelium, causing inflammation, increased mucus secretion, and impaired mucociliary function; other lung functions may also be affected. In severe bronchiolitis, inflammation and necrosis of the epithelium may block small airways leading to airway obstruction.Causative agents of lower respiratory infections are viral or bacterial. Viruses cause most cases of bronchitis and bronchiolitis. In community-acquired pneumonias, the most common bacterial agent is Streptococcus pneumoniae. Atypical pneumonias are cause by such agents as Mycoplasma pneumoniae, Chlamydia spp, Legionella, Coxiella burnetti and viruses. Nosocomial pneumonias and pneumonias in immunosuppressed patients have protean etiology with gram-negative organisms and staphylococci as predominant organisms.

Diseases includes LRTI are as follows:

- ➢ Bronchitis
- ➢ Bronchiolitis
- ➢ Pneumonia

Upper Respiratory Tract Infections:

Common Cold:

Etiology:

Common colds are the most prevalent entity of all respiratory infections and are the leading

cause of patient visits to the physician, as well as work and school absenteeism. Most colds are caused by viruses. Rhinoviruses with more than 100 serotypes are the most common pathogens, causing at least 25% of colds in adults. Coronaviruses may be responsible for more than 10% of cases. Parainfluenza viruses, respiratory syncytial virus, adenoviruses and influenza viruses have all been linked to the common cold syndrome. All of these organisms show seasonal variations in incidence. The cause of 30% to 40% of cold syndromes has not been determined.

Pathogenesis:

The viruses appear to act through direct invasion of epithelial cells of the respiratory mucosa, but whether there is actual destruction and sloughing of these cells or loss of ciliary activity depends on the specific organism involved. There is an increase in both leukocyte infiltration and nasal secretions, including large amounts of protein and immunoglobulin, suggesting that cytokines and immune mechanisms may be responsible for some of the manifestations of the common cold.

Clinical Manifestations:

After an incubation period of 48–72 hours, classic symptoms of nasal discharge and obstruction, sneezing, sore throat and cough occur in both adults and children. Myalgia and headache may also be present. Fever is rare. The duration of symptoms and of viral shedding varies with the pathogen and the age of the patient. Complications are usually rare, but sinusitis and otitis media may follow.

Microbiologic Diagnosis:

The diagnosis of a common cold is usually based on the symptoms (lack of fever combined with symptoms of localization to the nasopharynx). Unlike allergic rhinitis, eosinophils are absent in nasal secretions. Although it is possible to isolate the viruses for definitive diagnosis, that is rarely warranted.

Prevention and Treatment:

Treatment of the uncomplicated common cold is generally symptomatic. Decongestants, antipyretics, fluids and bed rest usually suffice. Restriction of activities to avoid infecting others,
along with good hand washing, are the best measures to prevent spread of the disease. No vaccine is commercially available for cold prophylaxis.

Sinusitis:

Sinusitis is an acute inflammatory condition of one or more of the paranasal sinuses. Infection plays an important role in this affliction. Sinusitis often results from infections of other sites of the respiratory tract since the paranasal sinuses are contiguous to, and communicate with, the upper respiratory tract.

Etiology:

Acute sinusitis most often follows a common cold which is usually of viral etiology. Vasomotor and allergic rhinitis may also be antecedent to the development of sinusitis. Obstruction of the sinusal ostia due to deviation of the nasal septum, presence of foreign bodies, polyps or tumors
can predispose to sinusitis. Infection of the maxillary sinuses may follow dental extractions or an extension of infection from the roots of the upper teeth. The most common bacterial agents responsible for acute sinusitis are Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. Other organisms including Staphylococcus aureus, Streptococcus pyogenes, gramnegative organisms and anaerobes have also been recovered. Chronic sinusitis is commonly a mixed infection of aerobic and anaerobic organisms.

Pathogenesis:

nfections caused by viruses or bacteria impair the ciliary activity of the epithelial lining of the sinuses and increased mucous secretions. This leads to obstruction of the paranasal sinusal ostia which impedes drainage. With bacterial multiplication in the sinus cavities, the mucus is converted to mucopurulent exudates. The pus further irritates the mucosal lining causing more edema, epithelial destruction and ostial obstruction. When acute sinusitis is not resolved and becomes chronic, mucosal thickening results and the development of mucoceles and polyps may ensue.

Clinical Manifestations:

The maxillary and ethmoid sinuses are most commonly involved in sinusitis. The frontal sinuses are less often involved and the sphenoid sinuses are rarely affected. Pain, sensation of pressure and tenderness over the affected sinus are present. Malaise and low grade fever may also occur. Physical examination usually is not remarkable with no more than an edematous and hyperemic nasal mucosa. In uncomplicated chronic sinusitis, a purulent nasal discharge is the most constant finding. There may not be pain nor tenderness over the sinus areas. Thickening of the sinus mucosa and a fluid level are usually seen in x-ray films or magnetic resonance imaging.

Microbiologic Diagnosis:

For acute sinusitis, the diagnosis is made from clinical findings. A bacterial culture of the nasal discharge can be taken but is not very helpful as the recovered organisms are generally contaminated by the resident flora from the nasal passage. In chronic sinusitis, a careful dental examination, with sinus x-rays may be required. An antral puncture to obtain sinusal specimens for bacterial culture is needed to establish a specific microbiologic diagnosis.

Prevention and Treatment

Symptomatic treatment with analgesics and moist heat over the affected sinus pain and a decongestant to promote sinus drainage may suffice. For antimicrobial therapy, a beta-lactamase resistant antibiotic such as amoxicillin-clavulanate or a cephalosporin may be used. For chronic sinusitis, when conservative treatment does not lead to a cure, irrigation of the affected sinus may be necessary. Culture from an antral puncture of the maxillary sinus can be performed to identify the causative organism for selecting antimicrobial therapy. Specific preventive procedures are not available. Proper care of infectious and/or allergic rhinitis, surgical correction to relieve or avoid obstruction of the sinusal ostia is important. Root abscesses of the upper teeth should receive proper dental care to avoid secondary infection of the maxillary sinuses.

Otitis:

Infections of the ears are common events encountered in medical practice, particularly in young children. Otitis externa is an infection involving the external auditory canal while otitis media denotes inflammation of the middle ear.

Etiology:

For otitis externa, the skin flora such as Staphylococcus epidermidis, Staphylococcus aureus, diphtheroids and occasionally an anaerobic organism, Propionibacterium acnes are major etiologic agents. In a moist and warm environment, a diffuse acute otitis externa (Swimmer's ear) may be caused by Pseudomonas aeruginosa, along with other skin flora. Malignant otitis externa is a severe necrotizing infection usually caused by Pseudomonas aeruginosa. For otitis media, the commonest causative bacteria are Streptococcus pneumoniae, Hemophilus influenzae and beta-lactamase producing Moraxella catarrhalis. Respiratory viruses may play a role in otitis media but this remains uncertain.Mycoplasma pneumoniae has been reported to cause hemorrhagic bullous myringitis in an experimental study among nonimmune human volunteers inoculated with M pneumoniae. However, in natural cases of M pneumoniae infection, clinical bullous myringitis or otitis media is uncommon.

Pathogenesis:

The narrow and tortuous auditory canal is lined by a protective surface epithelium. Factors that may disrupt the natural protective mechanisms, such as high temperature and humidity, trauma, allergy, tissue maceration, removal of cerumen and an alkaline pH environment, favor the development of otitis externa. Prolonged immersion in a swimming pool coupled with frequent ear cleansing increases the risk of otitis externa. Acute otitis media commonly follows an upper respiratory infection extending from the nasopharynx via the eustachian tube to the middle ear. Vigorous nose blowing during a common cold, sudden changes of air pressure, and perforation of the tympanic membrane also favor the development of otitis media. The presence of purulent exudate in the middle ear may lead to a spread of infection to the inner ear and mastoids or even meninges.

Clinical Manifestations:

Otitis externa:

Furuncles of the external ear, similar to those in skin infection, can cause severe pain and a sense of fullness in the ear canal. When the furuncle drains, purulent otorrhea may be present. In generalized otitis externa, itching, pain and tenderness of the ear lobe on traction are present. Loss of hearing may be due to obstruction of the ear canal by swelling and the presence of purulent debris. Malignant otitis externa tends to occur in elderly diabetic patients. It is characterized by severe persistent earache, foul smelling purulent discharge and the presence of granulation tissue in the auditory canal. The infection may spread and lead to osteomyelitis of the temporal bone or externally to involve the pinna with osteochondritis.

Otitis media:

Acute otitis media occurs most commonly in young children. The initial complaint usually is persistent severe earache (crying in the infant) accompanied by fever, and, and vomiting. Otologic examination reveals a bulging, erythematous tympanic membrane with loss of light reflex and landmarks. If perforation of the tympanic membrane occurs, serosanguinous or purulent discharge may be present. In the event of an obstruction of the eustachian tube, accumulation of a usually sterile effusion in the middle ear results in serous otitis media. Chronic otitis media frequently presents a permanent perforation of the tympanic membrane. A central perforation of the pars tensa is more benign. On the other hand, an attic perforation

of the pars placcida and marginal perforation of the pars tensa are more dangerous and often associated with a cholesteatoma.

Diagnosis:

The diagnosis of both otitis externa and otitis media can be made from history, clinical symptomatology and physical examinations. Inspection of the tympanic membrane is an indispensable skill for physicians and health care workers. All discharge, ear wax and debris must be removed and to perform an adequate otoscopy. In the majority of patients, routine cultures are not necessary, as a number of good bacteriologic studies have shown consistently the same microbial pathogens mentioned in the section of etiology. If the patient is immunocompromised or is toxic and not responding to initial antimicrobial therapy tympanocentesis (needle aspiration) to obtain middle ear effusion for microbiologic culture is indicated.

Prevention and Treatment:

Otitis externa:

Topical therapy is usually sufficient and systemic antimicrobials are seldom needed unless there are signs of spreading cellulitis and the patient appears toxic. A combination of topical antibiotics such as neomycin sulfate, polymyxin B sulfate and corticosteroids used as eardrops, is a preferred therapy. In some cases, acidification of the ear canal by applying a 2% solution of acetic acid topically may also be effective. If a furuncle is present in the external canal, the physician should allow it to drain spontaneously.

Otitis media:

Amoxicillin is an effective and preferred antibiotic for treatment of acute otitis media. Since beta-lactamase producing H influenzae and M catarrhalis can be a problem in some communities, amoxicillin-clavulanate is used by many physicians. Oral preparations of trimethoprim/sulfamethoxazole, second and third generation cephalosporins, tetracyclines and macrolides can also be used. When there is a large effusion, tympanocentesis may hasten the resolution process by decreasing the sterile effusion. Patients with chronic otitis media and frequent recurrences of middle ear infections may be benefitted by chemoprophylaxis with once daily oral amoxicillin or trimethoprim/sulfamethoxazole during the winter and spring months. In those patients with persistent effusion of the middle ear, surgical interventions with myringotomy, adenoidectomy and the placement of tympanotomy tubes has been helpful.

Use of polyvalent pneumococcal vaccines has been evaluated for the prevention of otitis media in children. However, children under two years of age do not respond satisfactorily to polysaccharide antigens; further, no significant reduction in the number of middle ear infections was demonstrable. Newer vaccines composed of pneumococcal capsular polysaccharides conjugated to proteins may increase the immunogenicity and are currently under clinical investigation for efficacy and safety.

Pharyngitis

Etiology:

Pharyngitis is an inflammation of the pharynx involving lymphoid tissues of the posterior pharynx and lateral pharyngeal bands. The etiology can be bacterial, viral and fungal infections as well as noninfectious etiologies such as smoking. Most cases are due to viral infections and accompany a common cold or influenza. Type A coxsackieviruses can cause a severe ulcerative

pharyngitis in children (herpangina), and adenovirus and herpes simplex virus, although less common, also can cause severe pharyngitis. Pharyngitis is a common symptom of Epstein-Barr virus and cytomegalovirus infections. Group A beta-hemolytic streptococcus or Streptococcus pyogenes is the most important bacterial agent associated with acute pharyngitis and tonsillitis.Corynebacterium diphtheriae causes occasional cases of acute pharyngitis, as do mixed anaerobic infections (Vincent's angina),Corynebacterium haemolyticum, Neisseria gonorrhoeae, and Chlamydia trachomatis. Outbreaks of Chlamydia pneumoniae (TWAR agent) causing pharyngitis or pneumonitis have occurred in military recruits. Mycoplasma pneumoniae andMycoplasma hominis have been associated with acute pharyngitis.Candida albicans, which causes oral candidiasis or thrush, can involve the pharynx, leading to inflammation and pain.

Pathogenesis:

As with common cold, viral pathogens in pharyngitis appear to invade the mucosal cells of the nasopharynx and oral cavity, resulting in edema and hyperemia of the mucous membranes and tonsils. Bacteria attach to and, in the case of group A beta-hemolytic streptococci, invade the mucosa of the upper respiratory tract. Many clinical manifestations of infection appear to be due to the immune reaction to products of the bacterial cell. In diphtheria, a potent bacterial exotoxin causes local inflammation and cell necrosis.

Clinical Manifestations:

Pharyngitis usually presents with a red, sore, or “scratchy” throat. An inflammatory exudates or membranes may cover the tonsils and tonsillar pillars. Vesicles or ulcers may also be seen on the pharyngeal walls. Depending on the pathogen, fever and systemic manifestations such as malaise, myalgia, or headache may be present. Anterior cervical lymphadenopathy is common in bacterial pharyngitis and difficulty in swallowing may be present.

Microbiologic Diagnosis:

The goal in the diagnosis of pharyngitis is to identify cases that are due to group A betahemolytic streptococci, as well as the more unusual and potentially serious infections. The various forms of pharyngitis cannot be distinguished on clinical grounds. Routine throat cultures for bacteria are inoculated onto sheep blood and chocolate agar plates. Thayer-Martin medium is used if N gonorrhoeae is suspected. Viral cultures are not routinely obtained for most cases of pharyngitis. Serologic studies may be used to confirm the diagnosis of pharyngitis due to viral, mycoplasmal or chlamydial pathogens. Rapid diagnostic tests with fluorescent antibody or latex agglutination to identify group A streptococci from pharyngeal swabs are available. Gene probe and polymerase chain reaction can be used to detect unusual organisms such as M pneumoniae, chlamydia or viruses but these procedures are not routine diagnostic methods.

Prevention and Treatment:

Symptomatic treatment is recommended for viral pharyngitis. The exception is herpes simplex virus infection, which can be treated with acyclovir if clinically warranted or if diagnosed in immunocompromised patients. The specific antibacterial agents will depend on the causative organism, but penicillin G is the therapy of choice for streptococcal pharyngitis. Mycoplasma and chlamydial infections respond to erythromycin, tetracyclines and the new macrolides. Epiglottitis and Laryngotracheitis.

Etiology:

Inflammation of the upper airway is classified as epiglottitis or laryngotracheitis (croup) on the basis of the location, clinical manifestations, and pathogens of the infection. Haemophilus influenzae type b is the most common cause of epiglottitis, particularly in children age 2 to 5 years. Epiglottitis is less common in adults. Some cases of epiglottitis in adults may be of viral origin. Most cases of laryngotracheitis are due to viruses. More serious bacterial infections have been associated with H influenzae type b, group A beta-hemolytic streptococcus and C diphtheriae. Parainfluenza viruses are most common but respiratory syncytial virus, adenoviruses, influenza viruses, enteroviruses and Mycoplasma pneumoniae have been implicated.

Pathogenesis:

A viral upper respiratory infection may precede infection with H influenzae in episodes of epiglottitis. However, once H influenzae type b infection starts, rapidly progressive erythema and swelling of the epiglottis ensue, and bacteremia is usually present. Viral infection of laryngotracheitis commonly begins in the nasopharynx and eventually moves into the larynx and trachea. Inflammation and edema involve the epithelium, mucosa and submucosa of the subglottis which can lead to airway obstruction.

Clinical Manifestations:

The syndrome of epiglottitis begins with the acute onset of fever, sore throat, hoarseness, drooling, dysphagia and progresses within a few hours to severe respiratory distress and prostration. The clinical course can be fulminant and fatal. The pharynx may be inflamed, but the diagnostic finding is a “cherry-red” epiglottis. A history of preceding cold-like symptoms is typical of laryngotracheitis, with rhinorrhea, fever, sore throat and a mild cough. Tachypnea, a deep barking cough and inspiratory stridor eventually develop. Children with bacterial tracheitis appear more ill than adults and are at greater risk of developing airway obstruction. Haemophilus influenzae type b is isolated from the blood or epiglottis in the majority of patients with epiglottis; therefore a blood culture should always be performed. Sputum cultures or cultures from pharyngeal swabs may be used to isolate pathogens in patients with laryngotracheitis. Serologic studies to detect a rise in antibody titers to various viruses are helpful for retrospective diagnosis. Newer, rapid diagnostic techniques, using immunofluorescent-antibody staining to detect virus in sputum, pharyngeal swabs, or nasal washings, have been successfully used. Enzyme-linked immunosorbent assay (ELISA), DNA probe and polymerase chain reaction procedures for detection of viral antibody or antigens are now available for rapid diagnosis.

Prevention and Treatment:

Epiglottitis is a medical emergency, especially in children. All children with this diagnosis should be observed carefully and be intubated to maintain an open airway as soon as the first sign of respiratory distress is detected. Antibacterial therapy should be directed at H influenzae. Patients with croup are usually successfully managed with close observation and supportive care, such as fluid, humidified air, and racemic epinephrine. For prevention, Haemophilus influenzae type b conjugated vaccine is recommended for all pediatric patients, as is immunization against diphtheria.

LOWER RESPIRATORY TRACT INFECTIONS:

Bronchitis and Bronchiolitis:

Etiology:

Bronchitis and bronchiolitis involve inflammation of the bronchial tree. Bronchitis is usually preceded by an upper respiratory tract infection or forms part of a clinical syndrome in diseases such as influenza, rubeola, rubella, pertussis, scarlet fever and typhoid fever. Chronic bronchitis with a persistent cough and sputum production appears to be caused by a combination of environmental factors, such as smoking, and bacterial infection with pathogens such as H influenzae and S pneumoniae. Bronchiolitis is a viral respiratory disease of infants and is caused primarily by respiratory syncytial virus. Other viruses, including parainfluenza viruses, influenza viruses and adenoviruses (as well as occasionally M pneumoniae) are also known to cause bronchiolitis.

Pathogenesis:

When the bronchial tree is infected, the mucosa becomes hyperemic and edematous and produces copious bronchial secretions. The damage to the mucosa can range from simple loss of mucociliary function to actual destruction of the respiratory epithelium, depending on the organisms(s) involved. Patients with chronic bronchitis have an increase in the number of mucusproducing cells in their airways, as well as inflammation and loss of bronchial epithelium, Infants with bronchiolitis initially have inflammation and sometimes necrosis of the respiratory epithelium, with eventual sloughing. Bronchial and bronchiolar walls are thickened. Exudate made up of necrotic material and respiratory secretions and the narrowing of the bronchial lumen lead to airway obstruction. Areas of air trapping and atelectasis develop and may eventually contribute to respiratory failure.

Clinical Manifestations:

Symptoms of an upper respiratory tract infection with a cough is the typical initial presentation in acute bronchitis. Mucopurulent sputum may be present, and moderate temperature elevations occur. Typical findings in chronic bronchitis are an incessant cough and production of large amounts of sputum, particularly in the morning. Development of respiratory infections can lead to acute exacerbations of symptoms with possibly severe respiratory distress. Coryza and cough usually precede the onset of bronchiolitis. Fever is common. A deepening cough, increased respiratory rate, and restlessness follow. Retractions of the chest wall, nasal flaring, and grunting are prominent findings. Wheezing or an actual lack of breath sounds may be noted, Respiratory failure and death may result.

Microbiologic Diagnosis:

Bacteriologic examination and culture of purulent respiratory secretions should always be performed for cases of acute bronchitis not associated with a common cold. Patients with chronic bronchitis should have their sputum cultured for bacteria initially and during exacerbations. Aspirations of nasopharyngeal secretions or swabs are sufficient to obtain specimens for viral culture in infants with bronchiolitis. Serologic tests demonstrating a rise in antibody titer to specific viruses can also be performed. Rapid diagnostic tests for antibody or viral antigens may be performed on nasopharyngeal secretions by using fluorescent-antibody staining, ELISA or DNA probe procedures.

Prevention and Treatment:

With only a few exceptions, viral infections are treated with supportive measures. Respiratory syncytial virus infections in infants may be treated with ribavirin. Amantadine and rimantadine are available for chemoprophylaxis or treatment of influenza type A viruses.

Selected groups of patients with chronic bronchitis may receive benefit from use of corticosteroids, bronchodilators, or prophylactic antibiotics.

Pneumonia:

Pneumonia is an inflammation of the lung parenchyma. Consolidation of the lung tissue may be identified by physical examination and chest x-ray. From an anatomical point of view, lobar pneumonia denotes an alveolar process involving an entire lobe of the lung while bronchopneumonia describes an alveolar process occurring in a distribution that is patchy without filling an entire lobe. Numerous factors, including environmental contaminants and autoimmune diseases, as well as infection, may cause pneumonia. The various infectious agents that cause pneumonia are categorized in many ways for purposes of laboratory testing, epidemiologic study and choice of therapy.

Pneumonias occurring in usually healthy persons not confined to an institution are classified as community-acquired pneumonias. Infections arise while a patient is hospitalized or living in an institution such as a nursing home are called hospital-acquired or nosocomial pneumonias. Etiologic pathogens associated with community-acquired and hospital-acquired pneumonias are somewhat different. However, many organisms can cause both types of infections.

Etiology:

1. Bacterial pneumonias:

Streptococcus pneumoniae is the most common agent of community-acquired acute bacterial pneumonia. More than 80 serotypes, as determined by capsular polysaccharides, are known, but 23 serotypes account for over 90% of all pneumococcal pneumonias in the United States. Pneumonias caused by other streptococci are uncommon.Streptococcus pyogenes pneumonia is often associated with a hemorrhagic pneumonitis and empyema. Community-acquired pneumonias caused by Staphylococcus aureus are also uncommon and usually occur after influenza or from staphylococcal bacteremia. Infections due to Haemophilus influenzae(usually nontypable) and Klebsiella pneumoniae are more common among patients over 50 years old who have chronic obstructive lung disease or alcoholism.

The most common agents of nosocomial pneumonias are aerobic gram-negative bacilli that rarely cause pneumonia in healthy individuals.Peudomonas aeruginosa, Escherichia coli, Enterobacter, Proteus, and Klebsiella ecies are often identified. Less common agents causing pneumonias include Francisella tularensis, the agent of tularemia;Yersinia pestis, the agent of plague; and Neisseria meningitidis, which usually causes meningitis but can be associated with pneumonia, especially among military recruits. Xanthomonas pseudomallei causes melioidosis, a chronic pneumonia in Southeast Asia.

Mycobacterium tuberculosis can cause pneumonia. Although the incidence of tuberculosis is low in industrialized countries,M tuberculosis infections still continue to be a significant public health problem in the United States, particularly among immigrants from developing countries, intravenous drug abusers, patients infected with human immunodeficiency virus (HIV), and the institutionalized elderly. Atypical Mycobacterium species can cause lung disease indistinguishable
from tuberculosis.

2. Aspiration pneumonias:

Aspiration pneumonia from anaerobic organisms usually occurs in patients with periodontal disease or depressed consciousness. The bacteria involved are usually part the oral flora and cultures generally show a mixed bacterial growth.Actinomyces, Bacteroides, Peptostreptococcus, Veilonella, Propionibacterium, Eubacterium, and Fusobacterium spp are often isolated.

3. Atypical pneumonias:

Atypical pneumonias are those that are not typical bacterial lobar pneumonias.Mycoplasma pneumoniae produces pneumonia most commonly in young people between 5 and 19 years of age. Outbreaks have been reported among military recruits and college students. Legionella species, including L pneumophila, can cause a wide range of clinical manifestations. The 1976 outbreak in Philadelphia was manifested as a typical serious pneumonia in affected individuals, with a mortality of 17% . These organisms can survive in water and cause pneumonia by inhalation from aerosolized tap water, respiratory devices, air conditioners and showers. They also have been reported to cause nosocomial pneumonias. Chlamydia spp noted to cause pneumonitis are C trachomatis, C psittaci and C pneumoniae. Chlamydia trachomatis causes pneumonia in neonates and young infants.C psittaci is a known cause for occupational pneumonitis in bird handlers such as turkey farmers.Chlamydia pneumoniae has been associated with outbreaks of pneumonia in military recruits and on college campuses. Coxiella burnetii the rickettsia responsible for Q fever, is acquired by inhalation of aerosols from infected animal placentas and feces. Pneumonitis is one of the major manifestations of this systemic infection.

Viral pneumonias are rare in healthy civilian adults. An exception is the viral pneumonia caused by influenza viruses, which can have a high mortality in the elderly and in patients with underlying disease. A serious complication following influenza virus infection is a secondary bacterial pneumonia, particularly staphylococcal pneumonia. Respiratory syncytial virus can cause serious pneumonia among infants as well as outbreaks among institutionalized adults. Adenoviruses may also cause pneumonia, serotypes 1,2,3,7 and 7a have been associated with a severe, fatal pneumonia in infants. Although varicella-zoster virus pneumonitis is rare in children, it is not uncommon in individuals over 19 years old. Morality can be as high as 10% to 30%. Measles pneumonia may occur in adults.

4. Other pneumonias and immunosuppression:

Cytomegalovirus is well known for causing congenital infections in neonates, as well as the mononucleosis-like illness seen in adults. However, among its manifestations in immunocompromised individuals is a severe and often fatal pneumonitis. Herpes simplex virus also causes a pneumonia in this population. Giant-cell pneumonia is a serious complication of measles and has been found in children with immunodeficiency disorders or underlying cancers who receive live attenuated measles vaccine.Actinomyces and Nocardia spp can cause pneumonitis, particularly in immunocompromised hosts. Among the fungi, Cryptococcus neoformans and Sporothrix schenckii are found worldwide, whereas Blastomyces dermatitidis, Coccidioides immitis, Histoplasma capsulatum and Paracoccidioides brasiliensis have specific geographic distributions. All can cause pneumonias, which are usually chronic and possible clinically inapparent in normal hosts, but are manifested as more serious diseases in immunocompromised patients. Other fungi, such as Aspergillus and Candida spp, occasionally

are responsible for pneumonias in severely ill or immunosuppressed patients and neonates. Pneumocystis carinii produces a life-threatening pneumonia among patients immunosuppressed by acquired immune deficiency syndrome (AIDS), hematologic cancers, or medical therapy. It is the most common cause of pneumonia among patients with AIDS when the CD4 cell counts drop below 200/mm3.

Pathogenesis and Clinical Manifestations:

Infectious agents gain access to the lower respiratory tract by the inhalation of aerosolized material, by aspiration of upper airway flora, or by hematogenous seeding. Pneumonia occurs when lung defense mechanisms are diminished or overwhelmed. The major symptoms or pneumonia are cough, chest pain, fever, shortness of breath and sputum production. Patients are tachycardic. Headache, confusion, abdominal pain, nausea, vomiting and diarrhea may be present, depending on the age of the patient and the organisms involved.

Microbiologic Diagnosis:

Etiologic diagnosis of pneumonia on clinical grounds alone is almost impossible. Sputum should be examined for a predominant organism in any patient suspected to have a bacterial pneumonia; blood and pleural fluid (if present) should be cultured. A sputum specimen with fewer than 10 while cells per high-power field under a microscope is considered to be contaminated with oral secretions and is unsatisfactory for diagnosis. Acid-fast stains and cultures are used to identify Mycobacterium and Nocardia spp. Most fungal pneumonias are diagnosed on the basis of culture of sputum or lung tissue. Viral infection may be diagnosed by demonstration of antigen in secretions or cultures or by an antibody response. Serologic studies can be used to identify viruses,M pneumoniae, C. burnetii, Chlamydia species, Legionella, Francisella, and Yersinia. A rise in serum cold agglutinins may be associated with M pneumoniae infection, but the test is positive in only about 60% of patients with this pathogen.

Rapid diagnostic tests, as described in previous sections, are available to identify respiratory viruses: the fluorescent-antibody test is used for Legionella. A sputum quellung test can specify S pneumonia by serotype. Enzyme-linked immunoassay, DNA probe and polymerase chain reaction methods are available for many agents causing respiratory infections. Some organisms that may colonize the respiratory tract are considered to be pathogens only when they are shown to be invading the parenchyma. Diagnosis of pneumonia due to cytomegalovirus, herpes simplex virus, Aspergillus spp. Or Candida spp require specimens obtained by transbronchial or open-lung biopsy.Pneumocystis carinii can be found by silver stain of expectorated sputum. However, if the sputum is negative, deeper specimens from the lower respiratory tract obtained by bronchoscopy or by lung biopsy are needed for confirmatory diagnosis.

Prevention and Treatment:

Until the organism causing the infection is identified, decisions on therapy are based upon clinical history, including history of exposure, age, underlying disease and previous therapies, past pneumonias, geographic location, severity of illness, clinical symptoms, and sputum examination. Once a diagnosis is made, therapy is directed at the specific organism responsible. The pneumococcal vaccine should be given to patients at high risk for developing pneumococcal infections, including asplenic patients, the elderly and any patients immunocompromised through disease or medical therapy. Yearly influenza vaccinations should

also be provided for these particular groups. An enteric-coated vaccine prepared from certain serotypes of adenoviruses is available, but is only used in military recruits. In AIDS patients, trimethoprim/sulfamethoxazole, aerosolized pentamidine or other antimicrobials can be given for prophylaxis of Pneumocystis carinii infections.

5. GASTROENTERITIS

PATHOPHYSIOLOGY

Adequate fluid balance in humans depends on the secretion and reabsorption of fluid and electrolytes in the intestinal tract; diarrhea occurs when intestinal fluid output overwhelms the absorptive capacity of the gastrointestinal tract.

The 2 primary mechanisms responsible for acute gastroenteritis are
(1) damage to the villous brush border of the intestine, causing malabsorption of intestinal contents and leading to an osmotic diarrhea, and
(2) the release of toxins that bind to specific enterocyte receptors and cause the release of chloride ions into the intestinal lumen, leading to secretory diarrhea.

Even in severe diarrhea, however, various sodium-coupled solute co-transport mechanisms remain intact, allowing for the efficient reabsorption of salt and water.

By providing a 1:1 proportion of sodium to glucose, classic oral rehydration solution (ORS) takes advantage of a specific sodium-glucose transporter (SGLT-1) to increase the reabsorption of sodium, which leads to the passive reabsorption of water.

Rice and cereal-based ORS may also take advantage of sodium-amino acid transporters to increase reabsorption of fluid and electrolytes.

CLINICAL MANIFESTATIONS

The history and physical examination serve 2 vital functions:
(1) differentiating gastroenteritis from other causes of vomiting and diarrhea in children and
(2) estimating the degree of dehydration. In some cases, the history and physical examination can also aid in determining the type of pathogen responsible for the gastroenteritis, although only rarely will this affect management.

Physical

Elements of the physical examination are as follows:

General - Weight, ill appearance, level of alertness, lethargy, irritability

HEENT (head, ears, eyes, nose, and throat) - Presence or absence of tears, dry or moist mucous membranes, and whether the eyes appear sunken

Cardiovascular - Heart rate and quality of pulses

Respiratory - Rate and quality of respirations (deep, acidotic breathing suggests severe dehydration).

Abdomen - Abdominal tenderness, guarding and rebound, and bowel sounds; abdominal tenderness on examination, with or without guarding, should prompt consideration of diseases other than gastroenteritis
Back - Flank/costovertebral angle tenderness increase the likelihood of pyelonephritis
Rectal - Quality and color of stool, presence of gross blood or mucous
Extremities - Capillary refill time, warm or cool extremities
Skin - Abdominal rash may indicate typhoid fever (infection with Salmonella typhi), while jaundice might make viral or toxic hepatitis more likely; slow return of abdominal skin pinch suggests decreased skin turgor and dehydration, while a doughy feel to the skin may indicate hypernatremia.

DIAGNOSIS

- Congenital secretory diarrheas
- Cryptosporidiosis
- Giardiasis
- Hemolytic-Uremic Syndrome
- Hepatitis
- Inflammatory Bowel Disease
- Pediatric Appendicitis
- Pediatric Crohn Disease
- Pediatric Diabetic Ketoacidosis
- Pediatric Lactose Intolerance
- Pediatric Pancreatitis
- Pediatric Pyelonephritis
- Pediatric Urinary Tract Infection
- Pediatrics, Foreign Body Ingestion
- Pediatrics, Intussusception
- Pediatrics, Pyloric Stenosis
- Peptic Ulcer Disease
- Pseudomembranous colitis
- Shock in Pediatrics
- Shock, Septic
- Sinonasal Manifestations of Cystic Fibrosis
- Toxic ingestion
- Toxic megacolon

PHARMACOTHERAPY

The goals of pharmacotherapy are to reduce morbidity, prevent complications, and provide prophylaxis. Antidiarrheal (ie, kaolin-pectin) and antimotility agents (ie, loperamide) are

contraindicated in the treatment of acute gastroenteritis in children because of their lack of benefit and increased risk of adverse effects, including ileus, drowsiness, and nausea.

Probiotics are live microbial feeding supplements commonly used in the treatment and prevention of acute diarrhea. Possible mechanisms of action include synthesis of antimicrobial substances, competition with pathogens for nutrients, modification of toxins, and stimulation of nonspecific immune responses to pathogens.

Two large systematic reviews have found probiotics (especiactobacillus GG) to be effective in reducing the duration of diarrhea in children presenting with acute gastroenteritis.

A recent meta-analysis found probiotics may be especially effective for the prevention of C difficile –associated diarrhea in patients receiving antibiotics. As probiotic preparations vary widely, it is difficult to estimate the effectiveness of any single preparation.

6. ENDOCARDITIS

Endocarditis is inflammation of the inside lining of the heart chambers and heart valves (endocardium). Endocarditis is inflammation of your heart's inner lining, called the endocardium. It's usually caused by bacteria. When the inflammation is caused by infection, the condition is called infective endocarditis. Endocarditis is uncommon in people with healthy hearts.

symptoms of endocarditis:

Common symptoms of endocarditis include:

- heart murmur, which is an abnormal heart sound of turbulent blood flow through the heart
- pale skin
- fever or chills
- night sweats
- muscle or joint pain
- nausea or decreased appetite
- a full feeling in the upper left part of your abdomen
- unintentional weight loss
- swollen feet, legs, or abdomen

Less common symptoms of endocarditis include:

- blood in urine
- weight loss
- an enlarged spleen, which may be tender to touch

Causes, Incidence, And Risk Factors:

Endocarditis can involve the heart muscle, heart valves, or lining of the heart. Most people who develop endocarditis have a

a) Birth defect of the heart
b) Damaged or abnormal heart valve
c) History of endocarditis
d) New heart valve after surgery

Endocarditis diagnosis:

a) Blood test
b) Transthoracic echocardiogram
c) Transoesophageal echocardiogram
d) Electrocardiogram
e) Chest X-ray

Pathophysiology:

Endocarditis comprises at least three critical elements:

STEP 1 -preparation of the cardiac valve for bacterial adherence
STEP 2 - adhesion of circulating bacteria to the prepared valvular surface
STEP 3 - survival of the adherent bacteria on the surface, with propagation of the infected vegetation.

Epidemiology:

Infective endocarditis is a rare disease, with an incidence of two to six episodes per 100,000 habitants/year. Incidence is higher in elderly people; besides, this group is often affected by many comorbidities. In India the ratio of this disease is 1: 10000.

Treatment:

Infectious endocarditis results from bacterial or fungal infection of the endocardial surface of the heart and is associated with significant morbidity and mortality. Antibiotic treatment of infectious endocarditis depends on whether the involved valve is native or prosthetic, as well as the causative microorganism and its antibiotic susceptibilities. Common blood culture isolates include Staphylococcus aureus, viridians Streptococcus, enterococci, and coagulase-negative staphylococci. Valvular structural and functional integrity may be adversely affected in infectious endocarditis, and surgical consultation is warranted in patients with aggressive or persistent infections, emboli, and valvular compromise or rupture.

Surgery:

The structural and functional integrity of cardiac valves may be damaged by infection. This may lead to valvular regurgitation or flow obstruction in valves with large vegetations. Surgery may need to be considered in selected patients; the benefits are greatest in patients with the most indications.

Surgical intervention should be considered in patients with fungal infection, infection with aggressive antibiotic-resistant bacteria or bacteria that respond poorly to antibiotics, left-sided infectious endocarditis caused by gram-negative bacteria, persistent infection with positive blood cultures after one week of antibiotic therapy, or one or more embolic events during the first two weeks of antibiotic therapy.

Surgical intervention is warranted for valve dehiscence, perforation, rupture or fistula, or a large perivalvular abscess. Peri annular extension of infection into the myocardium is associated with increased mortality and should be suspected in patients presenting with new atrioventricular block.

Anticoagulation:

Anticoagulation in patients with infectious endocarditis is controversial, particularly in those with mechanical valve endocarditis. In general, anticoagulation should be discontinued for at least the first two weeks of antibiotic therapy in patients with Staphylococcus aureus prosthetic valve endocarditis who have experienced a recent central nervous system embolic event.

Patient counseling:

- Need to continue IV therapy for up to 6 weeks at home
- Take the antibiotics until they are all gone. Take them even if you feel better. They treat the infection and prevent it from returning.
- Take good care of your teeth and mouth. Brush your teeth after meals.
- Visit your dentist every 6 months. Dental infection is a risk factor for bacterial endocarditis. See your dentist immediately if you have a toothache or abscess.
- You might need to take an antibiotic before dental visits. Ask your healthcare provider for more information.
- Take good care of yourself. Get regular exercise and eat a healthy diet. Ask your healthcare provider for help as needed.
- Stop smoking.
- Be careful to get proper treatment of any open cuts that develop

7. SEPTICEMIA

DEFINITION

Septicaemia (sepsis or blood poisoning) is the presence of disease-causing bacteria in the blood. The human body is host to a range of different bacteria that live harmlessly in various places such as the mouth, skin, bowel and genital tract. However, these bacteria can cause disease if they get into the bloodstream, particularly if a person is unwell or if their immune system isn't strong enough to keep the invading organisms under control.

This is why people with pre-existing medical conditions are most likely to get septicaemia. Severe infections, such as those of the lung, will also often give rise to septicaemia. Septicaemia is fatal in about one in four cases because of the effects of large numbers of multiplying bacteria and the toxins they release in the blood. Sepsis that progresses to septic shock has a death rate as high as 50%, depending on the type of organism involved. Other terms for septicaemia include bacteraemia and blood poisoning.

The bacteria strains most commonly responsible include

- Escherichia coli *(*E. coli*)*
- Pneumococcus,
- Klebsiella*,*
- Pseudomonas*,*
- Staphylococcus
- Streptococcus

Stages

PATHOPHYSIOLOGY

Sepsis is caused by a combination of factors related to the particular invading pathogen(s) and to the status of the immune system of the host. The early phase of sepsis characterized by excessive inflammation (sometimes resulting in a cytokine storm) may be followed by a prolonged period of decreased functioning of the immune system. Either of these phases may prove fatal. On the other hand, systemic inflammatory response syndrome (SIRS) occurs in people without the presence of infection, for example, in those with burns, polytrauma, or the initial state in pancreatitis and chemical pneumonitis. However, sepsis also causes similar response to SIRS.

1. Microbial factors

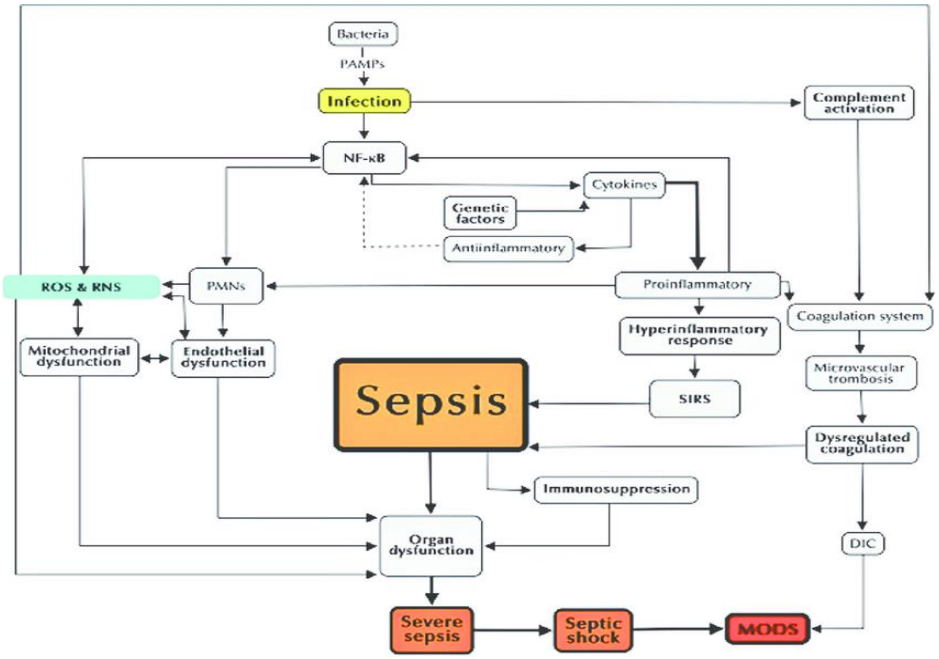
- Bacterial virulence factors, such as glycocalyx and various adhesins, allow colonization, immune evasion, and establishment of disease in the host. Sepsis caused by gram-negative bacteria is thought to be largely due to a response by the host to the lipid A component of lipopolysaccharide, also called endotoxin. Sepsis caused by gram-positive bacteria may result from an immunological response to cell wall lipoteichoic acid. Bacterial exotoxins that act as superantigens also may cause sepsis. Superantigens simultaneously bind major histocompatibility complex and T-cell receptors in the absence of antigen presentation. This forced receptor interaction induces the production of pro-inflammatory chemical signals (cytokines) by T-cells.
- There are a number of microbial factors that may cause the typical septic inflammatory cascade. An invading pathogen is recognized by its pathogen-associated molecular patterns (PAMPs). Examples of PAMPs include lipopolysaccharides and flagellin in gram-negative bacteria, muramyl dipeptide in the peptidoglycan of the gram-positive bacterial cell wall, and CpG bacterial DNA. These PAMPs are recognized by the pattern recognition receptors (PRRs) of the innate immune system, which may be membrane-bound or cytosolic. There are four families of PRRs: the toll-like receptors, the C-type lectin receptors, the NOD-like receptors, and the RIG-I-like receptors. Invariably, the association of a PAMP and a PRR will cause a series of intracellular signalling cascades. Consequentially, transcription factors such as nuclear factor-kappa B and activator protein-1, will up-regulate the expression of pro-inflammatory and anti-inflammatory cytokines.

2. Host factors

- Upon detection of microbial antigens, the host systemic immune system is activated. Immune cells not only recognise pathogen-associated molecular patterns, but also damage-associated molecular patterns from damaged tissues. An uncontrolled immune response is then activated because leukocytes are not recruited to the specific site of infection, but instead they are recruited all over the body. Then, an immunosuppression state ensues when the proinflammatory T helper cell 1 (TH1) is shifted to TH2, mediated by interleukin 10, which is known as "compensatory anti-inflammatory response syndrome".The apoptosis (cell death) of lymphocytes further worsens the immunosuppression. Subsequently, multiple organ failure ensues because tissues are unable to use oxygen efficiently due to inhibition of cytochrome c oxidase.
- Inflammatory responses cause multiple organ dysfunction syndrome through various mechanisms as described below. Increased permeability of the lung vessels causes leaking of fluids into alveoli, which results in pulmonary edema and acute respiratory distress syndrome (ARDS). Impaired utilization of oxygen in the liver impairs bile salt transport, causing jaundice (yellowish discoloration of skin). In kidneys, inadequate

oxygenation results in tubular epithelial cell injury (of the cells lining the kidney tubules), and thus causes acute kidney injury (AKI). Meanwhile, in the heart, impaired calcium transport, and low production of adenosine triphosphate (ATP), can cause myocardial depression, reducing cardiac contractility and causing heart failure. In the gastrointestinal tract, increased permeability of the mucosa alters the microflora, causing mucosal bleeding and paralytic ileus. In the central nervous system, direct damage of the brain cells and disturbances of neurotransmissions causes altered mental status. Cytokines such as tumor necrosis factor, interleukin 1, and interleukin 6 may activate procoagulation factors in the cells lining blood vessels, leading to endothelial damage. The damaged endothelial surface inhibits anticoagulant properties as well as increases antifibrinolysis, which may lead to intravascular clotting, the formation of blood clots in small blood vessels, and multiple organ failure.

- The low blood pressure seen in those with sepsis is the result of various processes, including excessive production of chemicals that dilate blood vessels such as nitric oxide, a deficiency of chemicals that constrict blood vessels such as vasopressin, and activation of ATP-sensitive potassium channels. In those with severe sepsis and septic shock, this sequence of events leads to a type of circulatory shock known as distributive shock.



Pathophysiology

CLINICAL MANIFESTATION

Common symptoms related to the actual cause, people with sepsis may have a fever, low body temperature, rapid breathing, a fast heart rate, confusion, and edema. Early signs include a rapid heart rate, decreased urination, and high blood sugar. Signs of established sepsis include confusion, metabolic acidosis (which may be accompanied by a faster breathing rate that leads

to respiratory alkalosis), low blood pressure due to decreased systemic vascular resistance, higher cardiac output, and disorders in blood-clotting that may lead to organ failure.The drop in blood pressure seen in sepsis can cause light headedness and is part of the criteria for septic shock.

There are three stages of sepsis

Sepsis

Symptoms of sepsis include:

- a fever above 101ºF (38ºC) or a temperature below 96.8ºF (36ºC)
- heart rate higher than 90 beats per minute
- breathing rate higher than 20 breaths per minute
- probable or confirmed infection

Septic shock

- Symptoms of septic shock include the symptoms of severe sepsis, plus a very low blood pressure.

Severe sepsis:

Severe sepsis occurs when there's organ failure. You must have one or more of the following signs to be diagnosed with severe sepsis:

- patches of discolored skin
  - decreased urination
  - changes in mental ability
  - low platelet (blood clotting cells) count
  - problems breathing
  - abnormal heart functions
  - chills due to fall in body temperature
  - unconsciousness
  - extreme weakness

CAUSES

Infections leading to sepsis are usually bacterial but may be fungal or viral. Gram-positive bacteria were the primary cause of sepsis before the introduction of antibiotics in the. After the introduction of antibiotics, gram-negative bacteria became the predominant cause of

sepsis. gram-positive bacteria, most commonly staphylococci, are thought to cause more than 50% of cases of sepsis. Other commonly implicated bacteria include *Streptococcus pyogenes*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella* species. Fungal sepsis accounts for approximately 5% of severe sepsis and septic shock cases; the most common cause of fungal sepsis is an infection by *Candida* species of yeast, a frequent hospital-acquired infection.

The most common sites of infection resulting in severe sepsis are the lungs, the abdomen, and the urinary tract. Typically, 50% of all sepsis cases start as an infection in the lungs. In one third to one-half of cases, the source of infection is unclear.

DIAGNOSIS

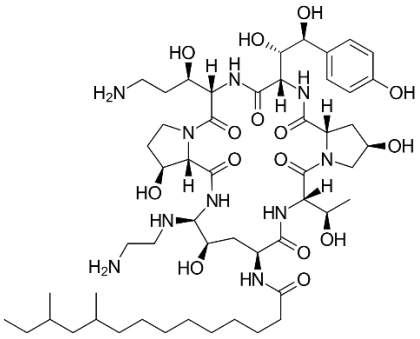
- Early diagnosis is necessary to properly manage sepsis, as the initiation of rapid therapy is key to reducing deaths from severe sepsis. Some hospitals use alerts generated from electronic health records to bring attention to potential cases as early as possible.
- Within the first three hours of suspected sepsis, diagnostic studies should include white blood cell counts, measuring serum lactate, and obtaining appropriate cultures before starting antibiotics, so long as this does not delay their use by more than 45 minutes. To identify the causative organism(s), at least two sets of blood cultures using bottles with media for aerobic and anaerobic organisms are necessary. At least one should be drawn through the skin and one through each vascular access device (such as an IV catheter) that has been in place more than 48 hours. Bacteria are present in the blood in only about 30% of cases. Another possible method of detection is by polymerase chain reaction. If other sources of infection are suspected, cultures of these sources, such as urine, cerebrospinal fluid, wounds, or respiratory secretions, also should be obtained, as long as this does not delay the use of antibiotics.
- Within six hours, if blood pressure remains low despite initial fluid resuscitation of 30 ml/kg, or if initial lactate is ≥ four mmol/l (36 mg/dl), central venous pressure and central venous oxygen saturation should be measured. Lactate should be re-measured if the initial lactate was elevated. Evidence for point of care lactate measurement over usual methods of measurement, however, is poor.
- Within twelve hours, it is essential to diagnose or exclude any source of infection that would require emergent source control, such as a necrotizing soft tissue infection, an infection causing inflammation of the abdominal cavity lining, an infection of the bile duct, or an intestinal infarction. A pierced internal organ (free air on an abdominal x-ray or CT scan), an abnormal chest x-ray consistent with pneumonia (with focal opacification), or petechiae, purpura, or purpura fulminans may indicate the presence of an infection.

PHARMACOTHERAPHY

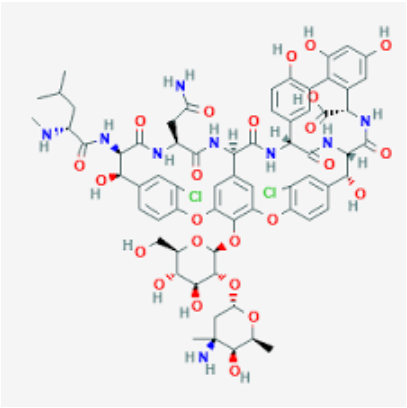
Antibiotics

- Two sets of blood cultures (aerobic and anaerobic) are recommended without delaying the initiation of antibiotics. Cultures from other sites such as respiratory secretions, urine, wounds, cerebrospinal fluid, and catheter insertion sites (in-situ more than 48 hours) are recommended if infections from these sites are suspected. In severe sepsis and septic shock, broad-spectrum antibiotics (usually two, a β-lactam antibiotic with broad coverage, or broad-spectrum carbapenem combined with fluoroquinolones, macrolides, or aminoglycosides) are recommended. However, combination of antibiotics is not recommended for the treatment of sepsis but without shock and immunocompromised persons unless the combination is used to broaden the anti-bacterial activity. The choice of antibiotics is important in determining the survival of the person. Some recommend they be given within one hour of making the diagnosis, stating that for every hour of delay in the administration of antibiotics, there is an associated 6% rise in mortality. Others did not find a benefit with early administration.
- Several factors determine the most appropriate choice for the initial antibiotic regimen. These factors include local patterns of bacterial sensitivity to antibiotics, whether the infection is thought to be a hospital or community-acquired infection, and which organ systems are thought to be infected. Antibiotic regimens should be reassessed daily and narrowed if appropriate. Treatment duration is typically 7–10 days with the type of antibiotic used directed by the results of cultures. If the culture result is negative, antibiotics should be de-escalated according to person's clinical response or stopped altogether if infection is not present to decrease the chances that the person is infected with multiple drug resistance organisms. In case of people having high risk of being infected with multiple drug resistance organisms such as Pseudomonas aeruginosa, Acinetobacter baumannii, addition of antibiotic specific to gram-negative organism is recommended. For Methicillin-resistant Staphylococcus aureus (MRSA), vancomycin or teicoplanin is recommended. For Legionella infection, addition of macrolide or fluoroquinolone is chosen. If fungal infection is suspected, an echinocandin, such as caspofungin or micafungin, is chosen for people with severe sepsis, followed by triazole (fluconazole and itraconazole) for less ill people. Prolonged antibiotic prophylaxis is not recommended in people who has SIRS without any infectious origin such as acute pancreatitis and burns unless sepsis is suspected.
- Once daily dosing of aminoglycoside is sufficient to achieve peak plasma concentration for clinical response without kidney toxicity. Meanwhile, for antibiotics with low volume distribution (vancomycin, teicoplanin, colistin), loading dose is required to achieve adequate therapeutic level to fight infections. Frequent infusions of beta-lactam

antibiotics without exceeding total daily dose would help to keep the antibiotics level above minimum inhibitory concentration (MIC), thus providing better clinical response. Giving beta-lactam antibiotics continuously may be better than giving them intermittently. Access to therapeutic drug monitoring is important to ensure adequate drug therapeutic level while at the same time preventing the drug from reaching toxic level.



Caspofungin



vancomycin

Intravenous fluids

- The Surviving Sepsis Campaign has recommended 30 ml/kg of fluid to be given in adults in the first three hours followed by fluid titration according to blood pressure, urine output, respiratory rate, and oxygen saturation with a target mean arterial pressure (MAP) of 65 mmHg. In children an initial amount of 20ml/kg is reasonable in shock. In cases of severe sepsis and septic shock where a central venous catheter is used to measure blood pressures dynamically, fluids should be administered until the central venous pressure (CVP) reaches 8–12 mmHg. Once these goals are met, the central venous oxygen saturation (ScvO2), i.e., the oxygen saturation of venous blood as it returns to the heart as measured at the vena cava, is optimized. If the ScvO2 is less than 70%, blood may be given to reach a hemoglobin of 10 g/dL and then inotropes are added until the ScvO2 is optimized. In those with acute respiratory distress syndrome (ARDS) and sufficient tissue blood fluid, more fluids should be given carefully.
- Crystalloid is recommended as the fluid of choice for resuscitation. Albumin can be used if large amount of crystalloid is required for resuscitaition. Crystalloid solutions shows little difference with hydroxyethyl starch in terms of risk of death. Starches also carry an increased risk of acute kidney injury, and need for blood transfusion. Various colloid solutions (such as modified gelatin) carry no advantage over crystalloid. Albumin also appears to be of no benefit over crystalloids.

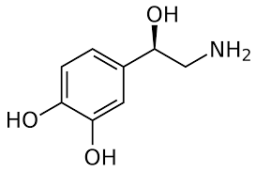
Blood products

- The Surviving Sepsis Campaign recommended packed red blood cells transfusion for hemoglobin levels below 70 g/L if there is no myocardial ischemia, hypoxemia, or acute bleeding. In a 2014 trial, blood transfusions to keep target hemoglobin above 70 or 90 g/L did not make any difference to survival rates; meanwhile, those with a lower threshold of transfusion received fewer transfusions in total. Erythropoietin is not recommended in the treatment of anemia with septic shock because it may precipitate blood clotting events. Fresh frozen plasma transfusion usually does not correct the underlying clotting abnormalities before a planned surgical procedure. However, platelet transfusion is suggested for platelet counts below (10×10^9/L) without any risk of bleeding, or (20×10^9/L) with high risk of bleeding, or (50×10^9/L) with active bleeding, before a planned surgery or an invasive procedure. IV immunoglobulin is not recommended because its beneficial effects are uncertain. Monoclonal and polyclonal preparations of intravenous immunoglobulin (IVIG) do not lower the rate of death in newborns and adults with sepsis. Evidence for the use of IgM-enriched polyclonal preparations of IVIG is inconsistent. On the other hand, the use of antithrombin to treat disseminated intravascular coagulation is also not useful. Meanwhile, the blood purification technique (such as hemoperfusion, plasma filtration, and coupled plasma filtration adsorption) to remove inflammatory mediators and bacterial toxins from the blood also does not demonstrate any survival benefit for septic shock.

Vasopressors

- If the person has been sufficiently fluid resuscitated but the mean arterial pressure is not greater than 65 mmHg, vasopressors are recommended. Norepinephrine (noradrenaline) is recommended as the initial choice.
- Norepinephrine is often used as a first-line treatment for hypotensive septic shock because evidence shows that there is a relative deficiency of vasopressin, when shock continues for 24 to 48 hours. Norepinephrine raises blood pressure through a vasoconstriction effect, with little effect on stroke volume and heart rate. In some people, the required dose of vasopressor needed to increase the mean arterial pressure can become exceedingly high that it becomes toxic. In order to reduce the required dose of vasopressor, epinephrine may be added. Epinephrine is not often used as a first-line treatment for hypotensive shock because it reduces blood flow to the abdominal organs and increases lactate levels. However, one of the adrenaline side effects is that it reduces blood flow to abdominal organs and may cause increased lactate levels. Vasopressin can be used in septic shock because studies have shown that there is a relative deficiency of vasopressin when shock continues for 24 to 48 hours. However,

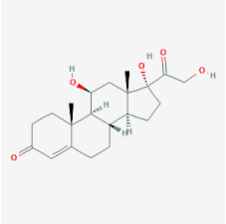
vasopressin reduces blood flow to the heart, finger/toes, and abdominal organs, resulting in a lack of oxygen supply to these tissues. Dopamine is typically not recommended. Although dopamine is useful to increase the stroke volume of the heart, it causes more abnormal heart rhythms than norepinephrine and also has an immunosuppressive effect. Dopamine is not proven to have protective properties on the kidneys. Dobutamine can also be used in hypotensive septic shock to increase cardiac output and correct blood flow to the tissues. Dobutamine is not used as often as epinephrine due to its associate side effects, which include reducing blood flow to the gut. Additionally, dobutamine increases the cardiac output by abnormally increasing the heart rate.



Norepinephrine

Steroids

- The use of steroids in sepsis is controversial. Studies do not give a clear picture as to whether and when glucocorticoids should be used. The 2016 Surviving Sepsis Campaign recommends low dose hydrocortisone only if both intravenous fluids and vasopressors are not able to adequately treat septic shock. A 2015 Cochrane review found low-quality evidence of benefit, as did two 2019 reviews.
- During critical illness, a state of adrenal insufficiency and tissue resistance to corticosteroids may occur. This has been termed critical illness–related corticosteroid insufficiency. Treatment with corticosteroids might be most beneficial in those with septic shock and early severe ARDS, whereas its role in others such as those with pancreatitis or severe pneumonia is unclear. However, the exact way of determining corticosteroid insufficiency remains problematic. It should be suspected in those poorly responding to resuscitation with fluids and vasopressors. Neither ACTH stimulation testing nor random cortisol levels are recommended to confirm the diagnosis. The method of stopping glucocorticoid drugs is variable, and it is unclear whether they should be slowly decreased or simply abruptly stopped. However, the 2016 Surviving Sepsis Campaign recommended to taper steroids when vasopressors are no longer needed.



Hydrocortisone

Anesthesia

- A target tidal volume of 6 mL/kg of predicted body weight (PBW) and a plateau pressure less than 30 cm H_2O is recommended for those who require ventilation due to sepsis-induced severe ARDS. High positive end expiratory pressure (PEEP) is recommended for moderate to severe ARDS in sepsis as it opens more lung units for oxygen exchange. Predicted body weight is calculated based on sex and height, and tools for this are available. Recruitment maneuvers may be necessary for severe ARDS by briefly raising the transpulmonary pressure. It is recommended that the head of the bed be raised if possible to improve ventilation. However, β2 adrenergic receptor agonists are not recommended to treat ARDS because it may reduce survival rates and precipitate abnormal heart rhythms. A spontaneous breathing trial using continuous positive airway pressure (CPAP), T piece, or inspiratory pressure augmentation can be helpful in reducing the duration of ventilation. Minimizing intermittent or continuous sedation is helpful in reducing the duration of mechanical ventilation.
- General anesthesia is recommended for people with sepsis who require surgical procedures to remove the infective source. Usually inhalational and intravenous anesthetics are used. Requirements for anesthetics may be reduced in sepsis. Inhalational anesthetics can reduce the level of proinflammatory cytokines, altering leukocyte adhesion and proliferation, inducing apoptosis (cell death) of the lymphocytes, possibly with a toxic effect on mitochondrial function. Although etomidate has a minimal effect on the cardiovascular system, it is often not recommended as a medication to help with intubation in this situation due to concerns it may lead to poor adrenal function and an increased risk of death. The small amount of evidence there is, however, has not found a change in the risk of death with etomidate.
- Paralytic agents are not suggested for use in sepsis cases in the absence of ARDS, as a growing body of evidence points to reduced durations of mechanical ventilation, ICU and hospital stays. However, paralytic use in ARDS cases remains controversial. When appropriately used, paralytics may aid successful mechanical ventilation, however

evidence has also suggested that mechanical ventilation in severe sepsis does not improve oxygen consumption and delivery.

8. URINARY TRACT INFECTIONS

The term urinary tract infection (UTI) usually refers to the presence of organisms in the urinary tract together with symptoms, and sometimes signs, of inflammation.

Epidemiology:

UTIs are among the most common infectious diseases occurring in either the community or health care setting. Uncomplicated UTIs typically occur in healthy adult nonpregnant women, whereas complicated UTIs are found in either sex and at any age, frequently associated with structural or functional urinary tract abnormalities.

Aetiology and risk factors:

In acute uncomplicated UTI acquired in the community, Escherichia coli is by far the most common causative bacterium, being responsible for about 80% of infections. The remaining 20% are caused by other Gram-negative enteric bacteria such as Klebsiella and Proteus species, and by Grampositive cocci, particularly enterococci and Staphylococcus saprophyticus. The latter organism is almost entirely restricted to infections in young, sexually active women. UTI associated with underlying structural abnormalities, such as congenital anomalies, neurogenic bladder and obstructive uropathy, is often caused by more resistant organisms such as Pseudomonas aeruginosa, Enterobacter and Serratia species. Organisms such as these are also more commonly implicated in hospital-acquired urinary infections, including those in patients with urinary catheters. Rare causes of urinary infection, nearly always in association with structural abnormalities or catheterisation, include anaerobic bacteria and

fungi. Urinary tract tuberculosis is an infrequent but important diagnosis that may be missed through lack of clinical suspicion. A number of viruses are excreted in urine and may be detected by culture or nucleic acid amplification methods, but symptomatic infection is confined to immunocompromised patients, particularly children following bone marrow transplantation, in whom adenoviruses and polyomaviruses such as BK virus are associated with haemorrhagic cystitis.

Pathogenesis:

There are three possible routes by which organisms might reach the urinary tract: the ascending, blood-borne and lymphatic routes. There is little evidence for the last route in humans. Blood-borne spread to the kidney can occur in bacteraemic illnesses, most notably Staphylococcus aureus septicaemia, but by far the most frequent route is the ascending route.

In women, UTI is preceded by colonisation of the vagina, perineum and periurethral area by the pathogen, which then ascends into the bladder via the urethra. Uropathogens colonise the urethral opening of men and women. That the urethra in women is shorter than in men and the urethral meatus is closer to the anus are probably important factors in explaining the preponderance of UTI in females.

Further, sexual intercourse appears to be important in forcing bacteria into the female bladder, and this risk is increased by the use of diaphragms and spermicides, which have both been shown to increase E. coli growth in the vagina. Whether circumcision reduces the risk of infection in adult men is not known, but it markedly reduces the risk of UTI in male infants.

Babies and infants:

Infections in newborn babies and infants are often overlooked or misdiagnosed because the signs may not be referable to the urinary tract. Common but non-specific presenting symptoms include failure to thrive, vomiting, fever, diarrhoea and apathy.

ChildrenAbove the age of 2:

children with UTI are more likely to present with some of the classic symptoms such as frequency, dysuria and haematuria. However, some children present with acute abdominal pain and vomiting, and this may be so marked as to raise suspicions of appendicitis or other intra-abdominal pathology. Again, however, it is extremely important that the diagnosis of UTI is made promptly to pre-empt the potential long-term consequences.

Adults:

In adults, the typical symptoms of lower UTI include frequency, dysuria, urgency and haematuria. Acute pyelonephritis (upper UTI) usually causes fever, rigors and loin pain in addition to lower tract symptoms. Systemic symptoms may vary from insignificant to extreme malaise. Importantly, untreated cystitis in adults rarely progresses to pyelonephritis, and bacteriuria does not seem to carry the adverse long-term consequences that it does in children. In about 40% of women with dysuria, urgency and frequency, the urine sample contains fewer than 100,000 bacteria/mL. These patients are said to have the urethral syndrome. Some have a true bacterial infection but with relatively low counts (100–1000 bacteria/mL). Some have urethral infection with Chlamydia trachomatis, Neisseria gonorrhoeae, mycoplasmas or other 'fastidious' organisms, any of which might give rise to symptoms indistinguishable from those of cystitis.

Elderly:

Although UTI is frequent in the elderly, the great majority of cases are asymptomatic, and even when present, symptoms are not diagnostic because frequency, dysuria, hesitancy and incontinence are fairly common in elderly people without infection. Further, there may be non-specific systemic manifestations such as confusion and falls, or alternatively the infection may be the cause of deterioration in pre-existing conditions such as diabetes mellitus or congestive cardiac failure, whose clinical features might predominate.

Diagonsis :

Current emphasis in the diagnosis of UTI rests with the detection of pyuria, as follow:

A positive leukocyte esterase dipstick test suffices in most instances.

In females with clinical findings suggestive of UTI, Urine microscopy may be indicated even if the leukocyte esterase dipstick test is negative

Pyuria is most accurately measured by counting leukocytes in unspun fresh urine using a hemocytometer chamber; more than 10 white blood cells (WBCs)/mL is abnormal.

Microscopic hematuria is found in about half of cystitis cases

Low-grade proteinuria is common

A positive nitrite test is highly specific for UTI

Recent urinary tract instrumentation

Recent exposure to antibiotics

Recurrent infection

Advanced age

Cystitis: More than 1000 colony-forming units (CFU)/ ml

Pyelonephritis: More than 10,000 CFU/ml

Treatment:

The mainstay of treatment is antibiotics. Phenazopyridine is occasionally prescribed during the first few days in addition to antibiotics to help with the burning and urgency sometimes felt during a bladder infection. However, it is not routinely recommended due to safety concerns with its use, specifically an elevated risk of methemoglobinemia (higher than normal level of methemoglobin in the blood). Acetaminophen (paracetamol) may be used for fevers. There is no good evidence for the use of cranberry products for treating current infections.

Asymptomatic bacteriuria

Those who have bacteria in the urine but no symptoms should not generally be treated with antibiotics. This includes those who are old, those with spinal cord injuries, and those who have urinary catheters. Pregnancy is an exception and it is recommended that women take 7 days of antibiotics. If not treated it causes up to 30% of mothers to develop pyelonephritis and increases risk of low birth weight and preterm birth. Some also support treatment of those with diabetes mellitus and treatment before urinary tract procedures which will likely cause bleeding.

Uncomplicated

Uncomplicated infections can be diagnosed and treated based on symptoms alone. Antibiotics taken by mouth such as trimethoprim/sulfamethoxazole (TMP/SMX), nitrofurantoin,

or fosfomycin are typically first line. Cephalosporins, amoxicillin/clavulanic acid, or a fluoroquinolone may also be used. However, resistance to fluoroquinolones among the bacteria that cause urinary infections has been increasing. The Food and Drug Administration (FDA) recommends against the use of fluoroquinolones when other options are available due to higher risks of serious side effects. These medications substantially shorten the time to recovery with all being equally effective. A three-day treatment with trimethoprim, TMP/SMX, or a fluoroquinolone is usually sufficient, whereas nitrofurantoin requires 5–7 days. Fosfomycin may be used as a single dose but has been associated with lower rates of efficacy.

With treatment, symptoms should improve within 36 hours. About 50% of people will recover without treatment within a few days or weeks. Fluoroquinolones are not recommended as a first treatment. The Infectious Diseases Society of America states this due to the concern of generating resistance to this class of medication. Amoxicillin-clavulanate appears less effective than other options. Despite this precaution, some resistance has developed to all of these medications related to their widespread use. Trimethoprim alone is deemed to be equivalent to TMP/SMX in some countries. For simple UTIs, children often respond to a three-day course of antibiotics. Women with recurrent simple UTIs are over 90% accurate in identifying new infections. They may benefit from self-treatment upon occurrence of symptoms with medical follow-up only if the initial treatment fails.

Complicated

Complicated UTIs are more difficult to treat and usually requires more aggressive evaluation, treatment and follow-up. It may require identifying and addressing the underlying complication. Increasing antibiotic resistance is causing concern about the future of treating those with complicated and recurrent UTI.

Pyelonephritis

Pyelonephritis is treated more aggressively than a simple bladder infection using either a longer course of oral antibiotics or intravenous antibiotics. Seven days of the oral fluoroquinolone ciprofloxacin is typically used in areas where the resistance rate is less than 10%. If the local resistance rates are greater than 10%, a dose of intravenous ceftriaxone is often prescribed. Trimethoprim/sulfamethoxazole or amoxicillin/clavulanate orally for 14 days is another reasonable option.[92] In those who exhibit more severe symptoms, admission to a hospital for ongoing antibiotics may be needed.[3] Complications such as urinary obstruction from a kidney stone may be considered if symptoms do not improve following two or three days of treatment.

9. MALARIA

It is an infection of liver and RBC's caused by the protozoan parasites of the genus plasmodium, transmitted to humans through the bite of an infected female anopheles mosquito.
It is caused by four species of plasmodium

- Plasmodium falciparum(the most common)
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malaria

Pathophysiology:

Life cycle of plasmodium: These parasites spend an asexual phase in man and sexual phase in female anopheles mosquito.

- The mosquito stores the sporozoite form of the protozoan in it's salivary glands.
- Through the bite of an infected mosquito the sporozoite enters the bloodstream and then into the paranchyma cell of host liver and becomes primary schizonts and then merozoites.
- Depending on the plasmodium, the merozoites either rupture the infected hepatocytes and enters systemic circulation or infect other liver cells(pre-erythrocytic stage)
- Merozoites which enters the circulation invades erythrocytes where they reside for 3to 4days and reproduce (erythrocytic stage)
- These erythrocytes may produce more merozoites or another form called gametocytes.
- Repeated multiplication causes the erythrocyte to rupture and release merozoites into the circulation and invades fresh erythrocytes, this phase is known as schizogony phase of infection causes severe fever and chills.
- Destruction of large number of infected RBC, thereby causing haemolytic anaemia.
- Haematin released from the ruptured RBC produces discoloration of spleen, liver, lymph nodes, bone marrow.
- Activation of defence mechanisms in host leads to a marked hyperplasia of mononuclear phagocytes Producing massive spleenomegaly and occasionally hepatomegaly.

Signs and symptoms:

➢ Cycles of shaking chill followed by fever and profuse sweating.
➢ Weight loss
➢ Headache
➢ Dry cough
➢ Weakness
➢ Muscle pain
➢ Dark pigmented urine

Risk factors:

➢ Living or visiting the region with high rate of malaria

➢ Availability of stagnant water
➢ People with low immunity.
➢ Lack of insect repellent.

Diagnosis:
➢ Physical examination
➢ Lab diagnosis
1. Films of blood(thick and thin blood smear study)
2. Quantitative buffy coat test
3. Antibody based techniques(serological test)
4. Antigen based techniques
5. Polymerase chain reaction.

Pharmacological treatment:
Antimalarial therapy:
Prophylactic agent: Kills the sporozoites injected by the mosquito or prevail the entering of sporozoites entering liver.
Schizonticidal agent: Drugs that are active against erythrocytic phase. Example:chloroquine, amodiaquine , quinine, pyrimethamine.
Suppressive agent: Kills merozoites in the blood or prevent their multiplication. Example: chloroquine, amodiaquine.
Gametocidal agents: Kills gametocytes before they enter the mosquito and reproduce into zygotes.

Classification of antimalarial drugs: Classified chemically as

1. Cinchona alkaloids: Ex:quinine, cinchonine
2. 4-amino quinolines: Ex:chloroquine, amodiaquine, hydroxychloroquine
3. 8-amino quinolones: Ex: bulaquine, primaquine, pamaquine
4. 9-aminoacridine: Ex:mepacrine
5. Biguanides: Ex: proguanil, cycloguanil
6. Pyrimidine analogue: Ex:pyrimethamine
7. Polycyclics: Ex: doxycycline, halofanyrine
8. Newer antimalarial agents: Ex:artemisinin, fosmidomycin
9. Sesquiterpene lactone: Ex:arteether, arteemether
10. Miscellaneous: Ex: metolamine, sulphadoxine

❖ Quinine:
It is used to treat chloroquine resistant strains of plasmodium falciparum
Dose:650 mg given 8 every hour for 7 days.

Adverse reactions: Cinchonism characterized by tinnitus, impaired hearing, disturbed vision, nausea and vomiting

❖ Chloroquine:
It prevents the development of malarial parasites in blood. They act by intercalating into the DNA of the parasite.chloroquine inhibits the action of heme polymerase in malarial trophozoites preventing the conversions of heme to hemazoin, accumulation of toxic heme kills parasite.
Dose:300 mg once weekly continued foe atleast 4 weeks after exposure.
Adverse effects: Retinopathy, hair loss, photosensitivity headache itching myopathy.

❖ Primaquine:
It is active against gametocytes and hypnozoites.
Dose:15 mg daily for 14 days
Adverse effects:
Nausea, vomiting, epigastric stress.

❖ Pyrimethamine:
It acts by interfering with tetrahydrofolic acid synthesis from folic acid by inhibiting the enzyme dihydrofolate reductase. Dose:25 mg as single dose
Adverse effects: Urticaria photosensitisation and arthralgia.

❖ Mefloquine:
It is effective against the erythrocytic form of malaria. It is used in combination with artemisinin.
Dose: 20 to 25 mg/kg as a single dose or preferably 2 or 3 divided doses
Adverse effects: Nausea , vomiting, abdominal pain, and diarrhoea.

10. HIV & OPPORTUNISTIC INFECTIONS

DEFINITION
Acquired immunodeficiency syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV). By damaging your immune system, HIV interferes with your body's ability to fight infection and disease.
EPIDEMIOLOGY
• Males are more prone to HIV than females
• Occurs in all ages and ethnic groups
• All areas of the country are affected
• AIDS is now the second leading cause of death for all men aged 25-44 years (Unintended injuries is #1 and heart disease is #3 for this age group)

Etiology:
• The HIV infection is caused by the human immunodeficiency virus (HIV).

• After HIV is in the body, it starts to destroy CD4+T cells , which are white blood cells that help the body fight infection and disease.

• HIV is spread when blood, semen, or vaginal fluids from an infected person enter another person's body, usually through sexual contact, from sharing needles when injecting drugs , or from mother to baby during birth.

Structure of HIV

• HIV belongs to a special class of viruses called retroviruses. Within this class, HIV is placed in the subgroup of lentiviruses

• All viruses except retroviruses contain DNA

• Other lentiviruses include SIV, FIV, Visna and CAEV, which cause diseases in monkeys, cats, sheep and goats .

• HIV particles surround themselves with a coat of fatty material known as the viral envelope.

• This envelope gives out lots of little spikes around 72 in number.

• These spikes are made of knobs and handles made of proteins gp120 and gp41 respectively.

• Just below the viral envelope is a layer called the matrix, which is made from the protein p17(Matrix proteins)

• Below the matrix is another layer of proteins P24 forming viral core (or capsid) and is usually bullet - shaped.

• Inside the core are three enzymes required for HIV replication called Reverse transcriptase, Integrase and protease

• Also held within the core is HIV's genetic material, which consists of two identical copies of single stranded RNA

PATHOGENESIS :

Attachment of virus at the CD4 receptor and chemokine co - receptors .

viral fusion and uncoating Reverse transcriptase .

Migration to nucleus

Integration of the viral DNA into cellular DNA by the enzyme integrase

Transcription and RNA processing Protein synthesis.

protease cleaves polypeptides into functional HIV proteins and the virion assembles

virion budding

Virion maturation

Pathogenesis of HIV

Incubation period
• The incubation period is from HIV infection till development of AIDS.
• It is from a few months to 10 years or even more.
• However it is estimated that 75% of people infected with HIV will develop AIDS at the end of 10 years.

Stages of HIV
Stage – 1(Primary)
• flu like illness - occurs two to six weeks after infection or there may be
• no symptoms at all
• Infected person can infect other people

STAGE2 ASYMPTOMATIC
This stage is free from symptoms
• There may be swollen glands.
• HIV antibodies are detectable in the blood
• This stage is last for about ten years

STAGE 3 – SYMPTOMATIC
• The person starts showing symptoms like fever, skin disease.
• The immune system deteriorates emergence of opportunistic infections and cancers

STAGE 4 - HIV - AIDS :
• The immune system weakens
• The illnesses become more severe leading to AIDS
• The illnesses become more severe leading to emergence of opportunistic infections and cancers

TRANSMISSION of HIV
• HIV virus is passed from one person to another through blood - to - blood and unprotected sex .

• In addition, infected pregnant women can pass HIV to their baby during pregnancy or delivery, as well as through breast – feeding

• The body fluids have been proven to spread HIV:
1. blood
2. semen
3. vaginal fluid
4. breast milk
5. other body fluids containing blood

6. cerebrospinal fluid surrounding the brain and the spinal cord
7. synovial fluid surrounding bone joints

SYMPTOMS :
The symptoms of this :
- Diarrhoea
- fatigue
- fever
- headache
- joint pain
- night sweat
- rash
- swollen glands
- weight loss
- yeast infections

Laboratory test
- Enzyme - Linked Immunosorbent Assay/Enzyme Immunoassay (ELISA/EIA)
- Western Blot

Opportunistic infections

Candidiasis of bronchi, trachea, esophagus, or lungs

This illness is caused by infection with a common (and usually harmless) type of fungus called Candida. Candidiasis, or infection with Candida, can affect the skin, nails, and mucous membranes throughout the body. Persons with HIV infection often have trouble with Candida, especially in the mouth and vagina. However, candidiasis is only considered an OI when it infects the esophagus (swallowing tube) or lower respiratory tract, such as the trachea and bronchi (breathing tube), or deeper lung tissue.

Coccidioidomycosis

This illness is caused by the fungus Coccidioides immitis. It most commonly acquired by inhaling fungal spores, which can lead to a pneumonia that is sometimes called desert fever, San Joaquin Valley fever, or valley fever. The disease is especially common in hot, dry regions of the southwestern United States, Central America, and South America.

Encephalopathy, HIV-related

This brain disorder is a result of HIV infection. It can occur as part of acute HIV infection or can result from chronic HIV infection. Its exact cause is unknown but it is thought to be related to infection of the brain with HIV and the resulting inflammation

Kaposi's sarcoma (KS)

This cancer, also known as KS, is caused by a virus called Kaposi's sarcoma herpesvirus (KSHV) or human herpesvirus 8 (HHV-8). KS causes small blood vessels, called capillaries, to grow abnormally. Because capillaries are located throughout the body, KS can occur anywhere. KS

appears as firm pink or purple spots on the skin that can be raised or flat. KS can be life-threatening when it affects organs inside the body, such the lung, lymph nodes, or intestines.

Tuberculosis (TB)

Tuberculosis (TB) infection is caused by the bacteria Mycobacterium tuberculosis. TB can be spread through the air when a person with active TB coughs, sneezes, or speaks. Breathing in the bacteria can lead to infection in the lungs. Symptoms of TB in the lungs include cough, tiredness, weight loss, fever, and night sweats. Although the disease usually occurs in the lungs, it may also affect other parts of the body, most often the larynx, lymph nodes, brain, kidneys, or bones.

Pneumocystis carinii pneumonia (PCP)

Pneumonia is an infection in one or both of the lungs. Many germs, including bacteria, viruses, and fungi can cause pneumonia, with symptoms such as a cough (with mucous), fever, chills, and trouble breathing. In people with immune systems severely damaged by HIV, one of the most common and life-threatening causes of pneumonia is infection with the bacteria Streptococcus pneumoniae, also called Pneumococcus.

TREATMENT

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (nrtis)

Nrtis force the HIV virus to use faulty versions of building blocks so infected cells can't make more HIV.

- Abacavir, or ABC (Ziagen)
- Emtricitabine, or FTC (Emtriva)
- Lamivudine, or 3TC (Epivir)
- Zidovudine or ZDV (Retrovir)

Non-nucleoside Reverse Transcriptase Inhibitors (nnrtis)

These are also called "non-nukes." nnrtis bind to a specific protein so the HIV virus can't make copies of itself, similar to jamming a zipper.

- Delavirdine or DLV (Rescripor)
- Doravirine, or DOR (Pifeltro)
- Efavirenz or EFV (Sustiva)
- Etravirine or ETR (Intelence)
- Nevirapine or NVP (Viramune)
- Rilpivirine or RPV (Edurant)

Protease Inhibitors (pis)

These drugs block a protein that infected cells need to put together new HIV virus particles.

- Atazanavir or ATV (Reyataz)
- Darunavir or DRV (Prezista)
- Fosamprenavir or FPV (Lexiva)
- Indinavir or IDV (Crixivan)
- Lopinavir + ritonavir, or LPV/r (Kaletra)

- Nelfinavir or NFV (Viracept)
- Ritonavir or RTV (Norvir)

Integrase Inhibitors

These stop HIV from making copies of itself by blocking a key protein that allows the virus to put its DNA into the healthy cell's DNA. They're also called integrase strand transfer inhibitors (instis).

- Bictegravir or BIC (combined with other drugs as Biktarvy)
- Dolutegravir or DTG (Tivicay)
- Elvitegravir or EVG (Vitekta),Raltegravir or RAL (Isentress)

Fusion Inhibitors

Unlike nrtis, nnrtis, pis, and instis -- which work on infected cells -- these drugs help block HIV from getting inside healthy cells in the first place.

Enfuvirtide, or ENF or T-20 (Fuzeon)

CCR5 Antagonist

Maraviroc, or MVC (Selzentry), also stops HIV before it gets inside a healthy cell, but in a different way than fusion inhibitors. It blocks a specific kind of "hook" on the outside of certain cells so the virus can't plug in.

Post-Attachment Inhibitor or Monoclonal Antibody

This is a new class of antiviral medication specifically for adults living with HIV who have tried multiple HIV medications and whose HIV has been resistant to current available therapies. Ibalizumab-uiyk (Trogarzo) blocks your body’s HIV infected cells from spreading the virus into those which are uninfected. It is administered by IV.

Fixed-Dose Combinations

Some drug manufacturers put together specific medicines into a single pill so they're easier to take, including:

Integrase strand transfer inhibitor (INSTI)-based:

- Dolutegravir + abacavir + lamivudine, or DTG/ABC/3TC (Triumeq)
- Dolutegravir + rilpivirine, or DTG/RPV (Juluca)
- Dolutegravir + lamivudine, or DTG/3TC (Dovato)

Protease inhibitor (PI)-based:

- Atazanavir + cobicistat, or ATV/c (Evotaz)
- Darunavir + cobicistat, or DRV/c (Prezcobix) Darunavir + cob

There's no vaccine to prevent HIV infection and no cure for AIDS. But it's possible to protect yourself and others from infection. That means educating yourself about HIV and avoiding any behavior that allows HIV - infected fluids: blood, semen, vaginal secretions and breast milk into your body.

11. FUNGAL INFECTIONS

Fungal infections are also known as mycoses,they represent the invasion of the tissues by one or more species of fungi.They range from superficial,localized skin conditions to deeper tissue infections to serious lung,blood(septicemia) or systemic diseases.

STUDY OF FUNGI:

Fungi reproduce by forming spores through mitosis giving rise to two daughter cells.They are known by given to this imperfect state(asexual reproduction), but the same fungus, for example, Scedosporium apiosperman(asexual state) is also known as Pseudoallescheria boydii(sexual form).

Fungi are broadly divided into yeasts and moulds.Yeasts are typically flat round colonies on culture plates and reproduce by forming buds from their cells.Moudls appear as a collection or mass(mycelium) of individual tubular structures called hyphae.

Epidemiology:

Fungal infections are acquired from the environment or may be endogenous in the few instances where they are members of the resident flora.Inhalation of infectious conidia generated from molds growing in the environment is a common mechanism. Some of these molds are ubiquitous, whereas others are restricted to geographic areas whose climate favors their growth. In the latter case, disease can be acquired only in the endemic area. Some environmental fungi produce disease after they are accidentally injected past the skin barrier. The pathogenic fungi represent only a small percentage of those found in the environment. Endogenous infections are restricted to a few yeasts, primarily Candida albicans. These yeasts have the ability to colonize by adhering to host cells and, given the opportunity, invade deeper structures.

PATHOGENESIS:

Superficial infection Candida infection:

Candida is a normal commensal of the human gastrointestinal tract and skin. Loss of skin and mucosal integrity or use of broad-spectrum antibiotics which alter normal bacterial flora allow overgrowth of endogenous Candida.Thrush is candidal infection of the mucous membrane. It can manifest as oral infection, for example, oral thrush in various patient groups, vulvo vaginal thrush in females, balanitis in the uncircumcised man or intertrigo infection in moist skin surfaces in close proximity, for example, groin area. Patients with diabetes and steroid users, whether inhaled or oral, are also prone to infections. Dysphagia due to candidal oesophagitis presents in patients with AIDS and cancer.

Clinical presentation:

Oral thrush typically presents as a sore mouth with white curd like patches on the tongue or oral mucosa which can bleed on scraping. Females with vaginal thrush present with itching and a creamy vaginal discharge.Candida folliculitis may present in unkempt, bearded men. Nail infection with Candida (onychomycosis), or subcutaneous tissue involvement under the nail (paronychia) is seen in people whose occupation involves prolonged hand immersion in water. In severe oesophageal candidiasis, ulceration or formation of pseudomembranes and, rarely, perforation of lower third of the oesophagus may occur

Treatment:

Oral and vaginal candidiasis may be treated by either topical or systemic antifungal agents. The drugs currently available for topical use fall into two groups: the polyenes, of which only amphotericin and nystatin are used clinically, and the imidazoles such as econazole, clotrimazole, miconazole and fenticonazole.The two systemic agents are both triazoles (fluconazole and itraconazole) and can be given by mouth.Three triazole agents: fluconazole, itraconazole and voriconazole are available for systemic treatment of oral and vulvo vaginal candidiasis (VVC).

Dermatophytosis:

Dermatophytosis, or tinea, is a condition caused by three genera of dermatophyte fungi: Trichophyton, Epidermophyton and Microsporum. Unlike Candida, these are moulds which have a predilection for keratinised tissue such as skin, nail and hair. These fungi are very widely distributed throughout the world and may be acquired from the soil (anthrophilic, e.g. Trichophyton rubrum), from animals (zoophilic) or from humans (geophilic) infected with the fungus.

Clinical presentation:

The classical clinical presentation of dermatophyte infection of the skin is ringworm (tinea), a circular, inflamed lesion with a raised edge and associated skin scaling. However, presentation is influenced by the site of infection, for example, tinea pedis (athlete's foot) between the toes. Dermatophytosis of the nail results in thickened, discoloured nails, while in the scalp, infection presents with itching, skin scaling and inflammation, and patchy hair loss (alopecia). Rarely, deep dermatophytosis may be seen in immunocompromised patients with involvement of subcutaneous tissue (granuloma).

diagnosis:

The diagnosis of dermatophyte infection is confirmed by collecting appropriate specimens such as material from infected nails and skin. The fungi can be seen microscopically and specimens may also be cultured, but antifungal susceptibility testing is not required.

Treatment:

The most commonly used topical agents are the imidazoles, of which a wide variety is available, including clotrimazole, ecoazole, miconazole, sulconazole and tioconazole.Other topical agents include amorolfine, terbinafine and tolnaftate. The main oral antifungals used for dermatophytosis are terbinafine, itraconazole and fluconazole. Griseofulvin is an alternative treatment for tinea capitis. Terbinafine. Terbinafine was the first member of a new class of antifungal agents, the allylamines, which became available for systemic use. These agents act by inhibition of the fungal enzyme squalene epoxidase, an enzyme involved in the synthesis of ergosterol, an essential component of the fungal cytoplasmic membrane.

Ptyriasis versicolor:

This is a common superficial skin infection caused by a yeast-like fungus, Malassezia furfur. The organism is a member of the normal skin flora and lives only on the skin because it has a growth requirement for medium-chain fatty acids present in sebum.

Clinical presentation:

The condition usually appears as patches scattered over the trunk, neck and shoulders. These patches produce scales and may be pigmented in light-skinned individuals, appearing light brown in colour. In dark-skinned patients, the lesions may lose pigment and appear lighter than normal skin. In some patients, Malassezia yeast is also associated with dandruff and seborrhoeic dermatitis, although the exact role of the yeast in causing this condition remains uncertain. In AIDS patients, seborrhoeic dermatitis may be quite extensive and sudden in onset.

diagosis:

The diagnosis is made by microscopy of scrapings from the lesion. The specimen is examined for the presence of yeast cells and short hyphae. Culture is not usually required for diagnosis and, since it requires special culture media, is not routinely attempted.

Treatment:

Pityriasis versicolor is treated with topical terbinafine cream or a topical imidazole cream such as clotrimazole, econazole or miconazole. Cheaper topical alternatives are 2% selenium sulphide lotion or 20% sodium thiosulphate applied daily for 10–14 days. Relapses are common and treatment may need to be repeated. In severe cases, oral itraconazole (200 mg once daily for 7 days) may be given. Treatment of seborrhoeic dermatitis and folliculitis is undertaken with topical azole creams and 1% hydrocortisone. This condition can also often relapse.

Ear infection:

Fungi sometimes infect the external auditory canal, causing otitis externa, the most common causative organisms being various species of Aspergillus (such as A. niger and A. fumigatus) and Candida albicans and other Candida species. A variety of other fungi found in the environment can also cause this condition. The use of topical antibacterial agents in the ear may predispose to local fungal infection.

Clinical presentation:

Fungal infection of the ear usually presents as pain and itching in the auditory canal, sometimes with a reduction in hearing due to blockage of the canal. There may be an associated discharge from the ear. Clinical examination shows a swollen red canal, and the fungal mycelium is sometimes visible as an amorphous white or grey mass.

Diagosis:

The diagnosis of a fungal infection of the external canal can be made by microscopy and culture of material obtained from the ear.

Treatment:

A topical antifungal agent such as nystatin or amphotericin, or an imidazole can also be applied. Infections with saprophytic fungi: Some saprophytic fungi (normally harmless human commensals) can cause significant infections. An example of such an infection in a host with a normal immune system is fusarium keratitis in contact lens wearers. Penicillium marneffei can cause skin infection and disseminated fatal infection in HIV-infected patients in South East Asia. Scedospermium pulmonary infections are seen in lung transplant recipients. A large retrospective data from the USA revealed that the three most common nonAspergillus moulds causing invasive fungal infection among patients receiving haemopoietic stem cell transplants (HSCT) were Fusarium, Scedospermium and Zygomycetes.

Deep seated fungal infection:

Most deep-seated or systemic fungal infections seen in the UK are the result of some breakdown in the normal body defenses, which may be due to disease or medical treatment. Fungi that cause superficial infections can also cause deep-seated infection in immunocompromised patients with leukaemia and lymphoma and those in the post-transplant period of immunosuppression. There are, however, a group of fungi, often referred to rather misleadingly as the pathogenic fungi, which are able to cause systemic infection in a previously healthy person. These infections, which are usually due to dimorphic fungi, include diseases such as histoplasmosis, blastomycosis and coccidioidomycosis. They are rare in the UK but rather more common in the USA and other parts of the world. Fungal infections in the

compromised host Epidemiology and predisposing factors: There are a large number of conditions which may predispose the individual to systemic or deep-seated fungal infection. A breach in the body's mechanical barriers may predispose to fungal infection. For example, fungal infection of the urinary tract occurs most commonly in catheterised patients who have received broad-spectrum antibiotics, while total parenteral nutrition (TPN) is strongly associated with fungaemia, sometimes with unusual fungi such as Malassezia furfur. This is due to the use of TPN infusions containing lipids, which are a growth requirement of this organism. Most cases of systemic fungal infection, however, are associated with a defect in the patient's immune system, and the nature of the organisms encountered is often related to the nature of the immunosuppression. Neutropenia, for example, is usually associated with Candida species, Aspergillus and mucormycosis, while defects of cell-mediated immunity, for example HIV infection, are strongly associated with infection by Cryptococcus neoformans. Prolonged diabetic ketoacidosis is a risk factor for developing rhinocerebral zygomycosis where mortality can be as high as 100% if there is significant underlying disease.

Clinical presentation:

Symptoms can be non-specific like low-grade fever, night sweats, weight loss, cough, chest pain and septic shock in extreme cases.

Diagnosis: Organ-specific radiological findings backed by laboratory tests, as discussed earlier in this chapter, are the mainstay of diagnosis.

Treatment:

Compared to the vast array of antibacterial agents available to treat bacterial infections, there are very few systemic antifungal agents available and these comprise four major categories: the polyenes (conventional and lipid formulations of Amphotericin B), the triazoles (fluconazole, itraconazole, voriconazole and posaconazole), the echinocandins (caspofungin, anidulafungin and micafungin) and flu-cytosine. To provide optimal therapy to the patient, it is necessary to understand the profile, properties and toxicity of these agents.Antifungal prophylaxis is commonly used to prevent invasive fungal infections in the ‘at risk’ group of patients.

12. VIRAL INFECTIONS

VIRUS :

Viruses are microscopic parasites, generally much smaller than bacteria. They lack the capacity to thrive and reproduce outside of a host body. The earliest indications of the biological nature of viruses came from studies in 1892 by the Russian scientist Dmitry I. Ivanovsky and in 1898 by the Dutch scientist Martinus W. Beijerinck. Beijerinck first surmised

that the virus under study was a new kind of infectious agent, which he designated contagium vivum fluidum, meaning that it was a live, reproducing organism that differed from other organisms. Both of these investigators found that a disease of tobaccoplants could be transmitted by an agent, later called tobacco mosaic virus, passing through a minute filter that would not allow the passage of bacteria. This virus and those subsequently isolated would not grow on an artificial medium and were not visible under the light microscope. In independent studies in 1915 by the British investigator Frederick W. Twort and in 1917 by the French Canadian scientist Félix H. d'Hérelle, lesions in cultures of bacteria were discovered and attributed to an agent called bacteriophage ("eater of bacteria"), now known to be viruses that specifically infect bacteria. Viruses occupy a special taxonomic position: they are not plants, animals, or prokaryotic bacteria (single-cell organisms without defined nuclei), and they are generally placed in their own kingdom. In fact, viruses should not even be considered organisms, in the strictest sense, because they are not freeliving; i.e., they cannot reproduce and carry on metabolic processes without a host cell.

STRUCTURE OF VIRUS :

All viruses contain nucleic acid, either DNA or RNA (but not both), and a protein coat, which encases the nucleic acid. Some viruses are also enclosed by an envelope of fat and protein molecules. In its infective form, outside the cell, a virus particle is called a virion.

• Capsid - The capsid is the protein shell that encloses the nucleic acid; with its enclosed nucleic acid, it is called the nucleocapsid. This shell is composed of protein organized in subunits known as capsomers. They are closely associated with the nucleic acid and reflect its configuration, either a rod-shaped helix or a polygonshaped sphere.

The capsid has three functions:

1) it protects the nucleic acid from digestion by enzymes

2) contains special sites on its surface that allow the virion to attach to a host cell,

3) provides proteins that enable the virion to penetrate the host cell membrane and, some cases, to inject the infectious nucleic acid into the cell's cytoplasm. Under the right conditions, viral RNA in a liquid suspension of protein molecules will self-assemble a capsid to become a functional and infectious virus.

• envelope - Many types of virus have a glycoprotein envelope surrounding the nucleocapsid. The envelope is composed of two lipid layers interspersed with protein molecules (lipoprotein bilayer) and may contain material from the membrane of a host cell as well as that of viral origin. The virus obtains the lipid molecules from the cell membrane during the viral budding process. However, the virus replaces the proteins in the cell membrane with its own proteins, creating a hybrid structure of cell-derived lipids and virus-derived proteins. Many viruses also develop spikes made of glycoprotein on their envelopes that help them to attach to specific cell surfaces.

• Nucleic Acid - Just as in cells, the nucleic acid of each virus encodes the genetic information for the synthesis of all proteins. While the double-stranded DNA is responsible for this in prokaryotic and eukaryotic cells, only a few groups of viruses use DNA. Most viruses maintain all their genetic information with the single-stranded RNA. There are two types of RNA-based viruses. In most, the genomic RNA is termed a plus strand because it acts as messenger RNA for direct synthesis (translation) of viral protein. A few, however, have negative strands of RNA. In these cases, the virion has an enzyme, called RNAdependent RNA polymerase (transcriptase), which must first catalyze the production of complementary messenger RNA from the virion genomic RNA before viral protein synthesis can occur.

VIRAL INFECTIONS :

A viral infection is a proliferation of a harmful virus inside the body. Viruses cannot reproduce without the assistance of a host. Viruses infect a host by introducing their genetic material into the cells and hijacking the cell's internal machinery to make more virus particles. With an active viral infection, a virus makes copies of itself and bursts the host cell (killing it) to set the newly-formed virus particles free. In other cases, virus particles “bud” off the host cell over a period of time before killing the host cell. Either way, new virus particles are then free to infect other cells. Symptoms of the viral illness occur as a result of cell damage, tissue destruction, and the associated immune response. Certain viruses -- like the ones that cause chickenpox and cold sores -- may be inactive or “latent” after the initial infection. For example, you may have a cold sore that erupts and then heals. The cold sore virus remains in your cells in a dormant state. At a later date, a trigger, such as stress, sunlight, or something else, may reactivate the virus and lead to new symptoms. The virus makes more copies of itself, releases new virus particles, and kills more host cells. Viruses can be transmitted in a variety of ways. Some viruses can spread through touch, saliva, or even the air. Other viruses can be transmitted through sexual contact or by sharing contaminated needles. Insects including ticks and mosquitoes can act as "vectors," transmitting a virus from one host to another. Contaminated food and water are other potential sources of viral infection.

Respiratory Viral Infections :

Respiratory viral infections affect the lungs, nose, and throat. These viruses are most commonly spread by inhaling droplets containing virus particles.

Examples include: Rhinovirus is the virus that most often causes the common cold, but there are more than 200 different viruses that can cause colds. Cold symptoms like coughing, sneezing, mild headache, and sore throat typically last for up to 2 weeks.

Seasonal influenza is an illness that affects about 5% to 20% of the population in the US every year. More than 200,000 people per year are hospitalized annually in the US due to complications of the flu. Flu symptoms are more severe than cold symptoms and often include body aches and severe fatigue. The flu also tends to come on more suddenly than a cold.

Respiratory Syncytial Virus (RSV) is an infection that can cause both upper respiratory infections (like colds) and lower respiratory infections (likepneumonia and bronchiolitis). It can be very severe in infants, small children, and elderly adults. Viral Skin Infections: Viral skin infections can range from mild to severe and often produce a rash.

Examples of viral skin infections include:

Molluscum contagiosum causes small, flesh-colored bumps most often in children ages 1 to 10 years old; however, people of any age can acquire the virus. The Page 8 bumps usually disappear without treatment, usually in 6 to 12 months.

• Herpes simplex virus-1 (HSV-1) is the common virus that causes cold sores. It's transmitted through saliva by kissing or sharing food or drink with an infected individual. Sometimes, HSV-1 causes genital herpes. An estimated 85% of people in the US have HSV-1 by the time they are in their 60s.

• Varicella-zoster virus (VZV) causes itchy, oozing blisters, fatigue, and high fever characteristic of chickenpox. The chickenpox vaccine is 98% effective at preventing infection. People who have had chickenpox (or in extremely rare instances, people who have received the chickenpox vaccine) are at risk for developing shingles, an illness caused by the same virus. Shingles can occur at any age, but it occurs most often in people age 60 or older. The best way to avoid viral skin infections is to avoid skinto-skin contact (especially areas that have a rash or sores) with an infected individual. Some viral skin infections, such as varicella-zoster virus, are also transmitted by an airborne route. Communal showers, swimming pools, and contaminated towels can also potentially harbor certain viruses.

Foodborne Viral Infections : Viruses are one of the most common causes of food poisoning. The symptoms of these infections vary depending on the virus involved.

• Hepatitis A is a virus that affects the liver for a few weeks up to several months. Symptoms may include yellow skin, nausea, diarrhea, and vomiting. Up to 15% of infected individuals experience recurrent illness within 6 months of infection.

• Norovirus has been reported to be responsible for outbreaks of severe gastrointestinal illness that happen on cruise ships, but it causes disease in many situations and locations. About 20 million people in the U.S. become sick from these highly contagious viruses every year

. • Rotavirus causes severe, watery diarrhea that can lead to dehydration. Anyone can get rotavirus, but the illness occurs most often in babies and young children.

Rotaviruses and noroviruses are responsible for many (but not all) cases of viral gastroenteritis, which causes inflammation of the stomach and intestines. People may use the terms “stomach virus” or “stomach flu” to refer to viral gastroenteritis, which causes nausea, vomiting, diarrhea, andabdominal pain. It's not pleasant to think about it, but foodborne viral illnesses are transmitted via the fecal-oral route. This means that a person gets the virus by ingesting virus particles that were shed through the feces of an infected person. Someone with

this type of virus who doesn't wash their hands after using the restroom can transfer the virus to others by shaking hands, preparing food, or touching hard surfaces. Contaminated water is another potential source of infection.

Sexually Transmitted Viral Infections :

Sexually transmitted viral infections spread through contact with bodily fluids. Some sexually transmitted infections can also be transmitted via the blood (bloodborne transmission).

• Human papillomavirus (HPV) is the most common sexually-transmitted infection in the US. There are many different types of HPV. Some cause genital warts while others increase the risk of cervical cancer. Vaccination can protect against cancer-causing strains of HPV.

• Hepatitis B is a virus that causes inflammation in the liver. It's transmitted through contaminated blood and bodily fluids. Some people with the virus don't have any symptoms while others feel like they have the flu. Thehepatitis B vaccine is more than 90% effective at preventing infection. Genital herpes is a common sexually-transmitted infection caused by herpes simplex virus-2 (HSV-2). Herpes simplex virus-1 (HSV-1), the virus responsible for cold sores, can also sometimes cause genital herpes. There's no cure for genital herpes. Painful sores often recur during outbreaks. Antiviral medications can decrease both the number and length of outbreaks.

Human immunodeficiency virus (HIV) is a virus that affects certain types of T cells of the immune system. Progression of the infection decreases the body's ability to fight disease and infection, leading to acquired immune deficiency syndrome (AIDS).

HIV is transmitted by coming into contact with blood or bodily fluids of an infected person. People can reduce the risk of getting a sexuallytransmitted viral infection by abstaining from sex or only having sex while in a monogamous relationship with someone who does not have a sexually-transmitted infection. Using a condom decreases, but doesn't entirely eliminate, the risk of acquiring a sexually-transmitted infection. Minimizing the number of sexual partners and avoiding intravenous drug use are other ways to reduce the risk of acquiring sexually-transmitted and bloodborne viral infections.

Signs and symptoms may include:

• Clear, white, greenish or yellowish vaginal discharge.
• Discharge from the penis.
• Strong vaginal odor.
• Vaginal itching or irritation.
• Itching or irritation inside the penis.

Other Viral Infections:

Viruses are abundant in the world and cause many other infections ranging from mild to life-threatening.

• Epstein-Barr virus (EBV) is a type of herpes virus that's associated with fever, fatigue, swollen lymph nodes, and an enlarged spleen. EBV is a very common virus that causes mononucleosis ("mono"). More than 90% of adults have been infected with this “kissing disease” that is spread primarily through saliva.

• West Nile virus (WNV) is a virus that's most commonly transmitted by infected mosquitos. Most people (70% to 80%) with WNV don't have any symptoms while others develop a fever, headache, and other symptoms. Less than 1% of people with WNV develop inflammation of the brain (encephalitis) or inflammation of the tissue surrounding the brain and spinal cord (meningitis).

• Viral meningitis is an inflammation of the lining of the brain and spinal cord that causes headache, fever, stiff neck, and other symptoms. Many viruses can cause viral meningitis, but a group of viruses called enteroviruses are most often to blame

VIRAL DISEASES IN MAN :

➢ Chikenpox
➢ Flu
➢ Herpes
➢ Human immune deficiency virus
➢ Humanpapilloma virus
➢ Infectious mononucleosis
➢ Mumps,measles,rubella
➢ Shingles
➢ Viral hepatits
➢ Viral meningitis
➢ Viral pneumonia
➢ SARS [Severe acute respiratory syndrome]
➢ Corona virus, etc…

STUDY OF HIV INFECTION:

HIV, in common with other retroviruses, possesses the enzyme reverse transcriptase and consists of a lipid bilayer membrane surrounding the capsid.

STRUCTURE OF HIV :

HIV is different in structure from other retroviruses. The HIV virion is ~100 nm in diameter. Its innermost region consists of a cone-shaped core that includes two copies of the

(positive sense) ssRNA genome, the enzymes reverse transcriptase, integrase and protease, some minor proteins, and the major core protein. HIV-1 viral particles have a diameter of 100 nm and are surrounded by a lipoprotein membrane.

Each viral particle contains 72 glycoprotein complexes, which are integrated into this lipid membrane, and are each composed of trimers of an external glycoprotein gp120 and a transmembrane spanning protein gp41.

The bonding between gp120 and gp41 is only loose and therefore gp120 may be shed spontaneously within the local environment.

Glycoprotein gp120 can be detected in the serum as well as within the lymphatic tissue of HIV-infected patients.

During the process of budding, the virus may also incorporate different host proteins from the membrane of the host cell into its lipoprotein layer, such as HLA class I and II proteins, or adhesion proteins such as ICAM-1 that may facilitate adhesion to other target cells.

The matrix protein p17 is anchored to the inside of the viral lipoprotein membrane. The p24 core antigen contains two copies of HIV-1 RNA. The HIV-1 RNA is part of a protein-nucleic acid complex, which is composed of the nucleoprotein p7 and the reverse transcriptase p66 (RT).

The viral particle contains all the enzymatic equipment that is necessary for replication: a reverse transcriptase (RT), an integrase p32 and a protease p11 (Gelderbloom 1993).

CLINICAL MANIFESTATIONS:

The sequelae of untreated HIV infection can be broadly considered in five categories:

• Opportunistic infections, that is, infections that would notnormally cause disease in an immunocompetent host, for example, P. jiroveci pneumonia and cytomegalovirus (CMV)

• Infections that can occur in immunocompetent patients but tend to occur more frequently, more severely .

• Malignancies, particularly those that occur rarely in the immunocompetent population, for example, Kaposi'ssarcoma and non-Hodgkin's lymphoma

• Direct manifestations of HIV infection per se, forexample, HIV encephalopathy, HIV myelopathy and HIVenteropathy Consequences chronic immune activation including premature cardiovascular disease, neuro cognitive dysfunction, bone mineral density loss.

INVESTIGATIONS AND MONITORING :

Current and previous infections : The initial diagnosis of HIV infection is made by the detection of antibodies against HIV. With improved technology, it is usually possible to detect antibodies within 3–4 weeks of infection,although individuals are advised that a ‘window period’ of upto 3 months after exposure is required before infection can be excluded. After confirmation of HIV infection, the patient is usually tested for prior exposure to a number of

potential pathogens, including syphilis, hepatitis A, B and C, CMV, varicella zoster (VZV), and T. gondii.

This can enable subsequent treatment (in the case of undiagnosed syphilis), vaccination (if no prior exposure to hepatitis A, B, or VZV), prevention (if no prior exposure to Toxoplasma and CMV), prophylaxis (if previous exposure to Toxoplasma) CD4 count : The level of immunosuppression is most easily estimated by monitoring a patient's CD4 count. This measures the number of CD4-positive T-lymphocytes in a sample of peripheral blood.

The normal range can vary between 500 and 1500 cells/ mm3. As HIV disease progresses, the number of cells falls. Particular complications of HIV infection usually begin to occur at similar CD4 differential diagnoses and enable the use of prophylactic therapies. For example, patients with a CD4 count of less than 200 cells/mm3 should always be offered prophylaxis against P. jiroveci pneumonia. Similarly, both patient and clinician are likely to use the CD4 count as the major indicator of when to consider starting antiretroviral therapy. The graph given below gives the detail about HIV and other related infections and the level of CD4 count in the human immune system and predictions of laboratory data are obtained.

TREATEMENT APPORACHES :

ANTIRETROVIRAL DRUGS :

Inhibiting viral replication with a combination of potent antiretroviral theraphy has been most clinically successful strategy in the treatement of hiv infection . Reverse transcriptase inhibitors are of two types : derived from purine and pyrmidine based nucleotides and nucleosides [NRTIs],and those of non nucleotide based [NNRTs]. Current treatement for initial theraphy includes minimum 3 drugs antiretroviral agents tenofir disoproxil fumarate, emtricitabine ,ritonavir enhanced pi etc….

POST EXPOSURE PROPHYLAXIS:

Post exposure prophylaxis with a three drug regimen consisting of two NRTIs and a boosted PI is recommended for a precutaneous blood exposure involving significant risk The optimal duration of the course is unknown but atleast 4 weeks of theraphy is advocated . ideally the treatement should be initiated within 1-2 hours of exposure but it is recommended upto 72 hours of postexposure.

1. PSORIASIS

DEFINITION:

• Psoriasis is a common chronic inflammatory disease characterized by recurrent exacerbations and remissions of thickened, erythematous, and scaling plaques.

PATHOPHYSIOLOGY:

• Cell-mediated immune mechanisms play a central role in psoriasis. Cutaneous inflammatory T-cell–mediated immune activation requires two Tcell signals mediated via cell–cell interactions by surface proteins and antigen-presenting cells such as dendritic cells or macrophages. The first signal is the interaction of the T-cell receptor with antigen presented by antigen-presenting cells. The second signal (called costimulation) is mediated through various surface interactions.

• Once T cells are activated, they migrate from lymph nodes and the bloodstream into skin and secrete various cytokines (e.g., interferon γ, interleukin 2 [IL-2]) that induce the pathologic changes of psoriasis. Local keratinocytes and neutrophils are induced to produce other cytokines, such as tumor necrosis factor-α (TNF-α), IL-8, and others.

• As a result of pathogenic T-cell production and activation, psoriatic epidermal cells proliferate at a rate sevenfold faster than normal epidermal cells. Epidermal proliferation is also elevated in apparently normal skin of psoriatic patients.

CLINICAL PRESENTATION:

• Psoriatic lesions are relatively asymptomatic, but about 25% of patients complain of pruritus.

• Lesions are characterized by sharply demarcated, erythematous papules and plaques often covered with silver-white fine scales. Initial lesions are usually small papules that enlarge over time and coalesce into plaques. If the fine scale is removed, a salmon-pink lesion is exposed, perhaps with punctate bleeding from prominent dermal capillaries (Auspitz sign).

• Scalp psoriasis ranges from diffuse scaling on an erythematous scalp to thickened plaques with exudation, microabscesses, and fissures. Trunk, back, arm, and leg lesions may be generalized, scattered, discrete, droplike lesions or large plaques. Palms, soles, face, and genitalia may also be involved. Affected nails are often pitted and associated with subungual keratotic material. Yellowing under the nail plate may be seen.

• Psoriatic arthritis is a distinct clinical entity in which both psoriatic lesions and inflammatory arthritis-like symptoms occur. Distal interphalangeal joints and adjacent nails are most commonly involved, but knees, elbows, wrists, and ankles may also be affected.

DIAGNOSIS:

• The diagnosis is based on physical examination findings of the characteristic lesions of psoriasis.

• The medical history of a patient with psoriasis should include information about the onset and duration of lesions, family history of psoriasis, presence of exacerbating factors, previous history of antipsoriatic treatment (if any) along with efficacy and adverse effect data, exposure to chemicals and toxins, and allergies (food, drugs, and environmental).
• Skin biopsy of lesional skin is useful in confirming the diagnosis.

PHARMACOTHERAPY

NONPHARMACOLOGIC THERAPY :

• Emollients (moisturizers) hydrate the stratum corneum and minimize water evaporation. They may enhance desquamation, eliminate scaling, and decrease pruritus. The lotions, creams, or ointments often need to be applied up to four times a day to achieve a beneficial response. Adverse effects include folliculitis and allergic or irritant contact dermatitis.
• Balneotherapy (and climatotherapy) involves bathing in waters containing certain salts, often combined with natural sun exposure. The salts in certain waters (e.g., the Dead Sea) reduce activated T cells in skin and may be remittive for psoriasis.

PHARMACOLOGICAL THERAPY:

FIRST-LINE TOPICAL PHARMACOTHERAPY :

Keratolytics :

• Salicylic acid is one of the most commonly used keratolytics. It causes a disruption in corneocyte-to-corneocyte cohesion in the abnormal horny layer of psoriatic skin. This serves to remove scales, smooth the skin, and decrease hyperkeratosis. The keratolytic effect enhances penetration and efficacy of some other topical agents such as corticosteroids. It is applied as a 2% to 10% gel or lotion two or three times a day. Salicylic acid produces local irritation. Application to large, inflamed areas may induce salicylism with symptoms of nausea, vomiting, tinnitus, or hyperventilation.

Corticosteroids :

• Topical corticosteroids may halt synthesis and mitosis of DNA in epidermal cells and appear to inhibit phospholipase A, lowering the amounts of arachidonic acid, prostaglandins, and leukotrienes in the skin. These effects, coupled with local vasoconstriction, reduce erythema, pruritus, and scaling. As antipsoriatic agents, they are best used adjunctively with a product that specifically functions to normalize epidermal hyperproliferation.

• Low-potency products (e.g., hydrocortisone 1%) have a weak antiinflammatory effect and are safest for long-term application, for use on the face and intertriginous areas, for use with occlusion, and for use in infants and young children.

• Medium-potency products are used in moderate inflammatory dermatoses. They may be used on the face and intertriginous areas for a limited time.

• High-potency preparations are used primarily as alternatives to systemic corticosteroids when local therapy is feasible.

• Very high potency products may be used for thick, chronic psoriatic lesions but for only short periods of time and on relatively small surface areas.

• Ointments are the most effective formulations for psoriasis because they have an occlusive oily phase that conveys a hydrating effect and enhances penetration of the corticosteroid into the dermis. They are not suited for use in the axilla, groin, or other intertriginous areas where maceration and folliculitis may develop secondary to the occlusive effect.

• Creams are more cosmetically desirable for some patients. They may be used in intertriginous areas even though their lower oil content makes them more drying than ointments.

• Topical corticosteroids are applied two to four times daily during longterm therapy.

• Adverse effects include local tissue atrophy, skin degeneration, and striae. If detected early, these effects may be reversible with discontinuation. Thinning of the epidermis may result in visibly distended capillaries (telangiectasias) and purpura. Acneiform eruptions and masking of symptoms of bacterial or fungal skin infections have been reported. Systemic consequences include risk of suppression of the hypothalamic-pituitary-adrenal axis, hyperglycemia, and development of cushingoid features. Tachyphylaxis and rebound flare of psoriasis after abrupt cessation of therapy can also occur.

Vitamin D Analogs :

• Vitamin D and its analogs inhibit keratinocyte differentiation and proliferation and have antiinflammatory effects by reducing IL-8, IL-2, and other cytokines. Use of vitamin D itself is limited by its propensity to cause hypercalcemia.

• Calcipotriene (Dovonex) is a synthetic vitamin D analog used for mild to moderate plaque psoriasis. Improvement is usually seen within 2 weeks of treatment, and approximately 70% of patients demonstrate marked improvement after 8 weeks. Adverse effects occur in about 10% of patients and include lesional and perilesional burning and stinging. Calcipotriene 0.005% cream, ointment, or solution is applied one or two times a day (no more than 100 g/wk).

• Calcitriol and tacalcitol are other vitamin D derivatives that have been studied for treatment of psoriasis. Tazarotene

• Tazarotene (Tazorac) is a synthetic retinoid that is hydrolyzed to its active metabolite, tazarotenic acid, which modulates keratinocyte proliferation and differentiation. It is available as a 0.05% or 0.1% gel and cream and is applied once daily (usually in the evening) for mild to moderate plaque psoriasis. Adverse effects are dose- and frequency related and include mild to moderate pruritus, burning, stinging, and erythema. Application of the gel to eczematous skin or to more than 20% of body surface area is not recommended because this may lead to

extensive systemic absorption. Tazarotene is often used with topical corticosteroids to decrease local adverse effects and increase efficacy.

SECOND-LINE TOPICAL PHARMACOTHERAPY :

Coal Tar:

• Coal tar contains numerous hydrocarbon compounds formed from distillation of bituminous coal. Ultraviolet B (UVB) light–activated coal tar photoadducts with epidermal DNA and inhibits DNA synthesis. This normalized epidermal replication rate reduces plaque elevation.

• Coal tar preparations of 2% to 5% tar are available in lotions, creams, shampoos, ointments, gels, and solutions. It is usually applied directly to lesions in the evening and allowed to remain in skin contact through the night. It may also be used in bathwater.

• Coal tar is an effective treatment, but it is time-consuming, causes local irritation, has an unpleasant odor, stains skin and clothing, and increases sensitivity to UV light (including the sun).

• The risk of carcinogenicity is low, but there may be a higher rate of nonmyeloma skin cancers in patients chronically exposed to coal tar and UV light.

Anthralin:

• Anthralin possesses antiproliferative activity on keratinocytes, inhibiting DNA synthesis by intercalation between DNA strands.

• Because anthralin exerts its clinical effects at low cellular concentrations, therapy usually starts with low concentrations (0.1% to 0.25%) with gradual increases to higher concentrations (0.5% to 1%). Cream and ointment formulations are usually applied in the evening and allowed to remain overnight.

• Alternatively, short-contact anthralin therapy (SCAT) with application for 10 to 20 minutes of higher concentrations (1% to 5%) in water-soluble vehicles is effective with decreased local adverse effects.

• Anthralin products must be applied only to affected areas because contact with uninvolved skin may result in excessive irritation and staining, which usually disappear within 1 to 2 weeks of discontinuation. Staining of affected plaques indicates a positive response because cell turnover has been slowed enough to take up the stain.

• Inflammation, irritation, and staining of skin and clothing are often therapylimiting effects.

FIRST-LINE SYSTEMIC PHARMACOTHERAPY:

• Biologic therapies—primarily immunomodulating agents designed to alter immune responses—comprise first-line systemic therapy.

• Infliximab (Remicade) is a chimeric monoclonal antibody directed against TNF-α. Adverse effects include headaches, fever, chills, fatigue, diarrhea, pharyngitis, upper respiratory and urinary tract infections.
• Etanercept (Enbrel) is a fusion protein that binds TNF-α, competitively interfering with its interaction with cell-bound receptors.
• Adalimumab (Humira) is a human immunoglobulin G1 monoclonal TNF-α antibody. The binding of adalimumab results in inactivation of the proinflammatory cytokine TNF-α.
• Alefacept (Amevive) is a dimeric fusion protein that binds to CD2 on T cells to inhibit cutaneous T-cell activation and proliferation.
• Efalizumab (Raptiva) is a humanized monoclonal antibody that inhibits CD11-α integrin, which is involved in T-cell activation, migration into skin, and cytotoxic function.

SECOND-LINE SYSTEMIC PHARMACOTHERAPY:

• Acitretin (Soriatane) is a retinoic acid derivative and the active metabolite of etretinate. The initial recommended dose is 25 or 50 mg; therapy is continued until lesions have resolved.
• Cyclosporine demonstrates immunosuppressive activity by inhibiting the first phase of T-cell activation. It also inhibits release of inflammatory mediators from mast cells, basophils, and polymorphonuclear cells.
• Tacrolimus, an immunosuppressant that inhibits T-cell activation, is a useful alternative in severe recalcitrant psoriasis.
• Methotrexate, an antimetabolite, is indicated for moderate to severe psoriasis. It is particularly beneficial for psoriatic arthritis.
• Mycophenolate mofetil (CellCept) inhibits DNA and RNA synthesis and has been shown to have a specific lymphocyte antiproliferative effect.
• Sulfasalazine is an antiinflammatory agent that inhibits 5-lipoxygenase. It is used selectively as an alternative treatment, particularly in patients with concurrent psoriatic arthritis.
• 6-Thioguanine is a purine analog that has been used as an alternative treatment for psoriasis when conventional therapies have failed.
• Hydroxyurea inhibits cell synthesis in the S phase of the DNA cycle.

PHOTOTHERAPY AND PHOTOCHEMOTHERAPY

• UVB light (290 to 320 nm) therapy is an important phototherapeutic intervention for psoriasis.

• PUVA is a photochemotherapeutic approach for selected patients. Candidates for PUVA therapy usually have moderate to severe, incapacitating psoriasis unresponsive to conventional topical and systemic therapies.

2. SCABIES

DEFINITION

A contagious, intensely itchy skin condition caused by a tiny , burrowing mite. Scabies us contagious and spreads quickly through close physical contact in a family, school or nursing home. The most common symptoms are severe itchiness and pimple like rash. Occasionally, tiny burrows may be seen in the skin. In the first ever infection a person will usually develop symptoms in between two and six weeks. During the second infection symptoms may began in as little as 24 hrs. These symptoms are can be present across most of the body or just certain areas such as wrist, between fingers, or along the waist line. The head may be affected but this is typically only in young children. The itch is often worse at night. Scratching may cause skin break down and an additional bacterial infection of the skin.

ETIOLOGY AND EPIDEMOLOGY

Scabies is caused by tiny mites that burrow into the skin . Scabies is an itchy skin condition is caused by an tiny burrowing mite called sarcoptes scabiei. Intense itchy occurs in the area where the mite burrows . The urge to scratch may be especially strong at night.

The world wide prevalence is estimated to be 100 million people , with wide variation in prevalence among individual geographic regions . A systematic review of population based studies from various region of the world [excluding North americs] found prevalence estimates ranging from 0.2 to 71%, with the highest prevalences in the pacific region and latin America.Scabies particularly common in resources limited region.

Signs and symptoms

Commonly involved sites of rashes of scabies The characteristic symptoms of a scabies infection include intense itching and superficial burrowsThe burrow tracks are often linear, to the point that a neat "line" of four or more closely placed and equally developed mosquito-like "bites" is almost diagnostic of the disease.[citation needed] Because the host develops the symptoms as a reaction to the mites' presence over time, typically a delay of four to six weeks occurs between the onset of infestation and the onset of itching.

Similarly, symptoms often persist for one to several weeks after successful eradication of the mites. As noted, those re-exposed to scabies after successful treatment may exhibit symptoms of the new infestation in a much shorter period—as little as one to four days **Itching** In the classic scenario, the itch is made worse by warmth, and is usually experienced as being worse at night, possibly because distractions are fewer As a symptom, it is less common in the elderly.

Rash The superficial burrows of scabies usually occur in the area of the finger webs, feet, ventral wrists, elbows, back, buttocks, and external genitals. Except in infants and the immunosuppressed, infection generally does not occur in the skin of the face or scalp. The

burrows are created by excavation of the adult mite in the epidermis. In most people, the trails of the burrowing mites are linear or S-shaped tracks in the skin often accompanied by rows of small, pimple-like mosquito or insect bites. These signs are often found in crevices of the body, such as on the webs of fingers and toes, around the genital area, in stomach folds of the skin, and under the breasts of women.

Symptoms typically appear two to six weeks after infestation for individuals never before exposed to scabies. For those having been previously exposed, the symptoms can appear within several days after infestation. However, symptoms may appear after several months or Years. Acropustulosis, or blisters and pustules on the palms and soles of the feet, are characteristic symptoms of scabies in infants.

Cause Scabies mite

Sarcoptes scabiei Life cycle of scabies. In the 18th century, Italian biologists Giovanni Cosimo Bonomo and Diacinto Cestoni (1637–1718) described the mite now called Sarcoptes scabiei, variety hominis, as the cause of scabies.

Sarcoptes is a genus of skin parasites and part of the larger family of mites collectively known as scab mites. These organisms have eight legs as adults, and are placed in the same phylogenetic class (Arachnida) as spiders and ticks. S. scabiei mites are under 0.5 mm in size, but are sometimes visible as pinpoints of white. Gravid females tunnel into the dead, outermost layer (stratum corneum) of a host's skin and deposit eggs in the shallow burrows. The eggs hatch into larvae in three to ten days.

These young mites move about on the skin and molt into a "nymphal" stage, before maturing as adults, which live three to four weeks in the host's skin. Males roam on top of the skin, occasionally burrowing into the skin. In general, the total number of adult mites infesting a healthy hygienic person with noncrusted scabies is small, about 11 females in burrows, on average. The movement of mites within and on the skin produces an intense itch, which has the characteristics of a delayed cell-mediated inflammatory response to allergens. IgE antibodies are present in the serum and the site of infection, which react to multiple protein allergens in the body of the mite. Some of these cross-react to allergens from house dust mites.

Immediate antibody-mediated allergic reactions (wheals) have been elicited in infected persons, but not in healthy persons; immediate hypersensitivity of this type is thought to explain the observed far more rapid allergic skin response to reinfection seen in persons having been previously infected (especially having been infected within the previous year or two.

Diagnosis:

A photomicrograph of an itch mite (*S. scabiei*) Scabies may be diagnosed clinically in geographical areas where it is common when diffuse itching presents along with either lesions in two typical spots or itchiness is present in another household member. The classical sign of

scabies is the burrow made by a mite within the skin. To detect the burrow, the suspected area is rubbed with ink from a fountain pen or a topical tetracycline solution, which glows under a special light. The skin is then wiped with an alcohol pad. If the person is infected with scabies, the characteristic zigzag or S pattern of the burrow will appear across the skin; however, interpreting this test may be difficult, as the burrows are scarce and may be obscured by scratch marks. A definitive diagnosis is made by finding either the scabies mites or their eggs and fecal pellets. Searches for these signs involve either scraping a suspected area, mounting the sample in potassium hydroxide and examining it under a microscope, or using dermoscopy to examine the skin directly.

Differential diagnosis

Symptoms of early scabies infestation mirror other skin diseases, including dermatitis, syphilis, erythema multiforme, various urticaria-related syndromes, allergic reactions, ringworm-related diseases, and other ectoparasites such as lice and fleas.

PATHOPHYSIOLOGY

In classic scabies infection, typically 10-15 mites (range, 3-50) live on the host. Little evidence of infection exists during the first month (range, 2-6 wk), but after 4 weeks and with subsequent infections, a delayed type IV hypersensitivity reaction to the mites, eggs, and scybala (feces) occurs. The time required to induce immunity in primary infestations probably accounts for the 4-week asymptomatic latent period. With reinfestation, the sensitized individual may develop a rapid reaction (within hours). The resultant skin eruption and its associated intense pruritus are the hallmarks of classic scabies.

The symptoms are caused by an allergic reaction of the host's body to mite proteins, though exactly which proteins remains a topic of study. The mite proteins are also present from the gut, in mite feces, which are deposited under the skin. The allergic reaction is both of the delayed (cell-mediated) and immediate (antibody-mediated) type, and involves IgE (antibodies are presumed to mediate the very rapid symptoms on reinfection).

The allergy-type symptoms (itching) continue for some days, and even several weeks, after all mites are killed. New lesions may appear for a few days after mites are eradicated. Nodular lesions from scabies may continue to be symptomatic for weeks after the mites have been killed. Rates of scabies are negatively related to temperature and positively related to humidity.

Transmission

Scabies is contagious and can be contracted through prolonged physical contact with an infested person. This includes sexual intercourse, although a majority of cases are acquired through other forms of skin-to-skin contact. Less commonly, scabies infestation can happen

through the sharing of clothes, towels, and bedding, but this is not a major mode of transmission; individual mites can survive for only two to three days, at most, away from human skin at room temperature.As with lice, a latex condom is ineffective against scabies transmission during intercourse,
because mites typically migrate from one individual to the next at sites other than the sex organs. Healthcare workers are at risk of contracting scabies from patients, because they may be in extended contact with them.

Management:

A number of medications are effective in treating scabies. Treatment should involve the entire household, and any others who have had recent, prolonged contact with the infested individual. Options to control itchiness include antihistamines and prescription anti-inflammatory agents. Bedding, clothing and towels used during the previous three days should be washed in hot water and dried in a hot dryer.

Permethrin Permethrin, a pyrethroid insecticide, is the most effective treatment for scabies,[34] and remains the treatment of choice. It is applied from the neck down, usually before bedtime, and left on for about eight to 14 hours, then washed off in the morning. Care should be taken to coat the entire skin surface, not just symptomatic areas; any patch of skin left untreated can provide a "safe haven" for one or more mites to survive. One application is normally sufficient, as permethrin kills eggs and hatchlings, as well as adult mites, though many physicians recommend a second application three to seven days later as a precaution. Crusted scabies may require multiple applications, or supplemental treatment with oral ivermectin (below Permethrin may cause slight irritation of the skin that is usually tolerable.

Ivermectin Oral ivermectin is effective in eradicating scabies, often in a single dose. It is the treatment of choice for crusted scabies, and is sometimes prescribed in combination with a topical agent. It has not been tested on infants, and is not recommended for children under six years of age.Topical ivermectin preparations have been shown to be effective for scabies in adults, though only one such formulation is available in the United States at present, and it is not FDA-approved as a scabies treatment. It has also been useful for sarcoptic mange (the veterinary analog of human scabies). conditions.

Others Other treatments include lindane, benzyl benzoate, crotamiton, malathion, and sulfur preparations. Lindane is effective, but concerns over potential neurotoxicity have limited its availability in many countries. it is banned in California, but may be used in other states as a second-line
treatment. Sulfur ointments or benzyl benzoate are often used in the developing world due to their low cost; Some 10% sulfur solutions have been shown to be effective, and sulfur ointments are typically used for at least a week, though many people find the odor of sulfur products unpleasant. Crotamiton has been found to be

less effective than permethrin in limited studies. Crotamiton or sulfur preparations are sometimes recommended instead of permethrin for children, due to concerns over dermal absorption of permethrin.

Prevention

Mass-treatment programs that use topical permethrin or oral ivermectin have been effective in reducing the prevalence of scabies in a number of populations.

No vaccine is available for scabies. The simultaneous treatment of all close contacts is recommended, even if they show no symptoms of infection (asymptomatic), to reduce rates of recurrence.

Since mites can survive for only two to three days without a host, other objects in the environment pose little risk of transmission except in the case of crusted scabies.

Therefore cleaning is of little importance. Rooms used by those with crusted scabies require thorough cleaning.

3. ECZEMA

Dermatitis, also known as eczema, is a group of diseases that result in inflammation of the skin. These diseases are characterized by itchiness, red skin and a rash. In cases of short duration, there may be small blisters, while in long-term cases the skin may become thickened. The area of skin involved can vary from small to the entire body.

Dermatitis is a group of skin conditions that includes atopic dermatitis, allergic contact dermatitis, irritant contact dermatitis and stasis dermatitis.The exact cause of dermatitis is often unclear.

Cases may involve a combination of irritation, allergy and poor venous return. The type of dermatitis is generally determined by the person's history and the location of the rash.[1] For example, irritant dermatitis often occurs on the hands of people who frequently get them wet

.Allergic contact dermatitis occurs upon exposure to an allergen, causing a hypersensitivity reaction in the skin.

Epidemiology:

Globally dermatitis affected approximately 230 million people as of 2010 (3.5% of the population). Dermatitis is most commonly seen in infancy, with female predominance of eczema presentations occurring during the reproductive period of 15–49 years. In the UK about 20% of children have the condition, while in the United States about 10% are affected.

Although little data on the rates of eczema over time exists prior to the 1940s, the rate of eczema has been found to have increased substantially in the latter half of the 20th century,

with eczema in school-aged children being found to increase between the late 1940s and 2000. In the developed world there has been rise in the rate of eczema over time. The incidence and lifetime prevalence of eczema in England has been seen to increase in recent times.

Dermatitis affected about 10% of U.S. workers in 2010, representing over 15 million workers with dermatitis. Prevalence rates were higher among females than among males, and among those with some college education or a college degree compared to those with a high school diploma or less. Workers employed in healthcare and social assistance industries and life, physical, and social science occupations had the highest rates of reported dermatitis. About 6% of dermatitis cases among U.S. workers were attributed to work by a healthcare professional, indicating that the prevalence rate of work-related dermatitis among workers was at least 0.6%.

Pathophysiology:

Acute eczema is an inflammatory process leading to oedema in the epidermis. The oedema is seen histologically in the epidermis as 'spongiosis'. Oedema manifests as fluid that collects into tiny blisters which may then coalesce. This is seen histologically as intraepidermal vesicles and clinically as pompholyx blisters on thicker palmar and plantar skin, and as excoriated, ruptured crusted vesicles elsewhere. Tightly packed keratinocyte cells in the epidermis usually prevent transepidermal fluid loss and the entry of pathogens. This barrier function of the skin is lost in eczema.

In the chronic form of eczema, prolonged rubbing and scratching results in a thickened epidermis and an increase in the upper horny cell layer of keratin, termed hyperkeratosis. Clinically, the skin appears thick, leathery, scaly and 'lichenified' with exaggerated skin markings, like tree bark. Both acute and chronic stages are accompanied by a heavy chronic inflammatory cell infiltration of the dermis and epidermis.

The main consequent symptom of these pathological processes is itch. The dictum of 'if it's not itchy, it's not eczema' holds true.

Clinical ypes

Atopic eczema

Atopic eczema is the commonest skin disorder of childhood, affecting between 10% and 20% of school age children in the UK. The aetiology is a combination of genetic, environmental and immunological factors.The term 'atopy' describes an exaggerated propensity to form IgE to common allergens. In later life, approximately half of eczema patients will develop associated atopic disorders such as asthma and allergic rhinitis. The molecular pathology in atopic eczema is complex. The epidermal Langerhans cells have high-affinity IgE receptors through which the T-helper cells (Th2 and Th1) release cytokines and mediate skin inflammation.

Contact dermatitis

Contact dermatitis is classified as either allergic contact dermatitis (ACD) or irritant contact dermatitis (ICD).

Allergic contact dermatitis

ACD is a delayed type IV hypersensitivity reaction that develops in response to an antigen to which the host immune system has been previously sensitised. As a consequence, symptoms rarely develop on first exposure to the stimulus and may only manifest months or years later following repeated re-exposure.

Irritant contact dermatitis

This is the most common form of occupational dermatitis and the commonest cause of hand eczema . Unlike ACD, ICD is not immunologically mediated. The mechanism involves disruption of the epidermal permeability barrier and a direct cytotoxic effect depending on the irritant. Patients with pre-existing epidermal barrier dysfunction such as atopic eczema are at higher risk. The occupation of the individual may also be a risk factor, especially those working as builders, hairdressers, gardeners, healthcare workers and chefs. Irritants include detergents, oils, water, inorganic acids, alcohols and plastics. Preventative skin care is key and this includes the use of barriers such as emollients or cotton gloves in addition to avoiding suspected irritants.

Discoid eczema

Discoid eczema is also known as ‘nummular dermatitis’ and is a type of chronic eczema presenting with disseminated coinshaped eczematous lesions of the extremities. Middle-aged males are most commonly affected.

Stasis eczema

Stasis eczema is also called stasis dermatitis, gravitational dermatitis or varicose eczema. It is a clinical component of chronic venous insufficiency seen in addition to other features which include varicose veins, skin discolouration, peripheral oedema, leg discomfort and non-healing ulcers. Clinical features include scaly eczematous plaques confined to the lower legs. Multiple topical medicines and dressings often lead to a secondary ACD. Management of stasis eczema should address the underlying cause.

Asteatotic eczema:

Asteatotic eczema, also called eczema craquele, usually affects the lower legs and appears as dry, cracked skin likened to ‘cracked paving’. This is associated with increasing age,

low humidity and frequent bathing. Treatment consists of emollients and mildly potent topical steroids.

Clinical manifestation:

Signs and symptoms:

The symptoms of atopic dermatitis can vary, depending on the age of the person with the condition.

Atopic dermatitis commonly occurs in infants, with dry and scaly patches appearing on the skin. These patches are often intensely itchy.

Most people develop atopic dermatitis before the age of 5 years. Half of those who develop the condition in childhood continue to have symptoms as an adult.

However, these symptoms are often different to those experienced by children. People with the condition will often experience periods of time where their symptoms flare up or worsen, followed by periods of time where their symptoms will improve or clear up.

Symptoms in infants under 2 years old

Rashes commonly appear on the scalp and cheeks.

Rashes usually bubble up before leaking fluid.

Rashes can cause extreme itchiness. This may interfere with sleeping. Continuous rubbing and scratching can lead to skin infections.

Symptoms in children aged 2 years until puberty

Rashes commonly appear behind the creases of elbows or knees.

They are also common on the neck, wrists, ankles, and the crease between buttock and legs.

Over time, the following symptoms can occur:

Rashes can become bumpy.

Rashes can lighten or darken in color.

Rashes can thicken in a process known as lichenification. The rashes can then develop knots and a permanent itch.

Symptoms in adults

Rashes commonly appear in creases of the elbows or knees or the nape of the neck.

Rashes cover much of the body.

Rashes can be especially prominent on the neck, face, and around the eyes.

Rashes can cause very dry skin.

Rashes can be permanently itchy.

Rashes in adults can be more scaly than those occurring in children.

Rashes can lead to skin infections.

Adults who developed atopic dermatitis as a child but no longer experience the condition may still have dry or easily-irritated skin, hand eczema, and eye problems.
The appearance of skin affected by atopic dermatitis will depend on how much a person scratches and whether the skin is infected. Scratching and rubbing further irritate the skin, increase inflammation, and make itchiness worse.

Causes:
The specific cause of eczema remains unknown, but it is believed to develop due to a combination of genetic and environmental factors.
Eczema is not contagious.

Children are more likely to develop eczema if a parent has had the condition or another atopic disease. If both parents have an atopic disease, the risk is even greater.
Environmental factors are also known to bring out the symptoms of eczema, such as:
Irritants: These include soaps, detergents, shampoos, disinfectants, juices from fresh fruits, meats, or vegetables.

Allergens: Dust mites, pets, pollens, mold, and dandruff can lead to eczema.

Microbes: These include bacteria such as Staphylococcus aureus, viruses, and certain fungi.

Hot and cold temperatures: Very hot or cold weather, high and low humidity, and perspiration from exercise can bring out eczema.

Foods: Dairy products, eggs, nuts and seeds, soy products, and wheat can cause eczema flare-ups.

Stress: This is not a direct cause of eczema but can make symptoms worse.

Hormones: Women can experience increased eczema symptoms at times when their hormone levels are changing, for example during pregnancy and at certain points in the menstrual cycle.

Diagnosis:

Your doctor will first examine your skin to determine whether you have allergic eczema. If they suspect you have the condition, they'll need to do further testing to find out exactly what you're allergic to. In most cases, a patch test will be used.
Patch test:
During this test, patches that contain common allergens are placed on your back. These patches remain in place for 48 hours. When your doctor removes the patches, they'll check for

symptoms of an allergic reaction. Your doctor will check your skin again after two more days to see if you have a delayed allergic reaction.

Biopsy

Other tests will be needed if your doctor isn't able to make a diagnosis based on the patch test. Your doctor may perform a skin lesion biopsy to make sure another health condition isn't causing your skin condition. During the biopsy, your doctor will remove a small sample of the affected skin. They'll then send it to a laboratory for testing.

Treatment:

First-line treatment of eczema should include an emollient and soap substitute for washing. Topical steroids are used for anti-inflammatory effect. Systemic treatments for adult atopic eczema include oral prednisolone, ciclosporin and azathioprine.If there is a secondary bacterial infection, then this should be treated with oral antibiotics. The antibiotic(s) should be chosen based on sensitivity determined by wound swab.

Emollients

Emollients, topical hydrating agents consisting of fat or oil to soften the skin, are the mainstay of eczema management.

Emollients are effective first-line treatments for all types of eczema, and regular, liberal use will reduce topical steroid requirements. The greasier products have more emollient effect. They are often underused and the need to educate the patient regarding use of sufficient quantities is vital. Dry skin is aggravated by soap and bath products, and therefore an emollient soap substitute for washing is advisable.

Topical corticosteroids

Topical steroids act as anti-inflammatory agents and are extremely useful and important in managing eczema. In recent years, the public have veered from overuse of topical steroids causing long-lasting side effects, to high levels of anxiety regarding possible side effects concerning their use.

This can commonly lead to under treatment in children. Therefore, patient/carer education regarding ppropriate topical steroid use is a crucial part of eczema management. Topical steroids are classified into four main groups according to potency: mild, moderately potent, potent and very potent. The choice of topical steroid is dependent on the site and severity of skin disease. Potent and very potent steroids should be avoided on delicate sites such as the face, genitals and flexures.

The periorbital region should be treated with caution due to the thin skin increasing the likelihood of absorption and risk of cataracts or glaucoma. Treatment should be reviewed regularly and tailored accordingly. It is also important to remember that any form of occlusion

will increase the absorption of steroid applied. Side effects are mainly local and include striae (stretch marks), telangiectasia (visible dilated small blood vessels), epidermal thinning, purpura (bruising), acne and perioral dermatitis. Lower frequency side effects include poor wound healing, spread or worsening of untreated infections and hypertrichosis. Hypopigmentation is a temporary side effect of long-term topical steroid use and is frequently exploited in illegal 'skin bleaching' agents. Rarely, adrenal suppression or Cushing's syndrome due to systemic absorption may occur.

Allergies

Both immediate and delayed hypersensitivity reactions to topical corticosteroids can occur, although not commonly. These can be reactions to either the steroid molecule itself or the vehicle in which it is found. Allergic reactions to one topical steroid may cross-react to others. Therefore, allergy testing is mandatory for such patients. Betamethasone may be less likely to cause allergic reactions than other topical preparations.

Antibiotics and steroid combinations

Combination preparations can be useful in treating mild bacterial infection of eczematous skin. Long-term use should be limited due to the risks of sensitisation and antibiotic resistance. In general, invasive infection is best managed with oral antibiotics.

Calcineurin inhibitors:

The past decade saw the introduction of topical calcineurin inhibitors for the treatment of chronic eczema. These non-steroid immunomodulators inhibit calcineurin phosphatase which is important in T-lymphocyte activation. The main side effect is burning or stinging on initial application, but this usually improves after a few days. Although a theoretical risk of increased malignancy exists with these agents, studies have not shown an association between exposures to topical calcineurin inhibitors and increased rates of cutaneous malignancy. Calcineurin inhibitors should not be used on infected skin and are generally not very useful in severely inflamed eczematous skin. Their greatest value appears to be in maintenance therapy.

Tacrolimus ointment:

It is a calcineurin inhibitor derived from the oral transplant medicine FK506. The 0.1% and 0.03% preparations are indicated in the treatment of moderate to severe atopic dermatitis in adults and children over the age of 2 years. Tacrolimus is now also used in clinical practice as a second-line agent for other steroid responsive dermatoses.

Pimecrolimus 1% cream:

It is indicated for short-term or intermittent long-term use in mild to moderate atopic dermatitis. Studies have shown that it is effective, well tolerated and has minimal adverse effects in the long-term control of eczema in children aged over 2 years (Langley et al., 2008). Furthermore, this has resulted in the reduced use of topical steroids leading to a lower risk of steroid-induced side effects (Kapp et al., 2002).

Antihistamines

Pruritis is the most distressing feature of eczema. Oral antihistamines have no direct effect on pruritis in eczema; their main effect is sedation. Sedating antihistamines may cause day time drowsiness, and caution should be taken when driving and also if prescribed to school age children.

Topical imidazoles:

Ketoconazole as a shampoo or cream is effective in reduction of Pityosporum ovale on the skin and is therefore useful in the treatment of seborrhoeic dermatitis. As the disease runs a chronic, relapsing course regular or intermittent use is usually necessary.

4. IMPETIGO

Introduction:

Impetigo (im-puh-TIE-go) is a highly contagious skin infection that mainly affects infants and children. Impetigo usually appears as red sores on the face, especially around a child's nose and mouth. The sores burst and develop honey-colored crusts. Impetigo may clear on its own in two to three weeks, but antibiotics can shorten the course of the disease and help prevent the spread to others. You may need to keep your child home from school or day care until he or she is no longer contagious, which is usually 24 to 48 hours after you begin antibiotic treatment. Without antibiotics, Impetigo is contagious until the sores go away.

Symptoms and signs:

Classic signs and symptoms of Impetigo involve red sores that quickly rupture, ooze for a few days and then form a yellowish-brown crust. The sores usually occur around the nose and mouth but can be spread to other areas of the body by fingers, clothing and towels. A less common form of the disorder, called bullous Impetigo, may feature larger blisters that occur on the trunk or diaper area of infants and young children. A more serious form of Impetigo, called ecthyma, penetrates deeper into the skin — causing painful Fluid- or pus-filled sores that turn into deep ulcers.

When to see a doctor If you suspect that you or your child has Impetigo, consult your family doctor, your child's pediatrician or a dermatologist. When exposed to the bacteria that cause Impetigo when you come into contact with the sores of someone who's infected or with items they've touched — such as clothing, bed linen, towels and even toys.

Risk factors:

Factors that increase the risk of Impetigo include:

• Age. Although anyone can develop Impetigo, it most commonly occurs in children ages 2 to 6.
• Crowded conditions. Impetigo spreads easily in schools and child care settings.
• Warm, humid weather. Impetigo infections are more common in summer.
• Certain sports. Participation in sports that involve skin-to-skin contact, such as football or wrestling, increases your risk of developing Impetigo.
• Broken skin. The bacteria that cause Impetigo often enter your skin through a small skin injury, insect bite or rash. Older adults and people with Diabetes or a compromised immune system are more likely to develop ecthyma, a deeper and more serious form of Impetigo.

Complications:

Impetigo typically isn't dangerous, but complications can sometimes occur. Examples include:

• Scarring. The ulcers associated with ecthyma, a deeper and more serious form of Impetigo, can leave scars.

• Cellulitis. This potentially serious infection affects the tissues underlying your skin and eventually may spread to your lymph nodes and into the bloodstream. Left untreated, Cellulitis can quickly become life-threatening.

• Kidney problems. One of the types of bacteria that cause Impetigo can also damage.

Test And Diagnosis:

Doctors usually diagnose Impetigo by looking at the distinctive sores. Usually, lab tests aren't necessary. But if the sores don't clear, even with antibiotic treatment, your doctor may take a sample of the liquid produced by a sore and test it to see what types of antibiotics might work best on it. Some types of the bacteria that cause Impetigo have become resistant to certain antibiotic drugs.

Treatment and drugs:

Antibiotics are the mainstay of Impetigo treatments. These drugs can be delivered by an ointment or cream that you apply directly to the sores. You may need to first soak the affected area in warm water or use wet compresses to help remove the overlying scabs. If you have more than just a few Impetigo sores, your doctor might recommend antibiotic drugs that

can be taken by mouth. Be sure to finish the entire course of medication even if the sores are healed. This helps prevent the infection from recurring and makes antibiotic resistance less likely.

Lifestyle and remedies:

Keeping the skin clean is the best way to keep it healthy. Treat cuts, scrapes, insect bites and other wounds right away by washing the affected areas. If someone in your family already has Impetigo, take these measures to help keep the infection from spreading to others:

- Gently wash the affected areas with mild soap and running water and then cover lightly with gauze.
- Wash an infected person's clothes, linens and towels every day and don't share them with anyone else in your family.
- Wear gloves when applying any antibiotic ointment and wash your hands thoroughly afterward.
- Cut an infected child's nails short to prevent damage from scratching.
- Wash hands frequently.
- Keep your child home until your doctor says he or she isn't contagious.

Impetigo is contagious,mostly from direct contact with someone else who has it transmitted through an

- Towels
- Toys
- Clothing
- Household itesms
- Types of impetigo has, bullous and non bullous Impetigo is a most common bacterial infection especially in child.

Therapaeutic managemant:

Emperic therapy regimens: Empiric therapeutic regimens for impetigo are outlined below, including those for localized, uncomplicated impetigo and those for widespread, or complicated, impetigo. Topical therapy is preferred for localized, uncomplicated nonbullous or bullous impetigo.Systemic antibiotics are used for widespread infections, complicated infections, outbreaks of poststreptococcal glomerulonephritis, or multiple incidents that have occurred within the home, daycare, or athletic-team settings. The duration of therapy should be based on clinical improvement; however, a 7-day regimen is recommended.As S aureus isolates from impetigo are usually methicillin-susceptible, cephalexin, amoxicillin-clavulanate, or dicloxacillin is usually recommended. Trimethoprim-sulfamethoxazole, clindamycin, or doxycycline is recommended for confirmed or highly suspected MRSA impetigo.

Impetigo is a contagious, superficial bacterial infection commonly seen in children. Treatment typically involves local wound care along with topical or systemic antibiotic therapy with activity against betahemolytic streptococci and Staphylococcus aureus.

Localized uncomplicated impetigo: Topical wound cleansing Mupirocin 2% cream/ointment applied topically BID for 5 days or Retapamulin 1% ointment applied topically BID for 5 days Ozenoxacin cream 1% thin layer BID for 5 days.

Widespread compilcated impetigo: Widespread (complicated) impetigo is treated as follows: The Infectious Diseases Society of America (IDSA) published 2014 guidelines for the treatment of impetigo.

• Cephalexin 250 mg PO QID for 7 days in adults or 25 mg/kg/day in 4 divided doses for 7 days in children or

➢ Dicloxacillin 250 mg PO QID for 7 days in adults/children >40 kg or 25 mg/kg/day PO divided QID for 7 days in patients < 40 kg or

➢ Amoxicillin-clavulanate 875 mg/125 mg PO BID for 7 days in adults or 25 mg amoxicillin/kg/day PO divided BID in children for 7 days.

Widespread complicated impetigo with confirmed MRSA:

➢ Clindamycin 300 mg PO QID for 7 days in adults or 10-20 mg/kg/dose PO TID for 7 days in children or

➢ Trimethoprim-sulfamethoxazole 160 mg PO BID for 7 days in adults or 8-12 mg TMP/kg/d PO BID for 7 days in infants >2 months or

➢ Doxycycline 100 mg PO BID for 7 days in patients >45 kg or 2 mg/kg/dose PO BID for 7 days in patients < 45 kg and >8 years.