SEMESTER- IV
MEDICAL MICROBIOLOGY
PAPER VIII- Medical Microbiology
Course Code: U-MIB-460
Dr.K.G.Maske

UNIT I: Disease process and kinds of diseases
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- Kinds of diseases –terms used to describe infections.
- Disease process, signs, symptoms and syndrome.
- Epidemiology-epidemic, endemic, pandemic, sporadic
- Reservoirs of infection.
- Modes of disease transmission, carriers and their types.

Infection refers to the multiplication of any parasitic organism within or on the host's body. (Sometimes the term **infestation** is used to refer to the presence of larger parasites, such as worms or arthropods, in or on the body.)

If an infection disrupts the normal functioning of the host, disease occurs.

Disease is a disturbance in the state of health wherein the body cannot carry out all its normal functions.

Both infection and disease result from interactions between parasites and their hosts. Sometimes an infection produces no observable effect on the host even though organisms have invaded tissues.

When an infection causes disease, the effects of the disease range from mild to severe.

KINDS OF DISEASES

- Human diseases are caused by infectious agents, structural or functional genetic defects, environmental factors,or any combination of these causes.
- **Infectious and Noninfectious Diseases**
- **Infectious diseases** are diseases caused by infectious agents such as bacteria, viruses, fungi, protozoa, and helminths.
- **Noninfectious diseases** are caused by any factor other than infectious organisms.

2. *Congenital diseases* are structural and function al defects present at birth,

1. Caused by drugs, excessive X-ray exposure, or certain infections.
2. When a mother has a rubella (German measles) or a syphilis infection, the infectious agent may cross the placenta and cause congenital defects.
3. Some medicines, such as the antiwrinkle Drug retinoid-A and the antibiotic tetracycline,

may cause congenital defects when taken by preg nant women.

Degenerative diseases

are disorders that develop in one or more body systems as aging occurs.

Patients with degenerative diseases such as emphysema or impaired kidney function are susceptible to infections.

Conversely, infectious agents can cause tissue damage that leads to degenerative disease, as occurs in bacterial endocarditis, rheumatic heart disease, and some kidney diseases.

Autoimmune diseases

4. *Nutritional deficiency diseases* lower resistance to infectious diseases and contribute to the severity of infections.

For example, the bacterium that causes diphtheria (*Corynebacterium diphtheriae*) produces more toxin in people with iron deficiencies than in those with normal amounts of iron.

Poor nutrition also increases the severity of measles and contributes to deaths from the disease.

5. *Endocrine diseases* are due to excesses or defi ciencies of hormones. Viral infection has been linked to pancreatic damage that leads to insulin-dependent diabetes

7. *Immunological diseases* such as allergies, auto immune diseases, and immunodeficiencies are caused by malfunction of the immune system; AIDS is a consequence of a viral infection and destruction of certain cells of the immune system.

8.Communicable and Noncommunicable Diseases

Infection :Lodgement and multiplication of any parasitic microorganism in or on body of the host is called as infection.

Infection may be classified in various ways

1. Primary infection: Initial infection with the parasite in the Host
2. Reinfection: Subsequent infection by **same** parasite in the host
3. Secondary infection: If resistance of the host is lowered infection by **one** parasite that is primary infection,**second** parasite set up infection it is called secondary infection.

4.Cross infection:When in a patient already suffering from disease a new parasite up a infection from another host or another external source ,it is termed as cross infection .

5.Nosocomial infection : cross infections occuring in hospital are called as nosocomial infection.

6.Iatrogenic infection:refers to physician induced infections resulting from investigative ,therapeutic or other procedures.

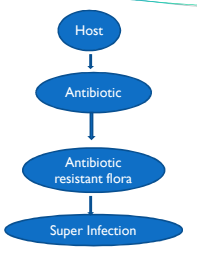
- Exogenous infections: Source of infection is out side the hosts own body.
- Endogenous infection: when source of infection is inside host.

Mixed infections

are caused by several species of organisms present at the same time.

A **superinfection**:

is a secondary infection that results from the destruction of normal microflora and often follows the use of broad-spectrum antibiotics.



Atypical infection: is one in which the typical or characteristic clinical manifestations /symptoms of particular infectious disease are not present

An **inapparent**, or **subclinical infection** is one that fails to produce the full range of signs and symptoms either because too few organisms are present or because host defences effectively combat the pathogens.

Latent infection

- Local infection :Infection confined to a small region of the body, such as a boil or bladder infection.

Multiplication—cells—damage---lesion

- Focal infection :Infection in a confined region from which pathogens travel to other regions of the body, such as an abscessed tooth or infected sinuses.**artritis**

Tonsilitis =infection

- **Systemic infection :** Infection in which the pathogen is spread throughout the body, often by travelling through blood or lymph

- Water,food----ingestion----intestine----multiply----Deep---blood –circulate all parts

- Acute disease--- Disease in which symptoms develop **rapidly** and that runs its course **quickly**. Cholera, dihaeria
- Chronic disease-- Disease in which symptoms develop **slowly** and disease persist for **prolonged period.**Tuberculosis,AIDS,Syphilis
- Subacute disease-- Disease with symptoms intermediate between acute and chronic

- Local infection Infection confined to a small region of the body, such as a boil or bladder infection
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Term Characteristic of Infection

- Acute disease Disease in which symptoms develop rapidly and that runs its course quickly
- Chronic disease Disease in which symptoms develop slowly and disease is slow to disappear
- Subacute disease Disease with symptoms intermediate between acute and chronic

Sources of infections===Reservoir of infection

SOURCE AND RESERVOIR

The source of infection is defined as the person, animal, object or substance from which an infectious agent passes or disseminated to the host.

A reservoir is defined as "any person, animal, arthropod, plant, soil or substance in which an infectious agent lives and multiplies, on which it depends primarily for survival, and where it reproduced itself in such manner that it can be transmitted to a susceptible host". In short the reservoir is the natural habitual in which the organism metabolized and replicates.

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CARRIERS

In some disease, either due to inadequate treatment or immune response, the disease agent is not completely eliminated, leading to a carrier state. A carrier is defined as an infected person or animal that harbors a specific infectious agent in the absence of discernible clinical disease and serves as a potential source of infection for others.

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Course of infection/Disease process

Outcome of disease depends upon

Virulence of pathogen, dose of infectionand host resistance.

1. **Route of infection**
2. **Infection dose:** ID50,LD50
3. **Adhesion**

- Specfic reaction between surface receptor on host cell and adhesive structures on the surface of bacteria
- Organized structures-Pili,fimbriae Antigenic.
- Loss of adhesion result in loss of virulence.
- **Invasiveness**
- Ability of pathogens to spread in tissues after establishing infection.

a. Highly invasive –pathogen produce characteristically spreading or generalized lesions.ex. Streptococcal septicaemia following wound infection.

b. Less invasive pathogens cause more locallize infections .Ex. *S. aureus*,Tetanus bacilli

- **4.Communicability**
- Ability of pathogen to spread from one person to anothercalled communicability.
- Respiratory and intestinal diseases are highly communicable
- Developement of epidemic and panemic require the pathogen to possess high degree of virulence and communicability.

- Spread of infection : Infection in which the pathogen is spread throughout the body, often by travelling through blood or lymph
- Septicemia Presence and multiplication of pathogens in blood
- Bacteremia Presence but not multiplication of bacteria in blood
- Viremia Presence but not multiplication of viruses in blood
- Toxemia Presence of toxins in blood
- Sapremia Presence of metabolic products of saprophytes

Pyaemia—septicaemia produced by pyogenic bacteria.

Depending upon spread of infection in community

Endemic diseases- dis constantly present in particular area. Typhoid in INDIA

2.Epidemic- spreads rapidly involving many persons in area at the same time

3.Pandemic –Epidemic that spreads through many areas of the world involving very large number of people within a short period.

4.sProsodemic diseases

Unit II

Etiology, pathogenesis, Clinical features, laboratory diagnosis, epidemiology,

treatment and prophylaxis of the following

2.1 Typhoid.

2.2 Cholera

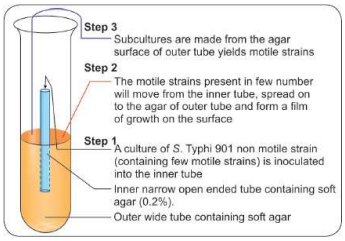
The antigens of salmonellae undergo phenotypic and genotypic variation:

1.H-O variation:This variation is associated with the loss of flagella.

- When salmonellae are grown on agar

containing phenol (1:800), flagella are inhibited.

- This change is phenotypic and temporary. Flagella reappear when the strain is sub cultured on media without phenol.
- Rarely,salmonellae may lose their flagella by mutation.
- Generally, the loss of flagella is not total .
- To obtain a population of motile cells rich in H antigen from such cultures,selection may be carried out by using Craigie's tube
- .



Phase variation:

- The flagellar antigens of most salmonellae occur in one of two phases.
- Phase 1 antigens are either specific for a species or shared by a few species only. Hence it is called the 'specific' phase.
- Phase 2 antigens are widely shared and hence this is called the 'non-specific' or 'group' phase.
- Strains that possess both phases are called diphasic.
- Some, like *S. Typhi*, occur only in Phase 1 and are called monophasic.

V-W variation:

Fresh isolates of *S. typhi* generally carry a surface layer of Vi antigen that completely masks the O antigen. Such bacilli are agglutinable with the **Vi antiserum** but not with the O antiserum. This is called the V form.

1 **Vi antiserum +,** O antiserum- V form

2. **Vi antiserum -,** O antiserum+ W form

- After serial sub culturing Vi antigen is lost Such cultures are not agglutinable with the Vi antiserum but readily agglutinable with the O antiserum. This is called the W form.

- Intermediate stages during the loss of the Vi antigen, when the bacillus is agglutinable with **both Vi and O antisera**, are called VW forms.
- S-R variation

- Typhoid-Salmonellae are strict parasites of animals or humans. *S. typhi*, *S.paratyphi A* and usually, but not invariably, *S. paratyphi B* are confined to human beings.

Pathogenasis:

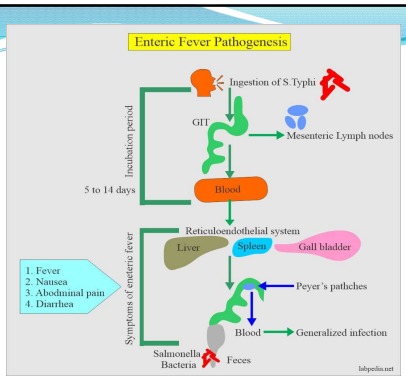
Enteric fever includes typhoid fever caused by *S.typhi* and paratyphoid fever caused by *Salmonella paratyphi A* and *S.paratyphi B*.

Name typhoid was given by Louis(1828) to distinguish it from typhus fever caused by Rickettsia.

1.Infection is acquired by **ingestion**

2.ID50 was found to be 10^3 to 10^6 bacilli in human volunteers.

3.



1. Ingestion----
2. GUT—
3. Attach to microvilli of the ileal mucosa—Penetrate to lamina propria and submucosa----They are phagocytosed there by macrophages and polymorphs----Resist killing—
4. Enter mesentric lymphnodes-----multiply---through thoracic duct ---enter blood stream
5. Transient bacterimia.
6. Bacilli seeded in the liver, gall bladder, spleen ,bone marrow, lymphnode ,lungs and kidney
7. Multiply
8. Massive bacterimia. Onset of clinical illness.
9. Bile is good culture medium for bacillus, it multiply abundantly in gall bladder and through bile discharged into intestine and affect Payers patches and lymphoid follicles of the ileum.

9. inflamed, necrosis=dead and slough off.

10. Typhoid ulcer complication, haemorhegic, perforation

Clinical Course of disease :

1. I. Period=7 to 14 days but range 3 to 56 days. I.D.

2 .Mild to fatal- severe disease

3.

Symptoms

Signs and symptoms are likely to develop gradually — often appearing one to three weeks after exposure to the disease.

Early illness

- Signs and symptoms include:
- Fever that starts low and increases daily, possibly reaching as high as 104.9 F (40.5 C) called step ladder pyrexia(fever).
- Headache
- Malaise or Weakness and fatigue-tiredness
- Muscle aches
- Sweating
- Dry cough
- Anorexia=Loss of appetite and weight loss
- Abdomenal pain =Stomach pain
- Diarrhea or constipation
- Rash-rose spots
- Extremely swollen stomach, hepatomegally liver

- Epidemiology:

S.paratyphi A is prevalent in India and other Asian countries.

Salmonella paratyphi B is common in Western Europe.

It is endemic in all parts of India.

Proportion of typhoid to Paratyphoid is 10:1.

All ages but common in 5-20 yr age group

Carriers

Convalscent carrier 3 wk to 3 months

Temporary-more than 3 month but less than a year.

Chronic-over a year.2-4 % become chronic carrier. Common in women. Typhoid Merry Intermittent shading.

- Laboratory diagnosis
- Microscopy-
- Culturing; Isolation- Fecal,blood clot, lengthy
- Serological test –ideal --serodiagnosis=AG/AB
- 1.Specimen-
- 2.Blood culture : 90%cases positive in first wk,75% = second wk, 60% =3 wk

Blood culture

- Blood and Clot culture sample-inoculate
- 0.5% bile broth 50 to 100ml
- Incubate, subculture on MacConkeys agar- Incubate- lac nonfermenting colonies,
- Castanadas method –bottle –slant, bile broth. Biochemical test.

Antigen testing

- Serotyping—O,H-antigen

Fecal culture

- Feces culture
- Urine culture

- Widal Test-

Serodiagnosis

- It measures H and O agglutinins for typhoid an paratyphoid bacilli.
- Two types of tubes are used

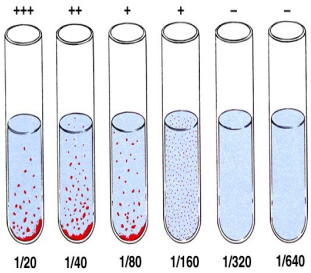
a.Dreyers agglutination tube for H agglutination.

b. Felix tube for O agglutination.

Procedure:

Serial dilutions 0.4 ml of serum 1:10 to 1:640 are mixed with H and O antigen. Incubated in water bath at **37**°C

- Use H and O antisera



Widal Test:

1. The Widal test performed reliably and interpreted with care, can be of value in the diagnosis of typhoid fever in endemic areas when facilities for culture are not available.
2. The patient's serum is tested for O and H antibodies against the antigen suspensions of *S. typhi* O 9, 12 & *S. typhi* Hd for diagnosis of typhoid fever.
3. The Widal test is reported by giving the titre for both O and H antibodies.
4. The antibody titre is taken as the highest dilution of serum in which agglutination occurs.
5. The type of agglutination seen with O reaction is granular while that seen with H reaction is more uneven type of clumping usually described as floccular.

Interpretation of the Widal test:

1. The agglutination titre will depend on the stage of the disease.
2. Agglutinins usually appear by the end of the first week.
3. The titre increases steadily till the third or the fourth week, after which it declines gradually.
4. The result of a single test should be interpreted with caution.
5. It is difficult to lay down levels of significance though it is generally stated that titres of 1/100 or more for O agglutinins and 1/200 or more for H agglutinins are significant.

- Prophylaxis:
- General measures
- Vaccination-

1.TAB vaccine is used for immunization. Heat killed vaccine developed by Almorth Wright in South Africa.

- S.typhi ,1000 million+S.paratyphi A and B 750 million. Inactivated by heating 50-60 ºC
- Dose two doses at the interval of 4-6 wk subcutaneously.

2.Live vaccine: live vavccine Typhoral is prepared from stable mutant of *S.typhi* strain Ty 2 la .It is Gal E mutant lact enzyme UDP galactose -4-epimerase

- Multiply for 4-6 cell generations and self distructs.
- Dose :1—3—5 day capsule containing 10^9bacilli.

3.Vi vaccine:Typhim Vi. *S.typhi* strain Ty 2

- Treatment:
- Ciprofoxacin
- Ceftriazone