Definitions

- **Infection**
The ability of a microorganism to invade a suitable host, evade host defenses, and to multiply and colonize host tissues. If an infection disrupts the normal functioning of the host, disease occurs.

- **Infectious disease**
Damage or alteration of host cells resulting from an infection.

There actually exist numerous variations on this infection theme including:

- **Symptomatic infection**
An infection by a microorganism which results in some sort of expression of lack of health (i.e., disease).

- **Asymptomatic infection**
Colonization of the body by a microorganism that does not cause symptoms.

- **Subclinical [inapparent] infection**
Asymptomatic infection by different names.

- **Opportunistic infection**
An infection by a microorganism that normally does not cause disease but becomes pathogenic when the body’s immune system is impaired and unable to fight off infection.

- **Latent infection**
An infection that is inactive though continuing to infect, and which remains capable of producing symptoms. "A latent disease is characterized by periods of inactivity either before signs and symptoms appear or between attacks."

- **Emerging infectious disease:**
An infectious disease that has newly appeared in a population or that has been known for some time but is rapidly increasing in incidence or geographic range.

- **Communicable disease**
An infectious disease that readily spreads from person to person.

- **Contagious disease**
An infectious disease that very readily spreads from person to person.

- **Noncommunicable disease**
A noncommunicable disease is an infectious disease that is not typically spread from person to person. "Such diseases may result from:

  1. infections caused by an individual's normal microbiota, such as an inflammation of the abdominal cavity lining following rupture of the appendix;
  2. poisoning following the ingestion of preformed toxins, such as staphylococcal enterotoxin, a common cause of food poisoning;
  3. infections caused by certain organisms found in the environment, such as tetanus, a bacterial infection resulting from spores in the soil gaining access to a wound.

  4. a disease caused by an opportunistic infection is an example of a noncommunicable disease.

- **Local infection**
an infection that is limited to a small area of the body

- **Systemic infection**
an infection that is found throughout the body

- **Focal infection**
**Systemic infection/local origin**: a systemic infection that originates from a local infection. All systemic infections are focal infections since they have to start somewhere. However, focal infection implies some amount of temporal difference between the start of the local and the systemic infections.

**Local infection/global symptoms**: focal infection is also another way of saying that a local infection is responsible for symptoms occurring in some other locality in the body. For example, tetanus is caused by the release of exotoxin from a local infection.

- **Nosocomial infections**
are infections which are a result of treatment in a hospital or a healthcare service unit, but secondary to the patient’s original condition. Infections are considered nosocomial if they first appear 48 hours or more after hospital admission or within 30 days after discharge.

**TYPES OF FEVER**

*Continuous fever*
Temperature remains above normal throughout the day and does not fluctuate more than 1 °C in 24 hours, e.g. lobar pneumonia, typhoid, urinary tract infection, brucellosis, or typhus.

*Remittent fever*
Temperature remains above normal throughout the day and fluctuates more than 1 °C in 24 hours, e.g., infective endocarditis.

*Intermittent fever*
Fever with regular shift of normal and high temperature with deviations of 3°- 4°C (malaria)

*Recurrent fever*
Fever with regular shift of high temperature, lasting for several days, and normal temperature, also of several days duration (recurrent typhus)

*Undulant fever*
Fever with several waves of gradual increase and decrease of temperature (Brucellosis, Leishmaniosis).

*Irregular fever*
Long lasting fever with irregular temperature deviations

*Fever inversa*
The morning temperature higher than the evening temperature

<table>
<thead>
<tr>
<th>Performance of the various types of fever</th>
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<tbody>
<tr>
<td>A</td>
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<td>B</td>
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**Types of prophylaxis**
- Chemoprophylaxis is the treatment with a drug before, during, or shortly after exposure to an infectious agent or agents in an attempt to prevent the development of infection.
- Chemoprophylaxis may be specific or nonspecific (preoperative use of antibiotics).
- Specific chemoprophylaxis has been shown to be effective in:
  - Cholera
  - Gonorrhea
  - Haemophilus influenzae
  - Influenza
  - Leprosy
  - Malaria
- Meningococcal infections
- Rheumatic fever
- Syphilis
- Tuberculosis
- Pneumocistis carinii

- **Immunoprophylaxis** against infectious disease includes the use of vaccines or antibody-containing preparations to provide immune protection against a specific disease.
  - Vaccine. A suspension of attenuated live or killed microorganisms (bacteria, viruses, rickettsiae), or fractions thereof, administered to induce immunity and thereby prevent infectious disease.
  - Toxoid. A modified bacterial toxin that has been rendered nontoxic but that retains the ability to stimulate the formation of antitoxin.
  - Specific immune globulin. Special preparations obtained from donor pools (human or equine) preselected for high antibody content against a specific disease.

- **Active prophylaxis**. Active immunization involves administering a preparation that stimulates the body’s immune system to produce its own specific immunity. Vaccines now available for use include the following types: (1) attenuated live microorganisms; (2) killed (inactivated) microorganisms; (3) recombinant produced antigens.

- **Passive prophylaxis**. Passive immunity is conferred by administering antibodies formed in another host. Human immunoglobulins remain a mainstay of passive prophylaxis (and occasionally therapy) they are usually used to protect individuals who have been exposed to a disease and cannot be protected by vaccination.

### Vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
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<tbody>
<tr>
<td>Adenovirus, types 4 and 7</td>
<td>Live viruses</td>
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<tr>
<td>Hepatitis A</td>
<td>Inactivated viral antigen</td>
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<tr>
<td>Hepatitis B</td>
<td>Recombinant DNA-derived protein</td>
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<tr>
<td>Influenza</td>
<td>Inactivated virus or viral components</td>
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<tr>
<td>IPV (inactivated poliovirus vaccine)</td>
<td>Inactivated virus of three serotypes</td>
</tr>
<tr>
<td>OPV (oral poliovirus vaccine)</td>
<td>Live viruses of three serotypes</td>
</tr>
<tr>
<td>Japanese Encephalitis</td>
<td>Inactivated virus</td>
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<tr>
<td>Measles, Mumps, Rubella (MMR)</td>
<td>Live viruses</td>
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<tr>
<td>Rabies</td>
<td>Inactivated virus</td>
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<tr>
<td>Smallpox</td>
<td>Live viruses</td>
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<tr>
<td>Varicella (Varivax)</td>
<td>Live viruses</td>
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<tr>
<td>Yellow fever</td>
<td>Live viruses</td>
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<tr>
<td>Meningococcal</td>
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<tr>
<td>Pneumococcal (pneumovax)</td>
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<tr>
<td>Rabies</td>
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<tr>
<td>Tetanus-diphtheria toxoids</td>
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<td>Typhoid</td>
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### Passive Immunization and Immunotherapy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Biologic</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Botulism antitoxin</td>
<td>specific equine Ig</td>
<td>treatment</td>
</tr>
<tr>
<td>CMV</td>
<td>Hyperimmune human Ig</td>
<td>Prophylaxis of renal transplant recipients</td>
</tr>
<tr>
<td>Diptheria antitoxin</td>
<td>specific equine Ig</td>
<td>treatment</td>
</tr>
<tr>
<td>Hepatitis A, measles</td>
<td>pooled human Ig</td>
<td>prophylaxis</td>
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<tr>
<td>Hepatitis B Ig</td>
<td>Immune human Ig</td>
<td>prophylaxis</td>
</tr>
<tr>
<td>Rabies (HRIG)</td>
<td>Immune human Ig</td>
<td>prophylaxis</td>
</tr>
<tr>
<td>Tetanus (TIG)</td>
<td>Immune human Ig</td>
<td>treatment</td>
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<tr>
<td>Tetanus antitoxin</td>
<td>equine</td>
<td></td>
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<tr>
<td>Vaccina (smallpox)</td>
<td>Immune human Ig</td>
<td>treatment</td>
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**Botulinum toxoid.** Pentavalent (ABCDE). The toxoid is used to protect individuals from accidental exposure to botulinum toxins. It should be administered only to individuals working in high risk laboratories who are actively working or expect to be working with cultures of Clostridium botulinum or the toxins.

**Primary and secondary immune responses.** A first exposure to antigen stimulates production of IgM antibodies, which become detectable within about a week. The antigen-specific B cells proliferate and some become memory cells. On subsequent exposure to the same antigen, these memory cells are rapidly activated. Antibodies, mainly of the IgG class, appear within about 2 days, and the quantity of antibody produced is much higher than is seen with the primary response. The affinity of the antibodies in the secondary response is also markedly higher than that seen in the primary response.

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**DESENSITIZE FRACTIONAL METHOD**

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<tr>
<td>1.</td>
<td>Intracutaneous, in forearm, is introduced 0.1 ml of diluted 1:100 heterogenous serum (red colored ampoule).</td>
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<td></td>
<td>Appreciate cutaneous reaction in 20 minutes.</td>
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<td>2.</td>
<td>If the diameter of edema or rash is &lt;10 cm - the reaction is considered negative.</td>
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**In case of negative reaction:**

1. Introduce subcutaneous 0.1 ml of undiluted heterogenous serum (blue or black colored ampoule).
2. Appreciate cutaneous reaction in 30 minutes.
3. If cutaneous reaction is negative - introduce intramuscular all therapeutic dose.

**In case of positive reaction:**

1. Introduce intramuscular 30 mg of prednysolon.
2. In 20 min introduce subcutaneous **0.5 ml of 1:100 diluted** heterogenous serum.
3. In 20 min, in case of negative reaction to previous injection, introduce subcutaneous **2 ml of 1:100** of diluted heterogenous serum.
4. In 20 min, in case of negative reaction to previous injection, introduce subcutaneous 5 ml of 1:100 of diluted heterogenous serum.
5. In 20 min, in case of negative reaction to previous injection, subcutaneous to introduce 0.1 ml of nondiluted serum.
6. In 30 min, in case of negative reaction to previous injection, introduce intramuscular all therapeutic dose.

**In case of positive reaction to one of the previous steps:**
1. Prescribe the remains doses of serum after intravenous introduction of 60-90 mg of prednysoloni and/or under narcosis.

**In case of anaphylaxis:**
1. Introduce intravenous 60-90 mg of prednysoloni (total maximum dose - 300 per day)
2. Introduce intravenous 0.5-1ml adrenalini 0.1% (or 1 ml noradrenalini 0.2%) in Sol. Glucosae 5%.

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**Laboratory Diagnosis of Infectious Diseases**

**A. Direct Microscopic Examination** - Using light microscopy (and occasionally electron microscopy) to directly observe microorganisms in wounds, bodily fluids, and tissues. This process is usually aided by using stains to help differentiate organisms.

- Examples include Gram staining of bacteria, dark field microscopic examination of spirochetes, acid-fast staining for mycobacteria, etc.

**B. Culturing Techniques** - Obtaining a pure culture of a microorganism by inoculating an appropriate nutrient media with infected tissue or bodily fluid (e.g., blood urine, sputum, wound, CSF, throat, and stool cultures).

- **Bacteria** - Bacteriologic culturing is frequently done on selective media - i.e., media which inhibits non-pathogenic "normal flora", but permits pathogenic bacteria to grow. Some bacteria require incubation in an aerobic environment, an anaerobic environment, or an environment with high levels of CO2. Identification of specific bacterial species is based on colony morphology as well as biochemical tests performed on bacterial isolates from culture.

- **Viruses** - Viruses are cultured in specialized media containing living cells. The presence of pathogenic virus is usually detected by observing the death of infected cells in culture (cytopathic effect). Immunologic techniques, PCR, or electron microscopy can be used to identify specific viruses after a positive culture has been obtained.

- **Antibiotic sensitivity testing** - Pure cultures of a bacteria can be directly exposed to paper disks impregnated with various antibiotics on an appropriate agar medium. Inhibition of growth around an antibiotic disk suggests sensitivity of the organism to the antibiotic. Antibiotic sensitivity can also be reported by the laboratory as the **minimal inhibitory concentration (MIC)**. This is the lowest concentration of a drug that inhibits the growth of an organism in culture. This information is useful for guiding physicians in choosing an antibiotic and its dose.

The success of culturing techniques depend on: (1) choosing an appropriate specimen for examination (based on the pathogenesis of the infection); (2) collecting the specimen properly and avoiding contamination; (3) prompt transport of the specimen to the laboratory, or proper storage of the specimen during transport.

**C. Immunologic Techniques** - These procedures utilize binding reactions between microbial antigens and their specific antibodies to infer the presence of infection in a host. A known antibody can be used to identify a specific microbial antigen in tissues, or a known antigen can be used to detect specific antibodies in a patient’s serum. Immunologic techniques have the advantage of providing more rapid diagnosis of infection. Currently, there are a number of commercially available rapid antigen detection tests available. However, many of these tests are expensive, and false positive and false negative results do occur.

- **Examples of common immunologic tests used for diagnosing infection:**
  - **Agglutination** tests are commonly used to identify a wide range of bacteria - E. coli, salmonella, shigella, haemophilus influenzae, streptococcus, etc. These tests can be
performed by mixing a pure isolate from culture with specific antibodies directed against bacterial antigens, or they can be performed by exposing a clinical specimen to latex beads that have been coated with specific antibody. A positive test is indicated by observing clumping (agglutination) of antigen-antibody complexes on a glass slide or test tube. The serologic tests for syphilis (RPR, VDRL) are agglutination tests.

- The **Enzyme-linked Immunosorbent Assay (ELISA)** is becoming one of the most commonly used immunologic methods for detecting infections. The procedure utilizes an easily assayed enzyme attached to a specific antigen. Presence of the complementary antibody in a clinical specimen (serum) activates the enzyme producing a chromogenic reaction (color change) in the specimen being examined. The screening test for HIV is an example of the ELISA.

- A relatively new procedure is the **optical immunoassay** which involves swabbing a clinical specimen on a silicon wafer that has been coated with specific bacterial antibody. The formation of an antigen-antibody complex on the wafer changes the color of light reflected from its surface allowing the technician to infer the presence of a specific organism. This technique is commonly used to rapidly diagnose group A streptococcal pharyngitis.

- **Fluorescent antibody tests** in which specific microbial antibodies labeled with fluorescent dye can be used to identify microorganisms in tissues. A positive test is indicated by observing fluorescence in a specimen using a microscope equipped with UV light. Fluorescent techniques can also be used to identify specific microbial antibodies in body fluids. For example, the, fluorescent treponemal antibody absorption test (FTA-ABS) is a very specific test used to confirm a diagnosis of syphilis.

- **Counter-immunoelectrophoresis** is a procedure in which a known antigen and samples of patient sera are placed in an agar medium and allowed to migrate towards each other in an electrical field. A positive test is indicated by precipitation of the antigen-antibody complex in the medium. This test can also use a known antibody to detect antigen from a clinical specimen.

- **Immunoblotting** - Electrophoresis techniques can be used for separating different proteins associated with an organism. For example, the **Western blot** technique is used to confirm a diagnosis of HIV after a positive antibody screening test is obtained. HIV proteins are separated electrophoretically in a gel medium resulting in discrete bands of viral proteins. These proteins are transferred to a paper strip which is then incubated with serum from a patient. If anti-HIV antibodies are present in the serum, they bind to specific HIV-associated proteins. An enzyme-linked reagent is then used to produce a color change in the strip to identify a positive test. (See Harrison’s, 16th ed., p 1100.)

- **Radioimmune assay** is a technique which uses a known antigen that has been "labeled" with a radioisotope to identify specific antibodies in a clinical specimen. Antigen-antibody complexes are separated from the specimen and the amount of radioactivity is measured and compared to known positive and negative standards. This method is also used to assay hormones and drugs in serum.

- **Acute and convalescent phase antibody testing** - Many viral infections can be diagnosed or staged by testing serum for IgM and IgG viral antibodies in the acute phase of a disease (onset of clinical disease), and the convalescent phase of the disease (14 days after onset of clinical disease). A 4-fold or greater rise in the IgM antibody titer between the two specimens indicates recent (acute) infection. If IgG concentrations of an antibody are greater than IgM concentrations, the patient either has immunity to the infection, or has a chronic infection.

D. **Genetic methods** - Highly specific gene amplification technologies such as **polymerase chain reaction (PCR)** are increasingly being used to identify the genetic signatures of organisms that grow slowly in culture (CMV, mycobacteria) - or those that do not culture at all (e.g., Hepatitis B and C viruses). These techniques are also used to determine the amount of an organism present in an infected patient (e.g.,
"viral load" of HIV and Hepatitis C). This ability to quantitate an infection is useful for staging the patient's disease.