MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

DISTANCE LEARNING CENTRE

DEPARTMENT OF INFECTIOUS DISEASES, EPIDEMIOLOGY, PARASITOLOGY AND TROPICAL MEDICINE

LECTURE № 3

FOR E-LEARNING IN EPIDEMIOLOGY OF INFECTIOUS DISEASES

FOR MEDICAL STUDENTS

TITLE: FACTORS AND ROUTES OF TRANSMISSION. SUSSCEPTIBLE HOST. HOST DEFENCES. IMMUNITY

PREPARED BY ASSOC. PROF. T. PETKOVA

PLEVEN, 2020

Communicable diseases may be transmitted from the reservoir or source of infection to a susceptible individual in many different ways, depending upon the infectious agent, portal of entry and the local ecological conditions.
As a rule, an infectious disease is transmitted by only one route, e.g. typhoid fever by vehicle transmission and common cold by direct contact. There are others which may be transmitted by several routes e.g. AIDS, hepatitis B, brucellosis. The multiple transmission routes enhance the survival of the infectious agent.

The mode of transmission of infectious diseases may be classified as **direct and indirect trasmission**.

Modes of transmission

A. Direct transmission

- Direct contact
- Droplet infection
- Contact with soil
- Inoculation into skin or mucosa
- Transplacental (vertical)

B. Indirect transmission

- Vehicle-borne
- Vector-borne – mechanical or biological
- Air-borne – dust
- Fomite-borne
- Unclean hands and fingers

Direct contact

Infection may be transmitted by direct contact from skin to skin, mucosa to mucosa, or mucosa to skin of the same or another person. This implies direct and essentially immediate transfer of infectious agent from the reservoir or source to a susceptible individual, without an intermediate agency. E.g. skin-to-skin contact as by touching, kissing or sexual intercourse or continued close contact.
Direct contact not only reduces the period for which the organism will have to survive outside the human host but also ensures a larger dose of infection. Diseases transmitted by direct contact include STD and AIDS, leprosy, skin and eye infections.

Droplet infection

This is direct projection of a spray of droplets of saliva and naso-pharyngeal secretions during coughing, sneezing or speaking and spitting talking in to the surrounding atmosphere.
The expelled droplets may impinge directly upon the conjunctiva, oro-respiratory mucosa or skin of close contact.
Particles of 10 μm or greater in diameter are filtered off by nose. Those 5 μm or less can penetrate deeply and reach the alveoli.
The droplet spread is usually limited to a distance of 50-100 cm between source and host.
In infectious diseases, this droplet which may contain millions of bacteria and viruses can be a source of infection to others. When a healthy susceptible person comes within the range of these infected droplets, he is likely to inhale some of them and acquire infection.
Diseases transmitted by droplet spread include many respiratory infections, eruptive fevers, many infections of the nervous system, common cold, diphtheria, whooping cough, meningococcal meningitis.
The potential for droplet spread is increased in conditions of close proximity, overcrowding and lack of ventilation.

Contact with soil

The disease agent may be acquired by direct exposure of susceptible tissue to the disease agent in soil, decaying vegetable matter in which it normally leads a saprophytic existence, e.g. tetanus, mycosis.

Inoculation into skin or mucosa
The disease agent may be inoculated directly in to the skin or mucosa e.g. rabies virus by dog bite, hepatitis B virus through contaminated needles and syringes.
Transplacental transmission
Disease agents can be transmitted transplacentally. Examples include toxoplasma gondii, rubella virus, cytomegalovirus, herpes virus, syphilis, hepatitis B, coxsackie B virus, HIV.
Some of the non-living agents (e.g. thalidomide) can also be transmitted vertically. In these cases, the disease agent produces malformations of the embryo by disturbing its development.

Indirect transmission embraces a variety of mechanisms including the traditional **5 F's** – flies, fingers, fomites, food and fluid.
An essential requirement for indirect transmission is that the infectious agent must be capable of surviving outside the human host in the external environment. Infectious agent retain its basic properties of pathogenesis and virulence till it finds a new host.
The depends upon the characteristics of the agent, the object and the influence of environmental factors such as temperature and humidity.

Indirect transmission can occur in a variety of settings.
Vehicle-borne
Vehicle-borne transmission implies transmission of the infectious agent through the agency of water, food (raw vegetables, fruits, milk and milk products), blood, serum, plasma or other biological products such as tissues and organs. Of these water and food are the most frequent vehicles of transmission, because they are used by everyone.
The infectious agent may have multiplied or developed in the vehicle (e.g. S. aureus in food) before being transmitted; or only passively transmitted in the vehicle (e.g. hepatitis A virus in water).
Diseases transmitted by water and food include infections of the alimentary tract – acute diarrhoeas, typhoid fever, cholera, polio, hepatitis A, food poisoning and intestinal parasites.
Those transmitted by blood include hepatitis B, hepatitis C, malaria, syphilis, HIV infection.
Organ transplantation may result in the introduction of the disease agent such as hepatitis B, hepatitis C, cytomegalovirus (with kidney transplants).
The *epidemiological features of vehicle transmission* are:

- If the dose of contamination is heavy, the outbreak may be explosive as in the case of cholera and hepatitis A epidemics;
- Cases are initially confined to those who are exposed to the contaminated vehicle;
- When secondary cases occur, the primary case may be obscured;
- The distance travelled by the infectious agent may be great, e.g. outbreaks of food poisoning;
- It is not always possible to isolate the infectious agent in the incriminated vehicle, e.g. typhoid bacilli in contaminated water;
- The common source of infection is often traceable.

Vector-borne
In infectious disease epidemiology, vector is defined as an arthropod or any living carrier that transports an infectious agent to a susceptible individual.
Transmission by a vector may be *mechanical* or *biological*.
When the transmission is biological, the disease agent passes through a developmental cycle or multiplication in the vector.
Epidemiological classification of vector-borne diseases
A. By vector:
Invertebrate type: arthropod vectors fall into 6 orders largely:

- Flies;
- Mosquitoes;
- Fleas;
- Cockroaches;
- Sucking lice;

- Ticks.

Vertebrate type – mice, rodents, bats

B. By transmission chain:

- Man – arthropod – man (malaria);
- Mammal – arthropod – man (plague);
- Bird - arthropod – man (encephalitis).

C. By methods in which vectors transmit agent:

- Biting;
- Regurgitation;
- Scratching-in of infectious agent;
- Contamination of host with body fluids of vectors

D. By methods in which vectors are involved in the transmission and propagation

- **Mechanical transmission** - the infectious agent is mechanically transported by a crawling or flying arthropod through soiling of its feet or by passage of organisms through its gastro-intestinal tract and passively excreted. There is no development or multiplication of the infectious agent on or within the vector.
- **Biological transmission** - the infectious agent undergoing replication or development in vector requires an incubation period before vector can transmit.
- ✓ When the infectious agent is transmitted vertically from the infected female to her progeny in the vector, it is known as transovarial transmission.
- ✓ Transmission of the disease agent from one stage of the life cycle to another as for example nymph to adult is known as trans-stadial transmission.

The factors which influence the ability of vectors to transmit disease are:

- Host feeding preferences;
- Infectivity - ability to transmit the disease agent;
- Susceptibility - ability to become infected;
- Survival rate of vectors in the environment;
- Suitable environmental factors.
- Seasonal occurrence of some diseases (e.g. lyme disease) may be related to intense breeding and thereby greater of the ticks during certain period of the year.

Airdust

Some of the larger droplet which are expelled during talking, coughing or sneezing, settle down by their sheer weight on the floor, clothes, bedding, linen and other objects in the immediate environment and become part of dust. A variety of infectious agent and skin squamae have been found in the dust of hospital wards and living rooms.

Some of them (tubercle bacilli) may survive in the dust for considerable periods under optimum conditions. During the act of sweeping, dusting and bed-making, the dust is released into the air and becomes once again airborne.

The diseases carried by infected dust are tuberculosis, Q-fever, psittacosis.

Fomite-borne

Fomites are articles or substances contaminated by the infectious discharges from a patient and capable of harbouring and transferring the infectious agent to a healthy person.

Fomites includes soiled clothes, towels, linen, handkerchiefs, cups, spoons, toys, glasses, door handles, syringes, instruments, surgical dressings.

Diseases transmitted by fomites include diphtheria, typhoid fever, dysentery, hepatitis A, eye and skin infections.

Unclean hands

Hands are the most common medium by which pathogenic agents are transferred to food from the skin, nose, bowel.

The transmission takes place both directly (hand-to-mouth) and indirectly.

Examples include staphylococcal and streptococcal infections, typhoid fever, dysentery, hepatitis A.

Lack of personal hygiene coupled with poor sanitation favour person-to-person transmission of infection.

Susceptible host
Successful parasitism
Four stages have been described in successful parasitism:

1. The infectious agent must find a **portal of entry** by which it may enter the host. There are many portals of entry, e.g. respiratory, alimentary, genitourinary tract, skin. Some organisms may have more than one portal of entry, e.g. hepatitis B, Q-fever, brucellosis.
2. On gaining entry into the host, the organisms must reach the appropriate tissue or "site of election" in the body of the host where it may find optimum conditions for its multiplication and survival.
3. The disease agent must find a way out of the body (portal of exit) in order that it may reach a new host and propagate its species. If there is no portal of exit, the infection becomes a dead-end infection as in rabies, bubonic plague, tetanus.
4. After leaving the human body, the organism must survive in the external environment for sufficient period till a new host is found.

A successful disease agent should not cause the death of the host but produce only a low-grade immunity so that the host is vulnerable again and again to the same infection – common cold virus.

Susceptible host – incubation period
An infection becomes apparent only after a certain incubation period, which is defined as "the time interval between invasion by an infectious agent and appearance of the first sign or symptom of the disease". During the incubation period, the infectious agent undergoes multiplication in the host.
Median incubation period - the time required for 50% of the cases to occur following exposure.
The factors which determine the incubation period include the generation time of the particular pathogen, infective dose, portal of entry and individual susceptibility.
Infectious diseases are not communicable during the incubation period, but there are exceptions – measles, chickenpox, hepatitis A. These diseases are communicable during the later part of the incubation period.
The length of the incubation period is characteristic of each disease.
There is a minimum incubation period for every disease before which no illness can occur.
Incubation period varies for different infectious diseases and also from one person to another with the disease.
In some diseases, the incubation period is very short ranging from a few hours to 2-3 days, e.g. staphylococcal food poisoning, cholera, influenza.
In some diseases, the incubation period is of median length ranging from 10 days to 3 weeks; in this category are many examples – typhoid fever, chickenpox, measles, mumps.
Then there are infections with longer incubation periods (ranging from weeks to months or year) and whose incubation time is difficult to measure precisely, e.g. hepatitis B, rabies, slow virus diseases.

The **communicable period** is defined as "the time during which an infectious agent may be transferred directly or indirectly from an infected person to another person, from an infected animal to man, or from an infected person to an animal".
Communicability varies in different diseases.
Some diseases are more communicable during the incubation period than during actual illness.
Communicability of some diseases can be reduced by early diagnosis and treatment.
Secondary attack rate (SAR) is defined as "the number of exposed persons developing the disease within the range of the incubation period, following exposure to the primary case".
SAR was initially developed to measure the spread of an infection within a family, household or any closed persons who have had contact with a primary case of disease.

Host defences against infection are at once local and systemic, non-specific and specific, and humoral and cellular.
It is difficult to identify any infectious agent that fails to stimulate multiple host defence mechanisms.

There is a phase of passive immunity transmitted to the baby from the mother across the placenta.
Maternal antibody transmitted to infant is gradually lost over a period of 6 months.
Thus a large proportion of infants remain free from potent infection up to 3 months, or even longer.
This protective "biological shield" is due to the presence of high levels of immunoglobulins IgG in the blood and plasma of infants born of immune mothers.
It has been postulated that some other factors (breast milk), are also responsible for the protection of infants.
A person is said to be immune when he possesses "Specific protective antibodies or cellular immunity as a result of previous infection or immunization. Or is so conditioned by such previous experience as to respond adequately to prevent infection following exposure to a specific infectious agent".

Specific defences
The specific defences may be discussed for convenience under the following heads:
1. Active immunity
    1.1 Humoral immunity
    1.2 Cellular immunity
    1.3 Combination of the above
2. Passive immunity
    2.1 Normal human Ig
    2.2 Specific human Ig
    2.3 Animal antitoxins or antisera

Active Immunity is the immunity which an individual develops as a result of infection or by specific immunization.
It is usually associated with presence of antibodies or cells having a specific action on the microorganism concerned with a particular infectious disease or on its toxin.
Active immunity depends upon the humoral and cellular responses of the host. The immunity produced is specific for a particular disease.
Active immunity may be acquired in 3 ways:

- Following clinical infection – chickenpox, rubella, measles;
- Following subclinical infection – polio, diphtheria;
- Following immunization with an antigen which may be a killed vaccine, a live attenuated vaccine or toxoid.

The immune response
Primary response
Primary response is when an antigen is administered for the first time to an animal or human who has never been exposed to it.
There is a latent period of induction of 3 to 10 days before antibodies appear in the blood. The antibody that is elicited first is entirely of the IgM type. The IgM antibody titre rises steadily during the next 2-3 days, reaches a peak level and then declines almost as fast as it developed.
If the antigen stimulus was sufficient, IgG antibody appears in a few days. IgG reaches a peak in 7-10 days and then gradually falls over a period of weeks or months.
The nature and extend of primary response to an antigen is determined by a number of factors, e.g. dose of antigen, nature of antigen, route of administration, adjuvants, nutritional status of the host.
An important outcome of primary antigenic challenge is education of the reticulo-endothelial system of the body. There is a production of what are known as "memory cells" by both B and T lymphocytes. These cells are responsible for the "immunological memory" which becomes established after immunization. In fact, the purpose of immunization is to develop immunological memory.
Secondary response - the response to a booster dose differs in a number of ways from the primary response – shorter latent period, production of antibody more rapid. Antibody response maintained at higher levels for a longer period of time and the antibody elicited tends to have a greater avidity to bind to the antigen.

The secondary response also involves the production of IgM and IgG antibody. Collaboration between B and T cells is necessary to initiate a secondary response. This response is attributed to immunological memory.
The immune response (primary and secondary) and immunological memory are the basis of vaccination and revaccination.

Humoral immunity comes from the B-cells which proliferate and manufacture specific antibodies after antigen presentation by macrophages. The antibodies are localized in the immunoglobulin fraction of the serum. Immuno-globulins are divided into 5 main classes – IgG, IgM, IgA, IgD and IgE. These antibodies circulate in the body and act directly by neutralizing the microbe or its toxin.
The complement system, together with antibodies is necessary for efficient phagocytosis of bacteria.
The antibodies are specific, they react with the same antigen which provoked their production, or a closely related one. As a result of this specificity, host response mediated by antibodies is limited and it will not provide protection against more than one antigen.
This specificity has been a problem in the production of vaccines. For example, there are numerous antigenic types of rhinoviruses, and it is not possible to expect a single vaccine to be effective against all these types.
Although antibodies are quite effective in combating most infectious diseases, humoral immunity does not cover all the situation than one finds in infectious diseases. Some pathogens (M. tuberculosis, S. typhi) escape the bacterial action of leukocyte. They can even multiply in the macrophages.The activated macrophages perform a much more efficient phagocytic function than non-activated macrophages.
It is now well-recognized that **cellular immunity** plays a fundamental role in resistance to infection. It is mediated by the T-cells which differentiate into sub-population able to help B-lymphocytes. The T-cells do not secrete antibody, but are responsible for recognition of antigen.
On contact with antigen, the T-cells initiate a chain of responses – activation of macrophages, release of cytotoxic factors, inflammatory reactions, secretion of immunological mediators (immune interferon). Cellular immunity is responsible for immunity against many diseases including tuberculosis, brucellosis.

Combination of the above. B- and T-lymphoid cells co-operate with one another and with certain accessory cells such as macrophages and killer cells and their joint functions constitute the complex events of immunity.
One subset of T-cells (T-helper) are required for the optimal production of antibody to most antigens. Another set of T-cells (T-suppressor) inhibit immunoglobulin synthesis.

Active immunity takes time to develop. It is superior to passive immunity because:

- The duration of protection, like that of the natural infection is frequently long-lasting;
- Severe reactions are rare;
- The protective efficacy of active immunization exceeds that of passive immunization – in some instances approaches 100%;
- Active immunization is less expensive than passive immunization. Vaccines are cheaper to produce than are antisera.

Passive immunity - when antibodies produced in one body (human or animal) are transferred to another to induce protection against disease. The body does not produce its own antibodies but depends upon ready-made antibodies.

Passive immunity may be induced:

- by administration of an antibody-containing preparation (immune globulin or antisera);
- by transfer of maternal antibodies across the placenta.
- by human milk - also contains protective antibodies – IgA.

Passive immunity differs from active immunity in the following respects:

- Immunity is rapidly established;

- Immunity produced is only temporary (days to months) till the antibody is eliminated from the body;
- There is no education of reticulo-endothelial system.

Passive immunization is useful for individual who cannot form antibodies or for the normal host who takes time to develop antibodies following active immunization.

Herd immunity is the level of resistance of a community or group of people to a particular disease. Herd immunity provides an immunological barrier to the spread of disease in the human herd.

For example, when an infectious disease is introduced into a "virgin" population, that is, population with a very low or no immunity, the attack and case fatality rates tend to be very high involving all susceptibles. For example, as it had happened in the very severe measles epidemic in the Faroe islands (1854), where the population had no previous experience of measles. The epidemic wave declined with a build-up of herd immunity following natural infection.

Elements which contribute to herd immunity are:

- Occurrence of clinical and subclinical infection in the herd;
- Immunization of the herd;
- Herd structure.

Herd structure is never constant. It is subject to constant variation because of new births, deaths and population mobility. An on-going immunization programme will keep up the herd immunity at a very high level.

The **herd structure** includes not only the hosts (population) belonging to the herd species but also the presence of alternative animal hosts and possible insect vectors as well as those environmental and social factors. These factors favour or inhibit the spread of infection from host to host.

If the herd immunity is sufficiently high, the occurrence of an epidemic is regarded as highly unlikely.

If that high level of immunity is maintained by an on-going immunization programme (to the point where the susceptible persons are reduced to a small proportion of the population), it may lead to elimination of the disease. This has been achieved in such disease as diphtheria and poliomyelitis. In the case of tetanus, herd immunity does not protect the individual.

Studies have shown that it is neither possible nor necessary to achieve 100% herd immunity in a population to halt an epidemic or control disease, as for example, eradication of smallpox.

Herd immunity may be determined by serological surveys – serological epidemiology.