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FOR E-LEARNING IN „INFECTIOUS DISEASE EPIDEMIOLOGY“

FOR MEDICAL STUDENTS

TITLE: EPIDEMIOLOGY AND PREVENTION OF SCARLET FEVER, DIPHTHERIA AND PERTUSSIS

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STREPTOCOCCAL INFECTIONS

Streptococcus pyogenes is a human pathogen. Group A streptococci (GAS) cause most streptococcal disease. GAS infections have the highest incidence in children younger than age 14. The asymptomatic prevalence is also higher (15-30%) in children, compared with that in adults (<5%). Crowded conditions in temperate climates during the winter months are associated with epidemics of pharyngitis and scarlet fever in school children.

Types of streptococcal infections

- Acute pharyngitis
- **Scarlet fever**
- Impetigo
- Erysipelas
- Cellulitis
- Streptococcal toxic shock syndrome
- Necrotizing fasciitis
- Rheumatic fever
- Post-streptococcal glomerulonephritis

SCARLET FEVER

Scarlet fever is an acute contagious disease of childhood. The disease is characterized by a bright punctiform eruption, diffused over the entire body. There are an angina more or less severe; a fever so variable in character and a marked tendency to nephritis. The disease finally terminating by desquamation of the skin. One attack renders the patient immune.

Today scarlet fever is endemic in the large cities of the world. The disease may occur sporadically or as an epidemic.

In Bulgaria (2018), there were 3 828 cases of scarlet fever, an incidence of 54,30‰. Compared to 2017, there is a slight increase in the number of morbidity and morbidity (registered 3 684 cases, incidence 51,87‰). Of the registered diseases, 95% are among children in pre-school and early school age (1-4 years and 5-9 years), (data from NCIPD).

Agent factors

Agent. Streptococci are gram-positive coccoid bacteria that grow in chains. On blood agar plates, streptococci may cause complete (β), incomplete (α), or no hemolysis (γ). R. Lancefield has allowed hemolytic streptococci to be classified into Group A through O-antigens of cell wall material.

Bacterial cell structure & extracellular products of S. Pyogenes:

- Capsule – some strains possess capsules of hyaluronic acid, resulting in large mucoid colonies on blood agar.
- Cell wall – lipoteichoic acid components have important interaction with the host.
- M-proteins – over 130 different M-protein types of GAS are currently described. M-protein protect bacteria against phagocytosis by polymorphonuclear leukocytes.
- Streptolysin O – cytolysins, causes the broad zone of β hemolysis surrounding colonies on blood agar plates. This is use for detection of anti-streptolysin O antibody (ASO).
- Hyaluronidase – extracellular enzyme hydrolyses hyaluronic acid in deeper tissues, facilitating the spread of infection along fascial planes.
- Pyrogenic (erythrogenic) exotoxins – 4 types: A, B, C and D. Because there are 4 types of pyrogenic exotoxins, some individuals may have multiple attacks of scarlet fever. They induce: lymphocyte blastogenesis, endotoxin-induced shock, fever, rash, suppress antibody synthesis, act as superantigens.
- **Source of infection** - may be a case or carrier. Mild infections are very common. These cases play a more important role than severe cases in spreading of infection. Carriers are common sources of infection. Carriers may be nasal or throat carriers. The incidence of carriers in a community may vary from 4 to 8% in non-epidemic situation up to 30-50% in epidemic focuses.

- **Infective material** - nasopharyngeal secretions.
- **Secondary attack rate** – 35-40%.
- **Mode of transmission**. Pharyngeal and cutaneous acquisition is spread person to person via aerosolized droplets and direct contact. Epidemics of scarlet fever have also resulted from ingestion of contaminated milk.

Host factors

- **Age.** Scarlet fever is a disease of childhood. The ages most susceptible are between 2 and 8 years. After 14 years the susceptibility diminishes, very few indeed contracting the disease after reaching adult life.
- Neither **sex** nor race seems to influence the predisposition.
- **Season** - Autumn and winter show a greater number of cases than summer.

Clinical features

- **Incubation period** – 1 to 10 days (average 3-5 days).
- Scarlet fever is mainly known for its sunburned-skin-colored sandpaper-like skin rash that is associated with fever. The classic description of the rash of scarlet fever has been described as “goose” bumps on a sunburned skin. Scarlet fever symptoms and signs may include a reddish sore throat, a fever and a red rash with a sandpaper-like texture, and a tongue that resembles a "strawberry".
- Complications from scarlet fever may include kidney disease (post-streptococcal glomerulonephritis) and rheumatic fever (an inflammatory disease caused by antibody cross-reactivity that the effects the heart, joints, skin and brain). Children between the ages of 6 and 15 are most susceptible to rheumatic fever development.
- The prognosis for scarlet fever, when treated appropriately with antibiotics, is usually excellent.
- Treatment. Penicillin is the drug of choice. Erythromycin is the drug of second choice.
- Currently, the mortality rate is less than 1% because of early recognition and early treatment with antibiotics.
- Diagnosis is possible by bacteriological examination of throat secretions which may be obtained by throat swabs.

Control of scarlet fever

- **Cases** - early diagnosis, isolation, treatment of cases, disinfection. The patient should be isolated 10 days and treated with antibiotics.
- **Contacts** - contacts are observed for 10 days.
- **No vaccine** is available for humans to prevent scarlet fever.

DIPHTHERIA

Diphtheria is an acute infectious disease caused by toxigenic strains of Corynebacterium diphtheriae. Three major clinical types have been described: nasal, pharyngeal and laryngeal. The skin, conjunctiva and other parts of the body may be affected. The bacilli multiply locally, usually in the throat.

Corynebacterium diphtheriae elaborate a powerful **exotoxin** which is responsible for:

- the formation of greyish membrane commonly over the tonsils, pharynx or larynx (or at the site of implantation), with well-defined edges and the membrane cannot be wiped away;
- marked congestion, oedema or local tissue destruction;
- enlargement of the regional lymph nodes;
- signs and symptoms of toxaemia.

Fatality rate on the average is about 10% which has changed little in the past 50 years in untreated cases and about 5% in treated cases.

Problem statement

- Diphtheria is a rare disease in most developed countries owing to routine children vaccination. In countries where satisfactory vaccination schemes have been instituted, the disease

has so declined that it is no longer regarded as a public health problem. Improved socio-economic conditions are changing the epidemiology of diphtheria.

- An example of waning immunity is the outbreak of diphtheria reported in Russia in 1990 and Thailand in 1996. These epidemics are largely due to decreasing immunization coverage among infants and children, waning immunity to diphtheria in adults, movement of large group of population in the last few years and an irregular supply of vaccine. These outbreaks highlight the need for booster vaccinations.
- Recent diphtheria outbreaks in a number of countries have demonstrated a shift in the age distribution of cases to older children and adults.
- The last cases in Bulgaria were introduced in the 1990s. There are no registered cases of diphtheria in Bulgaria in 2018, (data from NCIPD).

Agent factors

- **Agent.** C. diphtheriae is a gram-positive, non-motile organism. It produces a powerful **exotoxin**. Three types of diphtheria bacilli are differentiated – gravis, mitis and intermedius. In general, gravis infections tend to be more severe than mitis infections. Not all the strains of the organism are toxigenic. There is evidence that a non-toxigenic strain may become toxigenic when exposed to a particular bacteriophage, carrying the gene for toxin production. C. diphtheriae are sensitive to penicillin and are readily killed by heat and chemical agents. They may survive for short periods in dust and fomites.
- **Source of infection** may be a case or carrier. Cases range from subclinical to frank clinical cases.

Mild infections may exhibit no more than a running nose or sore throat. These cases play a more important role than frank cases in spreading the infection. Carriers are common sources of infection, their ratio is estimated to be 95 carriers for 5 clinical cases. Carriers may be temporary or chronic, nasal or throat carriers. The nasal carriers are particularly dangerous as source of infection because of frequent shedding of the organism into the environment, than do throat carriers. The temporary carrier state may last for about a month, but the chronic carrier state may persist for a year or so, unless the patient is treated. The incidence of carriers in a community may vary from 1 to 5%. Immunization does not prevent the carrier state.

Infective material - nasopharyngeal secretions, discharges from skin lesions, contaminated fomites, infected dust.

Period of infectivity. Unless treated, the period of infectivity may vary from 14 to 28 days from the onset of the disease, but carriers may remain infective for much longer periods. A case or carriers may be considered non-communicable, when at least 2 cultures obtained from nose and throat (24 hours apart) are negative for diphtheria bacilli.

Host factors

Age. Diphtheria particularly affects children aged 1 to 5. In countries where widespread immunization is practiced, a shift in age incidence has been observed from preschool to school age.

Sex. Both sexes are affected.

Immunity. A large proportion of population in developing countries seem to acquire active immunity through inapparent infection. A herd immunity of over 70% is considered necessary to prevent epidemic spread, but some believe that the critical level may be as high as 90%.

Environmental factors

- Cases of diphtheria occur in all seasons, although winter months favour its spread.

Mode of transmission

- The disease is spread mainly by droplet infection.
- It can also be transmitted directly to susceptible persons from infected cutaneous lesions.
- Transmission by objects (cups, toys), contaminated by the nasopharyngeal secretions of the patient is possible, but for only short periods.

Portal of entry

1. **Respiratory route**. Commonly the portal of entry is the respiratory tract.
2. **Non-respiratory routes**.

- The portal of entry may be the skin where cuts, wounds and ulcers not properly attended.
- The portal of entry sometimes may be the umbilicus in the newborn.
- The site of implantation may be the eye, genitalia or middle ear.
- The non-respiratory routes of infection are less common in developed countries where spread by droplet infection is more common.

Clinical features

Incubation period – 2 to 6 days, occasionally longer.

- Respiratory tract forms of diphtheria consist of pharyngotonsillar, laryngotracheal, nasal and combinations.
- **Pharyngotonsillar diphtheria**
- There are sore throat, difficulty in swallowing and low grade fever, mild erythema of throat, localized exudate or membrane. The membrane may be localized of the posterior pharynx or tonsil. May cover the entire tonsil or may spread to cover the soft and hard palates and the posterior portion of the pharynx.
- **Laryngotracheal diphtheria** most often is preceded by pharyngotonsillar disease, usually is associated with hoarseness and croupy cough. If the infection extends into bronchial tree, is the most severe form of disease.
- **Nasal diphtheria** is the mildest form of respiratory diphtheria, usually localized to the septum of one side of the nose.
- **Non-respiratory mucosal surface** – conjunctivae and genitals also be sites of infection.
- **Cutaneous diphtheria** is common in tropical areas. It often appears as a secondary infection of a previous skin abrasion or infection. The presenting lesion, often an ulcer, may be surrounded by erythema and covered with a membrane.
- Diagnosis is possible by bacteriological examination by nose and throat swabs and from the sites of infection for the other clinical forms.

Control of diphtheria

Cases and carriers

- **Early detection**. An active search for cases and carriers should start immediately among family and school contacts. Carriers can be detected only by cultural method. Swabs should be taken from both the nose and throat and examined by cultural methods for diphtheria bacilli.
- **Isolation**. All cases, suspected cases and carriers should be promptly isolated, preferably in a hospital, for at least 14 days. At least 2 consecutive nose and throat swabs, taken 24 hours apart, should be negative before terminating isolation.
- **Treatment**. Cases – diphtheria antitoxin; antibiotics. The carriers should be treated with 10 days course of antibiotics.

Contacts

- Contacts should be throat swabbed and their immunity status determined. If the immunization was received within the previous 2 years, no action would be needed. Non-immunized contacts should receive prophylactic antibiotics.
- Contacts should be placed under medical surveillance and examined daily for evidence of diphtheria for at least a week after exposure.

Community

- The only effective control is by active immunization with diphtheria toxoid of all infants as early in life as possible.
- **Diphtheria immunization** – Vaccines - DPTPHiB, DPTP, DPT, Td.

National policy is to immunize against diphtheria, whooping cough, tetanus, polio, haemophilus influenzae B (DPTPHiB) simultaneously, by administering 3 doses at 1 month interval, starting when the infant is 2 months old. Then there are reimmunizations.

WHOOPING COUGH (PERTUSSIS)

Pertussis is an acute infectious disease, usually of young children, caused by B. pertussis. It is clinically characterised by an insidious onset with mild fever and an irritating cough, gradually becoming paroxysmal with the characteristic "whoop". The spectrum of disease varies from severe illness to atypical and mild illness without whoop.

Problem statement

- Pertussis occurs in all countries. Since the beginning of last century, there was a marked and continuous drop in deaths from pertussis. In many parts of the world, pertussis is still a clinically serious illness, with high mortality and complication rates.
- Pertussis occurs endemically and epidemically. In tropical countries, it rivals measles in importance and severity among children. Since it became vaccine preventable around 1960, the worldwide number of cases and deaths has dropped dramatically.
- Pertussis occurs worldwide but most deaths are in countries of Africa, Asia and Latin America. Pertussis is one of the most lethal diseases of infants and young children who have not been immunized, particularly those with malnutrition and other respiratory infections. Case fatality rates in developing countries range from 4-15% in infants. About 10% of all pertussis cases and about 50% of the deaths occur in children under 1 year age.
- In 2018, 114 cases of pertussis were registered in Bulgaria (incidence $1.62\%_{000}$). Infants are most affected (incidence $53.30\%_{000}$), followed by the age group 1-4 years (incidence $13.26\%_{000}$). 61% of all cases are under 4 years of age, (data from NCIPD).

Agent factors

Agent

- The causative agent is **B. pertussis.** B. pertussis occurs in capsulated and non-capsulated forms and elaborates an endotoxin. Clinical disease is associated with encapsulated strains. B. pertussis carries 3 major agglutinogens. The bacterium survives only for very short periods outside the human body.

Source of infection

- B. pertussis infects only man. The source of infection is a case of pertussis. More often, the source of infection may be mild, missed and unrecognised cases. A chronic carrier state does not exist.
- **Infective material -** nasopharyngeal and bronchial secretions, which are infective. Objects contaminated by such discharges are also infective.
- **Infective period**. Pertussis is most infectious during catarrhal stage. The infective period may be considered to extend from a week after exposure to 3 weeks after the onset of paroxysmal stage.
- **Secondary attack rate** – 60-80% in unimmunized contacts.

Mode of transmission

- Pertussis is spread mainly by droplet infection and direct contact. Each time the patient coughs, sneezes or talks, the bacilli are sprayed into the air. Most children contract infection from their playmates who are in the early stages of the disease. The role of fomites in the spread of infection appears to be very small, unless they are freshly contaminated.

Host factors

Age

- Pertussis is primarily a disease of infants and preschool children. The highest incidence is found below the age of 5 years. Infants below 6 months have the highest mortality. Clinical disease may also occur in adults in whom the disease is often atypical.

Sex

- Both sexes are affected.

Immunity

- Recovery from pertussis or immunization is followed by immunity. Second attacks may occur in person with declining immunity, but usually mild. Infants are susceptible to infection from

birth because maternal antibody does not appear to give them protection. There is no cross immunity with B. parapertussis.

Environmental factors

- Pertussis occurs throughout the year, but the disease shows a seasonal trend with more cases occurring during spring months.
- Socioeconomic conditions and ways of life also play a role in the epidemiology of the disease. The risk of exposure is greater in the lower social classes living in overcrowded conditions than in well-to-do groups.

Clinical course

- **Incubation period** – 7 to 14 days, not more than 3 weeks.
- B. pertussis produces a local infection, the organism is not invasive. It multiplies on the surface epithelium of the respiratory tract and causes inflammation and necrosis of the mucosa leading to secondary bacterial invasion.
- **Three stages** are described:
    - Catarrhal stage, lasting for 1-2 weeks;
    - Paroxysmal stage, lasting for 2-6 weeks;
    - Convalescent stage, lasting for 1-2 weeks and more. The illness generally lasts 6 to 8 weeks.
- The chief complication are bronchitis, bronchopneumonia and bronchiectasis. The violence of the paroxysms may precipitate subconjunctival haemorrhages, epistaxis, punctate cerebral haemorrhages which may cause convulsion and coma.

Control of pertussis

Cases

- Early diagnosis, isolation, treatment of cases, disinfection of discharges from nose and throat. Early diagnosis is possible only by bacteriological examination of nose and throat secretions which may be obtained by nasopharyngeal swabs. The chances of isolating the organism are 80-90% if the material is obtained within 10-14 days from the onset of illness. PCR also can be used for the diagnosis of pertussis - nasopharyngeal swabs. The patient should be isolated until considered to be non-infectious.

Contacts

- Infants and young children should be kept away from cases. Contacts are observed for 21 days.

Prophylaxis

Pertussis vaccine is a killed whole cell preparation. The modern pertussis vaccines are acellular.

National policy is to immunize against diphtheria, whooping cough, tetanus, polio, haemophilus influenzae B (DPTPHiB) simultaneously, by administering 3 doses at 1 month interval, starting when the infant is 2 months old. Then there are reimmunizations.