MINISTRY OF HEALTH OF UKRAINE
DANYLO HALYTSKYI LVIV NATIONAL MEDICAL UNIVERSITY

PEDIATRIC INFECTIOUS DISEASES DEPARTMENT

GUIDELINES

FOR 6th YEAR STUDENTS
GENERAL MEDICINE FACULTY

«Differential diagnosis of diphtheria and infectious diseases with tonsillitis in children. Clinical features of diphtheria. Treatment. Prevention. Emergency states in toxic forms of diphtheria. Differential diagnosis of infectious mononucleosis. Clinical features in children. Treatment.»

LVIV-2021

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Guidelines on the course of Pediatric Infectious Diseases
for students of the 6th year of General Medicine Faculty
Approved at meeting of the
Pediatric infectious diseases department
Protocol № 229, 22.06.2021.
"Approved"
Methodical Commission of Pediatric disciplines
Protocol № 3, 07.09.2021.

Guidelines to lesson for 6th year students

(practical classes - 6 hours)

«Differential diagnosis of diphtheria and infectious diseases with tonsillitis in children. Clinical features of diphtheria. Treatment. Prevention. Emergency states in toxic forms of diphtheria. Differential diagnosis of infectious mononucleosis. Clinical features in children. Treatment.»

I.

Aim: to know diagnostic criteria of infectious diseases in children with tonzillitis; to perform differential diagnostics of them.

Professional motivation: Diphtheria is primarily a localized and generalized intoxication caused by diphtherial toxin, an extracellular protein metabolite elaborated by strains of *Corynebacterium diphtheria* that are lysogenic for corynephages that carry the tox+ structural gene in their genome. Classicaly, the diphtheric lesion is located in the pharynx and consists of a tightly adherent, grayish pseudomembrane within which the bacilli multiply and produce diphtherial toxin.

Basic level

1. To know how to ask about complaints, history of the disease and life in children with syndrome of tonzillitis [propedeutic pediatrics, children infectious diseases].
2. To perform clinical examination of the child with syndrome of tonzillitis [propedeutic pediatrics, children infectious diseases].
3. To diagnose infectious with syndrome of tonzillitis after clinical, laboratory and instrumental examination of the child [infectious diseases, propedeutic pediatrics, microbiology, and pathophysiology].
4. To give etiological, pathogenetical and symptomatical treatment [pharmacology, children infectious diseases].

II Primary aims of the study

A student should know:

1. Etiology and properties of the cause and causing factors of infectious.
2. Epidemiology (source of infection, ways of transmission, age-old receptivity and morbidity).
3. Pathogenesis of disease, pathomorphological changes in the staggered organs.
4. Classification of clinical forms of infectious.
5. Clinic of typical form of infectious.
6. Clinic of rare form of infectious.
7. Classification of toxic (severe) forms of infectious.
8. Clinic of toxic (severe) forms of infectious.
9. Complication of infectious
10. Methods of laboratory research.
11. Principles of therapy of d infectious.
12. Measures of prophylaxis of infectious.
13. Etiology of infectious**.**
14. Epidemiology infectious.
15. Characteristic of Epstein-Barr virus (EBV) and other infectious.
16. Pathogenesis of disease, pathomorphologic changes in the staggered organs and blood cells.
17. Classification of clinical forms of infectious mononucleosis and other infectious.
18. Clinic of infectious mononucleosis and other infectious.
19. Clinic of acute form infectious.
20. Clinic of chronic form infectious.
21. Other clinical forms of infectious
22. Hematologic disorders are typical for infectious
23. Methods of laboratory research.
24. Principles of therapy of infectious**.**

A student should be able:

1. 1.To follow the basic rules of work with a patient sick with diphtheria and other infectious.
2. To take anamnesis with the estimation of epidemiology information (taking into account seasonality, origin of febricities, polymorphism of clinical signs of illness).
3. To examine a patient and reveal the basic clinical signs of illness.
4. To represent information of anamnesis and objective inspection in a hospital chart and formulate the preliminary diagnosis.
5. To write a plan of examination.
6. To write a clinical diagnosis (form of disease, type, severity, course of disease).
7. To prescribe the treatment taking into account age, severity of illness.
8. To write out a prescription.
9. To organize disease measures in the hearth of infection (to find out the source of infection, fill an urgent report in SES, to set a quarantine, to define the circle of contact persons, conduct them bacteriological inspection).
10. To write epicrisis with the estimation of development of illness, results of inspection, efficiency of treatment, prognosis, by recommendations for a subsequent supervision or treatment depending on the form of diphtheria.
11. 11.To follow the basic rules of work with patients sick with infectious mononucleosis and mumps.
12. To take anamnesis with the estimation of epidemiology information (taking into account seasonality, origin of febricities, polymorphism of clinical signs of illness).
13. To examine patients and reveal the basic clinical signs of illness.
14. To represent information of anamnesis and objective inspection in a hospital chart and formulate the preliminary diagnosis.
15. To write a plan of examination.

16. To write a clinical diagnosis (form of disease, type, severity, course of disease).
17. To prescribe the treatment taking into account age, severity of illness.
18. To write out a prescription.
19. To organize disease measures in the hearth of infection (to find out the source of infection, fill an urgent report in SES, to set a quarantine, to define the circle of contact persons).
20. To write epicrisis with the estimation of development of illness, results of inspection, efficiency of treatment, prognosis, by recommendations for a subsequent supervision or treatment depending on the form of infectious mononucleosis and mumps.

III. Educational aims of the study

- forming the deontological presentations, skills of conduct with the patients
- to develop deontological presentations, be able to carry out deontology approach to the patient
- to develop the presentations of influence of ecological and socio-economic factors on the state of health
- to develop sense of responsibility for a time illness and loyalty of professional actions
- to be able to set psychological contact with a patient and his family

IV. Subject's integration

Table 1

Subjects	*To Know*	*To Know How*
1	2	3
Human Anatomy	*The main anatomic characteristics of respiratory tract and peculiarities in children*	
Physiology	*Respiratory, nervous and immune system function*	*To explain a variety of clinical signs and laboratory abnormalities*
Pathological Physiology	*Pathogenesis of disease. Pathogenesis of toxic shock syndrome.*	*To explain the main symptoms and signs appearance, causes of relapses, failure of inadequate therapy*
Pathological Anatomy	*Pathology*	*To explain the causes of complications and death*
Microbiology	*Etiology (classification, morphologic characteristic of the pathogen, methods of revealing and identification)*	*To culture the organism*
Pharmacology	*The main antibacterial agents. Regimens of treatment. Treatment of complicated diphtheria. Supportive care*	*To administer treatment of specific infection including ancillary therapy. To write the scheme of treatment of severe infection*
Histology	*Histological changes in different clinical forms of infections*	*Explanation of clinical signs appearance*
Propedeutics of Pediatric	*History of disease. Patient's examination.*	*To gather information about patient's history and chief*

Diseases		*complaints, to distinguish those, most important for diagnosis of different clinical forms of diphtheria. To examine the patient, to reveal the main symptoms and signs of disease. To distinguish the set of diagnostic features of infection. To argue the diagnosis.*
Pediatric Diseases	*Toxic syndrome, fever*	*To differentiate with other disorders of cardiovascular system*
Neurology	*Severe headache, vomiting, delirium, altered consciousness*	*Differential diagnosis with encephalitis, stroke*
Clinical immunology and allergology	*Immunologic changes as a part of pathogenesis and host defenses*	*To explain confirmative serologic tests*
Epidemiology	*The ways of transmission, main sources of infection*	*Epidemiological history*
Themes integration		
Sepsis, nephritis, heart failure, respiratory failure.	*To know peculiarities of manifestations, laboratory diagnosis, treatment*	*To differentiate diphtheria, pertussis, mumps infection with other infectious diseases with similar symptoms*

V. The contents of a theme

Diphtheria (Corynebacterium diphtheriae)

Diphtheria is an acute toxic infection caused by Corynebacterium diphtheriae. Diphtheria was the first infectious disease to be conquered on the basis of principles of microbiology and public health. Although diphtheria was reduced from a major cause of childhood death in the West in the early 20th century to a medical rarity, modern reminders of the fragility of such success underscore the need to apply those same principles assiduously in an era of vaccine dependence and a single global community.

ETIOLOGY.

Corynebacterium species are aerobic, nonencapsulated, non-spore-forming, mostly nonmotile, pleomorphic, gram-positive bacilli. Not fastidious in growth requirements, their isolation is enhanced by selective media (i.e., cystine-tellurite blood agar) that inhibit growth of competing organisms and, when reduced by C. dipththeriae, renders colonies gray-black. Three biotypes (i.e., mitis, gravis, and intermedius), each capable of causing diphtheria, are differentiated by colonial morphology, hemolysis, and fermentation reactions. A lysogenic bacteriophage carrying the gene that encodes for production of exotoxin confers diphtheria-producing potential to strains of C. diphtheriae, but it provides no essential protein to the bacterium. Investigation of outbreaks of diphtheria in England and the United States using a molecular technique suggested that indigenous nontoxigenic C. diphtheriae had been rendered toxigenic and disease producing after importation of toxigenic C. diphtheriae. Diphtheria toxin can be demonstrated in vitro by the agar immunoprecipitin technique (Elek test), by polymerase chain reaction, or by the in vivo toxin neutralization test in guinea pigs (lethality test). Toxigenic strains are indistinguishable by colony type, microscopy, or biochemical tests.

EPIDEMIOLOGY.

Unlike other diphtheroids (coryneform bacteria), which are ubiquitous in nature, C. diphtheriae is an exclusive inhabitant of human mucous membranes and skin. Spread is primarily by airborne respiratory droplets, direct contact with respiratory secretions of symptomatic individuals, or exudate from infected skin lesions. Asymptomatic respiratory tract carriers are important in transmission. Where diphtheria is endemic, 3-5% of healthy individuals may harbor toxigenic organisms, but carriage is exceedingly rare if diphtheria is rare. Skin infection and skin carriage are silent reservoirs of diphtheria. Viability in dust and on fomites for up to 6 mo has less epidemiologic significance. Transmission through contaminated milk and an infected food handler has been proved or suspected.

In the 1920s, more than 125,000 cases and 10,000 deaths due to diphtheria were reported annually in the United States, with highest fatality rates among very young and elderly patients. From 1921-1924, diphtheria was the leading cause of death among Canadian children 2-14 yr of age. The incidence began to fall, and with the widespread use of diphtheria toxoid in the United States after World War II, it declined steadily, with dramatic reductions in the latter 1970s. Since then, there have been zero to five cases per year and no epidemics of respiratory tract diphtheria. Similar decreases have occurred in Europe. Although disease incidence has fallen worldwide, diphtheria remains endemic in many developing countries. The sustained low incidence of diphtheria and high level of childhood vaccination have led authorities to set a goal to eliminate diphtheria among persons 25 yr of age or younger in the United States by the year 2000.

When diphtheria was endemic, it primarily affected children younger than 15 yr, but epidemiology has shifted to adults who lack natural exposure to toxigenic C. diphtheriae in the vaccine era and have low rates of booster vaccinations. In the 27 sporadic cases of respiratory tract diphtheria reported in the United States in the 1980s, 70% occurred in persons older than 25 yr. The largest outbreak of diphtheria in the developed world since the 1960s occurred from 1990-1995 throughout the states of the former Soviet Union, where more than 47,000 cases and 1,700 deaths occurred in 1994 alone. This outbreak was due to lack of

immunization, use of suboptimal antigen dose, and social factors (including population movements). Most affected individuals were older than 14 yr. Smaller epidemiologically similar outbreaks followed in Denmark and Sweden. Since 1994, public health authorities in the Russian federation have initiated aggressive efforts to vaccinate adults, and in 1995 the number of reported cases decreased.

Most proven cases of respiratory tract diphtheria in the United States in the past decade have been associated with importation of toxigenic C. diphtheriae, the organism believed to have become rare or to have disappeared from the United States. Enhanced surveillance surrounding the rare indigenous cases, however, shows that C. diphtheriae can continue to circulate in areas with previously endemic diphtheria. Protection from serious disease depends on immunization.

The estimated minimum protective level of diphtheria antitoxin is 0.01 IU/mL. It has been considered advisable that an antitoxin level of at least 0.1 IU/mL should be achieved after primary immunization to secure long-term protection. In serosurveys, in the United States and other developed countries with almost universal immunization during childhood, such as Sweden, Italy, and Denmark, significant percentages of adults and especially the elderly lack protective antitoxin levels. Booster doses of diphtheria-containing vaccine are recommended every 10 yr for adults in the United States.

Cutaneous diphtheria, a curiosity when diphtheria was common, accounted for more than 50% of C. diphtheriae isolates reported in the United States by 1975 and featured prominently in the changing epidemiology of diphtheria in the 1990s. An indolent local infection with infrequent toxic complications, cutaneous infection, compared with mucosal infection, is associated with more prolonged bacterial shedding, increased contamination of the environment, and increased transmission to the pharynx and skin of close contacts. Outbreaks are associated with homelessness, crowding, poverty, alcoholism, poor hygiene, contaminated fomites, underlying dermatosis, and introduction of new strains from exogenous sources. **PATHOGENESIS.**

Toxigenic and nontoxigenic C. diphtheriae organisms cause skin and mucosal infection and some cases of distant infection after bacteremia. The organism usually remains in the superficial layers of skin lesions or respiratory tract mucosa, inducing local inflammatory reaction. The major virulence of the organism lies in its ability to produce the potent 62-kd polypeptide exotoxin, which inhibits protein synthesis and causes local tissue necrosis. Within the first few days of respiratory tract infection, a dense necrotic coagulum of organisms, epithelial cells, fibrin, leukocytes, and erythrocytes forms, advances, and becomes a gray-brown adherent pseudomembrane. Removal is difficult and reveals a bleeding edematous submucosa. Paralysis of the palate and hypopharynx is an early local effect of the toxin. Toxin absorption can lead to necrosis of kidney tubules, thrombocytopenia, cardiomyopathy, and demyelination of nerves. Because the latter two complications can occur 2-10 wk after mucocutaneous infection, the pathophysiologic mechanism in some cases may be immunologically mediated.

CLINICAL MANIFESTATIONS.

The manifestations of C. diphtheriae infection are influenced by the anatomic site of infection, the immune status of the host, and the production and systemic distribution of toxin.

Respiratory Tract Diphtheria.

In the classic description of 1,400 cases of diphtheria in California in 1954, the primary focus of infection was the tonsils or pharynx in 94%, with the nose and larynx the next two most common sites. After an average incubation period of 2-4 days, local signs and symptoms of inflammation develop. Temperature is rarely higher than 39°C. Infection of the anterior nares (more common in infants) causes serosanguineous, purulent, erosive rhinitis with membrane formation. Shallow ulceration of the external nares and upper lip is characteristic. In tonsillar and pharyngeal diphtheria, sore throat is a universal early symptom, but only half of patients have fever, and fewer have dysphagia, hoarseness, malaise, or headache. Mild pharyngeal injection is followed by unilateral or bilateral tonsillar membrane formation, which extends variably to affect the uvula, soft palate, posterior

oropharynx, hypopharynx, and glottic areas. Underlying soft tissue edema and enlarged lymph nodes can cause a bull-neck appearance. The degree of local extension correlates directly with profound prostration, bull-neck appearance, and fatality due to airway compromise or toxin-mediated complications.

The leather-like adherent membrane, extension beyond the facial area, relative lack of fever, and dysphagia help differentiate diphtheria from exudative pharyngitis due to Streptococcus pyogenes and Epstein-Barr virus. Vincent's angina, infective phlebitis and thrombosis of the jugular veins, and mucositis in patients undergoing cancer chemotherapy are usually differentiated by the clinical setting. Infection of the larynx, trachea, and bronchi can be primary or a secondary extension from the pharyngeal infection. Hoarseness, stridor, dyspnea, and croupy cough are clues. Differentiation from bacterial epiglottitis, severe viral laryngotracheobronchitis, and staphylococal or streptococcal tracheitis hinges partially on the relative paucity of other signs and symptoms in patients with diphtheria and primarily on visualization of the adherent pseudomembrane at the time of laryngoscopy and intubation.

Patients with laryngeal diphtheria are highly prone to suffocation because of edema of soft tissues and the obstructing dense cast of respiratory epithelium and necrotic coagulum. Establishment of an artificial airway and resection of the pseudomembrane are lifesaving, but further obstructive complications are common, and systemic toxic complications are inevitable.

Cutaneous Diphtheria.

Classic cutaneous diphtheria is an indolent, nonprogressive infection characterized by a superficial, ecthymic, nonhealing ulcer with a gray-brown membrane. Diphtheritic skin infections cannot always be differentiated from streptococcal or staphylococcal impetigo, and they frequently coexist. In most cases, underlying dermatoses, lacerations, burns, bites, or impetigo have become secondarily contaminated. Extremities are more often affected than the trunk or

head. Pain, tenderness, erythema, and exudate are typical. Local hyperesthesia or hypesthesia is unusual. Respiratory tract colonization or symptomatic infection and toxic complications occur in the minority of patients with cutaneous diphtheria. Among infected Seattle adults, 3% with cutaneous infections and 21% with symptomatic nasopharyngeal infection, with or without skin involvement, had toxic myocarditis, neuropathy, or obstructive respiratory tract complications. All had received at least 20,000 U of equine antitoxin at the time of hospitalization.

Infection at Other Sites.

C. diphtheriae occasionally causes mucocutaneous infections at other sites, such as the ear (otitis externa), eye (purulent and ulcerative conjunctivitis), and genital tract (purulent and ulcerative vulvovaginitis). The clinical setting, ulceration, membrane formation, and submucosal bleeding help differentiate diphtheria from other bacterial and viral causes. Rare cases of septicemia are described and are universally fatal. Sporadic cases of endocarditis occur, and clusters among intravenous drug users have been reported in several countries; skin was the probable portal of entry, and almost all strains were nontoxigenic. Sporadic cases of pyogenic arthritis, mainly due to nontoxigenic strains, are reported in adults and children. Diphtheroids isolated from sterile body sites should not be dismissed as contaminants without careful consideration of the clinical setting.

Toxic Cardiomyopathy.

Toxic cardiomyopathy occurs in approximately 10-25% of patients with diphtheria and is responsible for 50-60% of deaths. Subtle signs of myocarditis can be detected in most patients, especially the elderly, but the risk for significant complications correlates directly with the extent and severity of exudative local oropharyngeal disease and delay in administration of antitoxin. The first evidence of cardiac toxicity characteristically occurs in the 2nd-3rd wk of illness as pharyngeal disease improves but can appear acutely as early as the 1st wk, when a

fatal outcome is likely, or insidiously as late as the 6th wk of illness. Tachycardia out of proportion to fever is common and may be evidence of cardiac toxicity or autonomic nervous system dysfunction. A prolonged PR interval and changes in the ST-T wave on an electrocardiographic tracing are relatively frequent findings, and dilated and hypertrophic cardiomyopathy detected by echocardiogram have been described. Single or progressive cardiac dysrhythmias can occur, such as first-, second-, and third-degree heart block; atrioventricular dissociation; and ventricular tachycardia. Clinical congestive heart failure may have an insidious or acute onset. Elevation of the serum aspartate aminotransferase concentration closely parallels the severity of myonecrosis. Severe dysrhythmia portends death. Histologic postmortem findings may show little or diffuse myonecrosis with acute inflammatory response. Survivors of more severe dysrhythmias can have permanent conduction defects; for others, recovery from toxic myocardiopathy is usually complete.

Toxic Neuropathy.

Neurologic complications parallel the extent of primary infection and are multiphasic in onset. Acutely or 2-3 weeks after onset of oropharyngeal inflammation, hypesthesia and local paralysis of the soft palate occur commonly. Weakness of the posterior pharyngeal, laryngeal, and facial nerves may follow, causing a nasal quality in the voice, difficulty in swallowing, and risk of death due to aspiration. Cranial neuropathies characteristically occur in the 5th wk and lead to oculomotor and ciliary paralysis, which are manifested as strabismus, blurred vision, or difficulty with accommodation. Symmetric polyneuropathy has its onset 10 days-3 mo after oropharyngeal infection and causes principally motor deficits with diminished deep tendon reflexes. Proximal muscle weakness of the extremities progressing distally and, more commonly, distal weakness progressing proximally are described. Clinical and cerebrospinal fluid findings in the latter are indistinguishable from those of polyneuropathy of Guillain-Barre syndrome. Paralysis of the diaphragm can ensue. Complete recovery is likely. Rarely, 2-3 wk

after onset of illness, dysfunction of the vasomotor centers can cause hypotension or cardiac failure.

DIAGNOSIS.

Specimens for culture should be obtained from the nose and throat and any other mucocutaneous lesion. A portion of membrane should be removed and submitted with underlying exudate. The laboratory must be notified to use selective medium. C. diphtheriae survives drying. In remote areas, a swab specimen can be placed in a silica gel pack and sent to a reference laboratory. Evaluation of a direct smear using Gram stain or specific fluorescent antibody is unreliable. Culture isolates of coryneform organisms should be identified to the species level, and toxigenicity and antimicrobial susceptibility tests should be performed for C. diphtheriae isolates.

TREATMENT.

Specific antitoxin is the mainstay of therapy and should be administered on the basis of clinical diagnosis, because it neutralizes only free toxin. Efficacy diminishes with elapsing time after the onset of mucocutaneous symptoms. Diphtheria antitoxin is no longer commercially available in the United States but may be obtained for treatment of suspected cases of diphtheria through the CDC (24-hr telephone [404] 639-2889). Antitoxin is administered once at empirical dose based on the degree of toxicity, site and size of the membrane, and duration of illness. Antitoxin is probably of no value for local manifestations of cutaneous diphtheria, but its use is prudent because toxic sequelae can occur. Commercially available immunoglobulin preparations for intravenous use contain low titers of antibodies to diphtheria toxin; their use for therapy of diphtheria is not proved or approved. Antitoxin is not recommended for asymptomatic carriers.

Antimicrobial therapy is indicated to halt toxin production, treat localized infection, and prevent transmission of the organism to contacts. C. diphtheriae is usually susceptible to various agents in vitro, including penicillins, erythromycin, clindamycin, rifampin, and tetracycline. Resistance to erythromycin is common in closed populations if the drug has been used broadly. Only penicillin or

erythromycin is recommended; erythromycin is marginally superior to penicillin for eradication of nasopharyngeal carriage. Appropriate therapy is erythromycin given orally or parenterally (40-50 mg/kg/24 hr; maximum, 2 g/24 hr), aqueous crystalline penicillin G given intramuscularly or intravenously (100,000-150,000 U/kg/24 hr divided in four doses), or procaine penicillin (25,000-50,000 U/kg/24 hr divided in two doses) given intramuscularly. Antibiotic therapy is not a substitute for antitoxin therapy. Therapy is given for 14 days. Some patients with cutaneous diphtheria have been treated for 7-10 days. Elimination of the organism should be documented by at least two successive cultures from the nose and throat (or skin) taken 24 hr apart after completion of therapy. Treatment with erythromycin is repeated if the culture result is positive.

Patients with pharyngeal diphtheria are placed in respiratory isolation, and patients with cutaneous diphtheria are placed in contact isolation until the cultures taken after cessation of therapy are negative. Cutaneous wounds are cleaned thoroughly with soap and water. Bed rest is essential during the acute phase of disease, usually for at least 2 wk until the risk of symptomatic cardiac damage has passed, with a return to physical activity guided by the degree of toxicity and cardiac involvement.

COMPLICATIONS.

Respiratory tract obstruction by pseudomembranes may require bronchoscopy or intubation and mechanical ventilation to maintain a patent airway. Recovery from the myocarditis and neuritis is often slow but usually complete. Corticosteroids do not diminish these complications and are not recommended.

PROGNOSIS.

The prognosis for patients with diphtheria depends on the virulence of the organism (subspecies gravis has the highest fatality), age, immunization status, site of infection, and speed of administration of the antitoxin. Mechanical obstruction from laryngeal diphtheria or bull-neck diphtheria and the complications of

myocarditis account for most diphtheria-related deaths. The case-fatality rate of almost 10% for respiratory tract diphtheria has not changed in 50 yr; the rate was 18% in the Swedish outbreak. At recovery, administration of diphtheria toxoid is indicated to complete the primary series or booster doses of immunization, because not all patients develop antibodies after infection.

PREVENTION.

Local public health officials should be notified promptly when a diagnosis of diphtheria is suspected or proved. Investigation is aimed at preventing secondary cases in exposed individuals and at determining the source and carriers to halt spread to unexposed individuals. Reported rates of carriage in household contacts of case patients have been 0-25%. The risk of developing diphtheria after household exposure to a case is approximately 2%, and the risk is 0.3% after similar exposure to a carrier.

Asymptomatic Case Contacts.

All household contacts and those who have had intimate respiratory or habitual physical contact with a patient are closely monitored for illness through the 7-day incubation period. Cultures of the nose, throat, and any cutaneous lesions are performed. Antimicrobial prophylaxis is given, regardless of immunization status, using oral erythromycin (40-50 mg/kg/24 hr for 7-10 days; maximum, 2 g/24 hr) or, if intolerant of erythromycin or if complete compliance is not ensured, using intramuscular benzathine penicillin (600,000 U for those <30 kg or 1,200,000 U for those

30 kg). The efficacy of antimicrobial prophylaxis is presumed but not proved. Diphtheria toxoid vaccine, in age-appropriate form, is given to immunized individuals who have not received a booster dose within 5 yr. Some experts suggest that the longevity of protective antibody is variable enough that a booster should be given to close contacts if 1 year has elapsed since immunization. Children who have not received their fourth dose should be vaccinated. Those who have received fewer than three doses of diphtheria toxoid or with uncertain

immunization status are immunized with age-appropriate preparation on a primary schedule.

Asymptomatic Carriers.

When an asymptomatic carrier is identified, antimicrobial prophylaxis is given for 7-10 days and an age-appropriate preparation of diphtheria toxoid is administered immediately if a booster has not been given within 1 yr. Individuals are placed in respiratory isolation (respiratory tract colonization) or contact isolation (cutaneous colonization only) until at least two subsequent cultures taken 24 hr apart after cessation of therapy are negative. Repeat cultures are performed 2 week or more after completion of therapy for cases and carriers, and if positive, an additional 10-day course of oral erythromycin should be given and follow-up cultures performed. Neither antimicrobial agent eradicates carriage in 100% of individuals. In one report, 21% of carriers had failure of eradication after a single course of therapy. Antitoxin is not recommended for asymptomatic close contacts or carriers, even if inadequately immunized. Transmission of diphtheria in modern hospitals is rare. Only those with an unusual contact with respiratory or oral secretions should be managed as contacts. Investigation of the casual contacts of patients and carriers or persons in the community without known exposure has yielded extremely low carriage rates and is not routinely recommended.

Vaccine.

Universal immunization with diphtheria toxoid throughout life to provide constant protective antitoxin levels and to reduce indigenous C. diphtheriae is the only effective control measure. Although immunization does not preclude subsequent respiratory or cutaneous carriage of toxigenic C. diphtheriae, it decreases local tissue spread, prevents toxic complications, diminishes transmission of the organism, and provides herd immunity when at least 70-80% of a population is immunized. Serum antitoxin concentration of 0.01 IU/mL is conventionally accepted as the minimum protective level, and 0.1 IU/mL provides the certain protective level.

Diphtheria toxoid is prepared by formaldehyde treatment of toxin, standardized for potency, and adsorbed to aluminum salts, which enhance immunogenicity. Two preparations of diphtheria toxoids are formulated according to the limit of flocculation (Lf) content, a measure of the quantity of toxoid. The pediatric preparation (i.e., DTaP, DT, DTP) contains 6.7-12.5 Lf units of diphtheria toxoid per 0.5-mL dose; the adult preparation (i.e., Td) contains no more than 2 Lf units of toxoid per 0.5-mL dose. The higher-potency (i.e., D) formulation of toxoid is used for primary series and booster doses for children through 6 yr of age because of superior immunogenicity and minimal reactogenicity. For individuals 7 yr of age and older, Td is recommended for the primary series and booster doses, because the lower concentration of diphtheria toxoid is adequately immunogenic and because increasing the content of diphtheria toxoid heightens reactogenicity with increasing age.

For children from 6 week to the seventh birthday, five 0.5-mL doses of diphtheria-containing (D) vaccine are given in a primary series, including three doses at approximately 2, 4, and 6 mo of age, with a fourth dose, an integral part of the primary series, at 6-12 mo after the third dose. A booster dose is given at 4-6 yr (unless the fourth primary dose was administered after the fourth birthday). For persons 7 yr of age or older, three 0.5-mL doses of diphtheria-containing (D) vaccine are given in a primary series of two doses 4-8 week apart and a third dose 6-12 mo after the second dose. The only contraindication to tetanus and diphtheria toxoid is a history of neurologic or severe hypersensitivity reaction after a previous dose. For children in whom pertussis immunization is contraindicated, DT or Td is used. Those begun with DTaP, DTP, or DT at before 1 year of age should have a total of five 0.5-mL doses of diphtheria-containing (D) vaccines by 6 yr. For those beginning at or after 1 yr of age, the primary series is three 0.5-mL doses of diphtheria-containing (D) vaccine, with a booster given at 4-6 yr, unless the third dose was given after the fourth birthday.

Further reduction in the number of cases of diphtheria in industrialized countries will require universal booster immunization throughout life. Booster

doses of 0.5 mL of Td should be given every 10 yr starting at 11-12 yr of age. Vaccination with diphtheria toxoid should be used whenever tetanus toxoid is indicated to ensure continuing diphtheria immunity.

There is no known association of DT or Td with increased risk of convulsions. Local side effects alone do not preclude continued use. Persons who experience Arthus-type hypersensitivity reactions or a temperature of 103°F (39.4°C) after a dose of Td (rare in childhood) usually have high serum tetanus antitoxin levels and should not be given Td more frequently than every 10 yr, even if a significant tetanus-prone injury is sustained. DT preparations and Td can be given concurrently with other vaccines. Haemophilus influenzae conjugate vaccines containing diphtheria toxoid (PRP-D) or the variant of diphtheria toxin, CRM197 protein (HbOC), are not substitutes for diphtheria toxoid immunization and do not affect reactogenicity.

Group A Streptococcus

Streptococci are among the most common causes of bacterial infection in infancy and childhood. Group A Streptococcus, the most common bacterial cause of acute pharyngitis, also produces diverse other infections as well as nonsuppurative sequelae such as rheumatic fever and glomerulonephritis. Infection during the first 3 mo of life with group B beta-hemolytic streptococci is common and may present as bacteremia, meningitis, osteomyelitis, or septic arthritis.

ETIOLOGY.

Streptococci are gram-positive cocci that grow in pairs or variable-length chains, classified on the basis of their ability to hemolyze red blood cells: those with hemolysins producing complete hemolysis beta- hemolytic), those producing partial (green) hemolysis (alpha- hemolytic), and those producing no hemolysis (gamma- hemolytic).

Because hemolysis alone does not define pathogenicity, Lancefield further separated the streptococci on the basis of differences in carbohydrate components (C-carbohydrate) within the cell wall; streptococcal groups A through H and K

through V have been identified so. In group A streptococci, the cell wall is composed of three distinct layers. The outer portion contains several antigenic proteins; the most important is M protein. Group A beta-hemolytic streptococci can be divided into more than 80 immunologically distinct types based on differences in the M protein. M antigen appears to be the major virulence factor, having a role in attachment to epithelial cells and resistance to phagocytosis. Lipoteichoic acid, another cell wall constituent, is another virulence factor that promotes colonization by binding to fibronectin on the surface of epithelial cells. The hyaluronic acid capsule resists phagocytosis, further facilitating virulence. Acquired immunity is directed at the M protein.

Streptococci elaborate toxins, enzymes, and hemolysins. More than 20 extracellular antigens released by group A hemolytic streptococci growing in human tissues have been identified. The extracellular products of greatest clinical significance are pyrogenic (formerly erythrogenic) exotoxins (A, B, and C), streptolysin O, streptolysin S, streptokinases, deoxyribonuclease (DNase), hyaluronidase, and proteinase. Pyogenic exotoxins are responsible for the rash of scarlet fever and for shock in toxic shock-like illness. Generally, the elaboration of pyogenic exotoxins depends on bacteriophage infection (lysogeny) of the streptococcus. Streptolysin S is largely cell bound and damages the membranes of neutrophils and platelets. Streptolysin O is produced by most group A and some group G streptococci. It lyses red blood cells and is toxic to neutrophils, platelets, and mammalian heart muscle. Elaboration of streptolysins S and O produces the clear zone of hemolysis permitting classification of the organisms as beta-hemolytic strains. Extracellular digestive enzymes facilitate rapid spreading of streptococci through tissue planes: Streptokinase lyses fibrin, DNase B helps liquefy pus, and hyaluronidase breaks down ground substance. The proteinase, in particular, is associated with tissue destruction of severe invasive streptococcal disease. Antibodies to streptolysin O (ASO), DNase B, hyaluronidase, and streptokinase are useful in the serodiagnosis of group A streptococcal disease. M-

type specific antibodies are detectable 4-8 wk after infection; antibiotic therapy ablates this response.

EPIDEMIOLOGY.

The incidence of suppurative and nonsuppurative sequelae from group A streptococci increased in the late 1980s and 1990s. The reason for this resurgence of serious streptococcal disease is unknown but is suspected to be related to an increased prevalence of streptococcal strains that produce more of the aforementioned virulence factors. Group A streptococci are normal inhabitants of the oropharynx; colonization rates in children vary from 15-20%. The incidence of disease depends on the age of the child, the season of the year, the climate and geographic location, and the degree of contact with infected individuals.

Generally, incidence is lowest among infants, who may be protected by transplacental acquisition of type-specific antibodies and a lack of pharyngeal receptors for streptococcal binding. Streptococcal infection of the skin is most common in children younger than 6 yr; streptococcal pharyngitis is most common between 5 and 15 yr of age. Streptococcal disease, including scarlet fever, is uncommon in children younger than 3 yr, but in families with known streptococcal infection, it may present as nonspecific upper respiratory tract infection, pharyngitis, and otitis media, with or without impetigo. Severe, invasive group A streptococcal infection can occur at any age. The incidence of streptococcal pharyngitis is higher in temperate climates; incidence and severity appear to increase in cold weather, typically during the school year. Impetigo is more prevalent in tropical climates and in warmer weather in temperate climates.

Group A beta-hemolytic streptococci are spread from person to person. Infection may be spread by droplets; pharyngeal carriers are effective disseminators. Infection also may be spread by contact with skin lesions or transmitted by food, milk, and water.

Acquisition of streptococci generally is associated with crowding in the home, school, military installation, or other institution. Disruption of the cutaneous epithelium predisposes to streptococcal pyoderma or impetigo. Concomitant

varicella creates many breaks in the integument; these serve as a portal of entry and may decrease the host response to subsequent streptococcal infection. Acquisition from an infected individual is most common during the acute illness (3-5 days) and decreases during the colonization stage. Colonization (pharyngeal) may precede or follow (2-6 wk) overt infection. Immunity,which is type specific, may be induced either by carriage of the organism or by overt infection. The risk of streptococcal disease diminishes during adult life as immunity develops to the more prevalent serotypes.

PATHOGENESIS.

After inhalation or ingestion, streptococci attach themselves to respiratory epithelial cells by their surface fibrils and cell wall lipoteichoic acid. Fibrils contain antiphagocytic epitopes of type-specific M proteins, which with capsular hyaluronic acid resist phagocytosis. Extracellular digestive enzymes facilitate the spread of infection by interfering with local thrombosis (streptolysins) and pus formation (DNase) and enhancing connective tissue digestion (hyaluronidase, proteinase). Suppurative complications follow local inflammation (peritonsillar abscess, retropharyngeal abscess), direct extension (otitis media, sinusitis), lymphangitic spread (lymphadenitis), or bacteremia (sepsis, osteomyelitis, pneumonia).

Scarlet fever-producing streptococci lead to clinical manifestations that are similar to those produced by nonpyrogenic exotoxin-containing strains with the addition of a scarlatiniform rash. Serologically distinct pyrogenic exotoxins (A-C) produce the rash in nonimmune hosts. Rash production is dependent in part on a host hypersensitivity reaction and is decreased by host synthesis of specific antitoxins. These toxins also exhibit pyrogenicity and cytotoxicity, enhance the effects of endotoxin, and have been associated with toxic shock-like illness. Streptococcal pyrogenic exotoxin A has partial amino acid homology with staphylococcal enterotoxin B, which is associated with staphylococcal toxic shock syndrome (TSS).

CLINICAL MANIFESTATIONS.

The most common infections caused by group A beta-hemolytic streptococci involve the respiratory tract, skin, soft tissues, and blood.

Skin Infections.

The most common form of skin infection due to group A beta-hemolytic streptococci is superficial pyoderma (impetigo). Colonization of unbroken skin precedes pyoderma by about 10 days. Skin lesions such as impetigo, ecthyma, and cellulitis develop after intradermal inoculation by insect bites, scabies, or minor trauma. Skin colonization or pyoderma may predispose patients to later pharyngeal colonization with the same strain.

Deeper soft tissue infections may occur. Erysipelas is an acute, well-demarcated infection of the skin with lymphangitis involving the face (associated with pharyngitis) and extremities (wounds). The skin is erythematous and indurated; the advancing margins of the lesions have raised, firm borders. The skin lesion usually is associated with fever, vomiting, and irritability.

Streptococcal cellulitis is a painful, erythematous, indurated infection of the skin and subcutaneous tissues that commonly follows some injury to the skin. Certain streptococcal strains (i.e., those producing proteinase) may cause a more severe necrotizing fasciitis or myositis that results in a rapidly spreading tissue-destructive process that causes necrosis of involved soft tissues including skin, fat, fascia, and muscle. Lymphangitis and regional lymphadenitis are common.

In some cases, streptococci break through the lymphatic barrier, and subcutaneous abscesses, bacteremia, and metastatic foci of infection are observed. Bacteremia and death have been associated with streptococcal cellulitis, and progression may be so rapid that there is no response to treatment with penicillin.

Bacteremia and Sepsis.

Bacteremia may follow a localized cutaneous (wounds, cellulitis, varicella lesions, hemangioma, abscess) or respiratory (pharyngitis, otitis media, sinusitis, pneumonia) infection in previously healthy or immunocompromised (malnutrition, malignancy) patients. It has also occurred in children with no obvious focus of infection . Sepsis may be rapidly progressive, leading to a toxic shock-like illness

with hypotension, fever, leukocytosis, disseminated intravascular coagulation, and peripheral gangrene. Metastatic foci may result in meningitis, brain abscess, osteomyelitis, septic arthritis, pneumonia, and peritonitis. Rarely, endocarditis may complicate group A streptococcal bacteremia. The prognosis is poorest for patients with an underlying disease such as malignancy.

Scarlet Fever.

This disease is a result of infection by streptococci that elaborate one of three pyrogenic (erythrogenic) exotoxins. The incubation period ranges from 1-7 days, with an average of 3 days. The onset is acute and is characterized by fever, vomiting, headache, toxicity, pharyngitis, and chills. Abdominal pain may be present; when this is associated with vomiting before the appearance of the rash, an abdominal surgical condition may be suggested. Within 12-48 hr, the typical rash appears.

Generally, temperature increases abruptly, may peak at 39.6-40°C (103-104°F) on the 2nd day, and gradually returns to normal within 5-7 days in untreated patients; it is usually normal within 12-24 hr after initiation of penicillin therapy. The tonsils are hyperemic and edematous and may be covered with a gray-white exudate. The pharynx is inflamed and covered by a membrane in severe cases. The tongue may be edematous and reddened. During the early days of illness, the dorsum of the tongue has a white coat through which the red and edematous papillae project (i.e., white strawberry tongue). After several days, the white coat desquamates; the red tongue studded with prominent papillae persists (i.e., red strawberry tongue, raspberry tongue). The palate and uvula may be edematous, reddened, and covered with petechiae.

The exanthem is red, is punctate or finely papular, and blanches on pressure. In some individuals, it may be palpated more readily than it is seen, having the texture of gooseflesh or coarse sandpaper. The rash appears initially in the axillas, groin, and neck but within 24 hr becomes generalized. Punctate lesions generally are not present on the face. The forehead and cheeks appear flushed, and the area around the mouth is pale (i.e., circumoral pallor). The rash is most intense in the

axillas and groin and at pressure sites. Petechiae may occur owing to capillary fragility. Areas of hyperpigmentation that do not blanch with pressure may appear in the deep creases, particularly in the antecubital fossae (i.e., Pastia's lines). In severe disease, small vesicular lesions (miliarysudamina) may appear over the abdomen, hands, and feet.

Desquamation begins on the face in fine flakes toward the end of the 1st wk and proceeds over the trunk and finally to the hands and feet. The duration and extent of desquamation vary with the intensity of the rash; it may continue for as long as 6 wk.

Scarlet fever may follow infection of wounds (i.e., surgical scarlet fever), burns, or streptococcal skin infection. Clinical manifestations including the strawberry tongue are similar to those just described, but the tonsils and posterior pharynx generally are not involved. A similar picture may be observed with certain strains of staphylococci that produce an exfoliative toxin, although a strawberry tongue is usually absent.

Scarlet fever must be differentiated from other exanthematous diseases, including measles (characterized by its prodrome of conjunctivitis, photophobia, dry cough, and Koplik spots), rubella (disease is mild, postauricular lymphadenopathy usually is present, and throat culture is negative), and other viral exanthems. Patients with infectious mononucleosis have pharyngitis, rash, lymphadenopathy, and splenomegaly as well as atypical lymphocytes. The exanthems produced by several enteroviruses can be confused with scarlet fever, but differentiation can be established by the course of the disease, the associated symptoms, and the results of culture. Roseola usually occurs in younger children and is characterized by the cessation of fever with the onset of rash and the transient nature of the exanthem. Kawasaki disease, drug eruption, and TSS must also be considered.

Scarlet fever may be differentiated from Kawasaki's disease by an older age at onset, absence of conjunctival involvement, and recovery of group A streptococci. Arcanobacterium haemolyticum (formerly Corynebacterium

haemolyticum) also produces tonsillitis, pharyngitis (without a strawberry tongue), and a scarlatiniform rash in adolescents and young adults. Severe sunburn can also be confused with scarlet fever.

Streptococcal Toxic Shock-Like Syndrome.

Streptococcal toxic shock-like syndrome is associated with streptococcal strains that produce the pyrogenic exotoxins and is characterized by hypotension accompanied by multiorgan-system dysfunction (Table 184-2) . It is often difficult to distinguish from staphylococcal TSS until results of cultures are obtained. A focus of group A streptococcal infection is usually present (e.g., bacteremia, pneumonia, cellulitis). Pharyngitis is commonly absent, and results of throat cultures may be negative despite isolation of the organism from other sites.

DIAGNOSIS.

Colonization of the throat with group A streptococci may occur in 10-20% of normal school-aged children. These carriers are not actively infected and are not at risk of developing rheumatic fever. Although 30% of children with sore throat have a positive throat culture result for group A streptococci, only half of these have a positive antibody response indicative of active infection rather than colonization. Streptococcal pharyngitis is suggested by age greater than 5 yr, high fever, exudates, tender anterior cervical lymphadenopathy, scarlatiniform rash, and a history of exposure. However, many children with active infection may have milder symptoms. Clinical judgment does not predict which children may have streptococcal infection and which must undergo throat culture or antigen detection.

Throat culture is the most useful laboratory aid in reaching a diagnosis in patients with acute tonsillitis or pharyngitis. Vigorous swabbing of the tonsils and posterior pharynx is essential to get an adequate sample for testing. Selective media culture often gives a higher yield than sheep blood agar plates. beta-Hemolytic colonies can be confirmed as streptococci by the absence of bubbling in the presence of 3% hydrogen peroxide (a negative catalase test) and confirmed as group A streptococci by inhibition by a bacitracin disk or latex agglutination. Because hemolytic streptococci are common inhabitants of the pharynx in well

children, isolation of group A Streptococcus from the pharynx of a child with pharyngeal infection does not necessarily indicate that the disease is caused by this organism. When streptococci are isolated from children who have moderate or severe exudative pharyngitis and who have petechiae on the palate and cervical adenitis, the diagnosis is more secure. Current rapid antigen detection tests are not sufficiently sensitive to be used without a backup culture; however, a positive result is usually reliable. Treatment is, however, recommended for all children with pharyngitis and a positive result of throat culture or rapid antigen test for group A streptococci, even though in some cases the streptococci represent colonization.

The white blood cell count may or may not be elevated in patients with streptococcal disease. Because leukocytosis may occur in many bacterial and viral diseases, this finding is nonspecific. Similarly, elevations in the erythrocyte sedimentation rate (ESR) and C-reactive protein (CPR) do not help to establish a specific diagnosis.

The immunologic response of the host after exposure to streptococcal antigen can be assessed by measuring ASO and anti-DNase B (ADB) titers. An increase in ASO titer to greater than 166 Todd units occurs in more than 80% of untreated children with streptococcal pharyngitis within the first 3-6 wk after infection. This response may be modified or abolished by early and effective antibiotic therapy. ASO titers may be very high in patients with rheumatic fever; in contrast, they are weakly positive or not elevated at all in patients with streptococcal pyoderma; responses in patients with glomerulonephritis are variable. Group A beta-hemolytic streptococci also may be recovered from the pharynx of asymptomatic individuals who develop an antibody response to this organism, indicating that subclinical infection has occured.

Individuals with impetigo may react more strongly to stimulation by other streptococcal extracellular products. Anti-DNase B provides the best serologic test for streptococcal pyoderma; levels begin to rise 6-8 wk after infection. Many patients with streptococcal pharyngitis also develop elevated titers to this enzyme. Patients with pyoderma and pharyngitis also may develop antibody responses to

hyaluronidase, but antihyaluronidase (AH) titers are elevated with less regularity than are ASO titers. When it is important to document a recent streptococcal infection, titers to multiple streptococcal products should be considered (e.g., ASO and ADB).

Differential Diagnosis.

Acute pharyngitis that is indistinguishable clinically from that caused by group A beta-hemolytic streptococci may be caused by many viruses, including adenovirus and Epstein-Barr virus (infectious mononucleosis). A viral cause may be suggested by failure to isolate streptococci and can be identified specifically by viral culture and serologic studies. Infectious mononucleosis may be suggested by the clinical manifestations, the presence of atypical lymphocytes in the peripheral blood, and a rise in heterophil and Epstein-Barr viral antibody titers. Acute pharyngitis similar to that caused by beta-hemolytic streptococci may rarely occur in patients with diphtheria, tularemia, and mycoplasmal infections. These diseases can be differentiated by appropriate cultures and serologic tests.

Streptococcal pyoderma must be differentiated from staphylococcal skin disease. These bacterial species often coexist. The lesions produced are clinically indistinguishable; distinction is made only by culture.

Streptococcal septicemia, meningitis, septic arthritis, and pneumonia present signs and symptoms similar to those produced by other bacterial organisms. The offending pathogen can be established only by culture.

COMPLICATIONS.

Complications generally reflect extension of streptococcal infection from the nasopharynx. This may result in sinusitis, otitis media, mastoiditis, cervical adenitis, retropharyngeal or parapharyngeal abscess, or bronchopneumonia. Hematogenous dissemination of streptococci may cause meningitis, osteomyelitis, or septic arthritis. Nonsuppurative late complications include rheumatic fever and glomerulonephritis.

TREATMENT.

The goals of therapy are to decrease symptoms and prevent septic, suppurative, and nonsuppurative complications. Penicillin is the drug of choice for the treatment of streptococcal infections. All strains of group A beta-hemolytic streptococci isolated to date have been sensitive to concentrations of penicillin (and many cephalosporins) achievable in vivo. Variable levels of resistance have been reported to erythromycin, depending on the frequency of that antibiotic's use, and rarely to clindamycin. Failure to respond to penicillin treatment owing to slowly growing organisms at the site of deep group A streptococcal infections (e.g., necrotizing fasciitis) has been called the "eagle effect."

Blood and tissue levels of penicillin sufficient to kill streptococci should be maintained for at least 10 days. Children with streptococcal pharyngitis should be treated with penicillin (250-500 mg/dose bid-tid) for 10 days. Penicillin G or penicillin V may be used; the latter is preferable because satisfactory blood levels are achieved even when the stomach is not empty. A single intramuscular injection of a long-acting benzathine penicillin G (600,000 U for children <60 lb and 1,200,000 U for children >60 lb) may be more effective for treatment or prevention of relapse and is indicated for all noncompliant patients or those having nausea, vomiting, or diarrhea.

Erythromycin (40 mg/kg/24 hr), clindamycin (30 mg/kg/24 hr), or the first-generation cephalosporins may be used for treating streptococcal pharyngitis in patients who are allergic to penicillin. Generally, relapse rates are lower with regimens other than penicillin. Tetracyclines and sulfonamides should not be used for treatment, although sulfonamides may be used for prophylaxis of rheumatic fever. Successful treatment with shorter courses (5 days) of azithromycin or cefpodoxime has been reported.

Treatment failure, defined as persistence of streptococci after a complete course of penicillin, occurs in 5-20% of children and is more common with oral than with intramuscular therapy. It may be due to poor compliance, reinfection, the presence of beta-lactamase-producing oral flora, tolerant streptococci, or the presence of a carrier state. Persistent carriage of streptococci predisposes a small

number of patients to symptomatic relapse. Repeating the throat culture after a course of penicillin therapy is indicated only in high-risk situations, such as in patients with a history of previous rheumatic fever or apparent frequent streptococcal infections. If the throat culture result is again positive for group A streptococci, some clinicians recommend a second course of treatment. Persistence after a second course of antibiotics probably indicates a carrier state, which poses a low risk for development of rheumatic fever and does not require further therapy.

Patients with severe scarlet fever, streptococcal bacteremia, pneumonia, meningitis, deep soft tissue infections, erysipelas, streptococcal toxic shock-like syndrome, or complications of streptococcal pharyngitis should be treated parenterally with penicillin, preferably intravenously. The dose and duration of therapy must be tailored to the nature of the disease process, with daily doses as high as 400,000 U/kg/24 hr required in the most severe infections. One study suggests that deep or necrotizing infections may require the addition of a second antibiotic (e.g., clindamycin) to ensure complete bacterial killing. TSS may require additional therapies (Chapter 182 .2) that may include aggressive fluid management, intravenous immunoglobulin, or steroids.

PREVENTION.

Administration of penicillin prevents most cases of streptococcal disease if the drug is provided before the onset of symptoms. Except for rheumatic fever, indications for prophylaxis are not clear. Oral penicillin G or V (400,000 U/dose) may be provided four times each day for 10 days. Alternatively, 600,000 U of benzathine penicillin in combination with 600,000 U of aqueous procaine penicillin may be given as a single intramuscular injection. This approach should be used for institutional epidemics. Children exposed to an individual case at school may be observed carefully.

Treatment of carriers of group A beta-hemolytic streptococci is controversial. It has been suggested that treatment of the carrier precludes the development of type-specific immunity, thereby leaving the individual susceptible to reinfection later in life. It is probably unnecessary to re-treat asymptomatic convalescent

patients with persistently positive throat cultures for group A streptococci, because they are generally carriers who do not have persistent or recurrent streptococcal infections. Children thought to have recurrent streptococcal infections may be carriers who have frequent viral respiratory infections masquerading as streptococcal infections. Parental anxiety may be high after several such episodes. Treatment with a nonpenicillin antibiotic (e.g., cephalosporin, erythromycin, clindamycin) may be useful in eradicating the carrier state but should be reserved for the rare problem case.

No group A streptococcal vaccines are available for clinical use.

PROGNOSIS.

The prognosis for adequately treated streptococcal infections is excellent; most suppurative complications are prevented or readily treated. When therapy is provided promptly, nonsuppurative complications are prevented and complete recovery is the rule. In rare instances, particularly in neonates or in children whose response to infection is compromised, fulminant pneumonia, septicemia, and death may occur despite usually adequate therapy.

Adenoviruses

Adenoviruses cause 5-8% of acute respiratory disease in infants, plus a wide array of other syndromes, including pharyngoconjunctival fever, follicular conjunctivitis, epidemic keratoconjunctivitis, myocarditis, hemorrhagic cystitis, acute diarrhea, intussusception, and encephalomyelitis. Only a third of the 49 serotypes have been associated with disease. Fatal disease is rare, but is associated with infection by certain serotypes (particularly type 7) and infection in severely immunocompromised hosts.

ETIOLOGY.

The Adenoviridae are DNA viruses of intermediate size, which are classified into subgenera A to F. The virion has an icosahedral coat (capsid) made up of 252 subunits (capsomers) of which 240 are "hexons" and 12 are "pentons." The hexons have a cross reacting antigen common to all mammalian adenoviruses. The penton confers type specificity, and antibody to it is protective. It is cytotoxic in tissue

culture, and toxic properties have been ascribed to it in vivo as well. Adenoviruses can also be classified by their characteristic DNA "fingerprints" on gels after being digested with restriction endonucleases, and this classification generally conforms to their antigenic types.

All adenovirus types, except types 40 and 41, grow in primary human embryonic kidney cells, and most grow in HEp-2 or HeLa cells, producing a typical destructive cytopathic effect. Types 40 and 41 (and other serotypes as well) grow in 293 cells, a line of human embryonic kidney cells into which certain "early" adenovirus genes have been introduced.

Many adenovirus types, but particularly the common childhood types (1, 2, and 5), are shed for prolonged periods from both the respiratory and gastrointestinal tracts. These types also establish low-level and chronic infection of the tonsils and adenoids.

EPIDEMIOLOGY.

Adenoviral infections are distributed worldwide. They occur year-round but are most prevalent in spring or early summer and again in midwinter in temperate climates. Certain types tend to occur in epidemics, notably types 4 and 7 in outbreaks of febrile respiratory disease, types 3, 7, and 21 in severe pneumonia; type 3 in pharyngoconjunctival fever; type 11 in hemorrhagic cystitis; and types 8, 19, and 37 in epidemic keratoconjunctivitis. For unexplained reasons, adenovirus types 3 and 7 cause severe epidemics of pneumonia in the children of northern China and Korea, with mortality rates of 5-15%.

More than 60% of school-age children have antibodies to the common respiratory types. Almost all adults have serum antibody to types 1-7. Infections with types 1 and 2 tend to occur during the 2nd yr of life, and types 3 and 5 occur a little later. Spread occurs by the respiratory and fecal-oral routes, although it is not clear whether spread is by large- or small-particle aerosol. Hospital outbreaks of respiratory disease and keratoconjunctivitis have been described.

PATHOGENESIS.

Adenoviruses are among the few "respiratory" viruses that grow well in the epithelium of the small intestine. Although mucosal surfaces are the primary target early in infection and typically the site of the most common pathology, viremia probably occurs frequently, with accompanying fever.

Adenoviral pneumonia produces characteristic microscopic changes, with dense lymphocytic infiltrates, destruction of the bronchial and bronchiolar epithelium, focal necrosis of mucous glands, hyaline membrane formation, and several types of nuclear inclusion bodies.

CLINICAL MANIFESTATIONS.

Adenoviruses cause a wide array of clinical syndromes.

Acute Respiratory Disease.

This is the most common manifestation of adenovirus infection in children and adults. Acute adenovirus respiratory tract infections in infants and children are not clinically distinctive and are usually caused by types 1, 2, 3, 5, or 6. Primary infections in infants are frequently associated with fever and respiratory symptoms and are complicated by otitis media in more than half of the patients. Adenovirus respiratory infections are associated with a significant incidence of diarrhea.

Pharyngitis due to adenovirus typically has symptoms of coryza, sore throat, and fever. Adenoviruses can be identified in 15-20% of children with isolated pharyngitis, mostly in preschoolers and infants.

Pneumonia is uncommon, but 7-9% of hospitalized children with acute pneumonia have adenovirus infection. Any of the "respiratory" types can cause pneumonia, but severe infections are most likely due to type 3, 7, or 21. Such infections have a mortality as high as 10%, and survivors may have residual airway damage, manifested by bronchiectasis, bronchiolitis obliterans, or, rarely, pulmonary fibrosis. Neonatal adenovirus pneumonia occurs rarely, but may be severe or fatal.

A pertussis-like syndrome has been described in association with adenovirus infections. In these cases, adenoviruses frequently accompany Bordetella pertussis as coinfecting agents, but occasionally they may also be causative on their own.

Pharyngoconjunctival fever is a clinically distinct syndrome that occurs particularly in association with type 3 adenovirus. Features include a high temperature that lasts 4-5 days, pharyngitis, conjunctivitis, preauricular and cervical lymphadenopathy, and rhinitis. Nonpurulent conjunctivitis occurs in 75% of patients and is manifested by inflammation of both the bulbar and palpebral conjunctivae of one or both eyes; it often persists after the fever and other symptoms have resolved. Headache, malaise, and weakness are common, and there is considerable lethargy after the acute stage.

Conjunctivitis and Keratoconjunctivitis.

Adenovirus is one of the most common causes of follicular conjunctivitis and keratoconjunctivitis. The former is a relatively mild illness. The latter, which may occur, in epidemics, is associated with infection by adenovirus types 8, 19, and 37. Keratitis begins as the conjunctivitis wanes, and may cause corneal opacities that last several years.

Myocarditis.

In several series of acute myocarditis or idiopathic cardiomyopathy, investigated by the application of polymerase chain reaction (PCR) in the search for microbial agents, adenovirus has been found as commonly as, or more commonly than, nonpolio enteroviruses. It is widely assumed that adenovirus has an important etiologic role in this disease. It has also been associated with heart transplant rejection and with some cases of endocardial fibroelastosis.

Gastrointestinal Infections.

Adenoviruses can be found in the stools of 5-9% of children with acute diarrhea. About one half of these are the "enteric" types, 40 or 41. It is also clear that enteric infection with any adenovirus serotype is often asymptomatic, so the causative role in these episodes is frequently uncertain.

The pathogenesis of intussusception is thought by many to include enlarged lymph nodes as an initiating factor. Adenoviruses have been recovered from mesenteric lymph nodes or appendices at surgery and also from surface cultures in

a higher percentage of children with intussusception than of controls. Adenoviruses have also been found in the appendices of children with appendicitis.

Hemorrhagic Cystitis.

This syndrome has a sudden onset of bacteriologically sterile hematuria, dysuria, frequency, and urgency lasting 1-2 wk. Infection with adenovirus types 11 and 21 has been found in some affected children and young adults.

Reye's Syndrome and Reye's-like Syndromes.

Typical Reye's syndrome has followed confirmed adenovirus infection of several serotypes, particularly in very young children. In addition, several cases of a Reye's-like syndrome have been reported, all of which are caused by infection with adenovirus type 7. The latter disease, which is frequently fatal, is characterized by severe bronchopneumonia, hepatitis, seizures, and disseminated intravascular coagulation. Circulating adenovirus penton antigen has been found in several patients and has been implicated in the pathogenesis.

Infections in Immunocompromised Hosts.

Adenoviruses are important pathogens in immunocompromised hosts with either B- or T-cell deficiencies. In B-cell-deficient (hypogammaglobulinemic) patients, a chronic meningoencephalitis similar to that caused by enteroviruses has been described. In T-cell-deficient patients, regardless of whether this deficiency is congenital, acquired, or iatrogenic, fulminant hepatitis and pneumonia, frequently with a fatal outcome, have been described. There is also a close association between adenovirus infection and both hemorrhagic cystitis and tubulointerstitial nephritis in immunosuppressed children.

DIAGNOSIS.

The laboratory diagnosis of adenovirus infection in children may be made by suggestive pathologic changes in biopsy material, detection of virus by culture or PCR, demonstration of a rise in antibody titers, or a combination of virus detection and serologic testing. PCR has proven a very useful method in the detection of adenovirus in biopsy tissues. If virus is found in a "privileged" site, such as blood, urine, or cerebrospinal fluid, or in a biopsy of the lung or liver, the implication of

infection with disease and organ damage is strong. Likewise, detection of certain adenovirus types in respiratory secretions (type 7 or 21) probably indicates their etiologic involvement. The presence of untyped virus or the common childhood types (1, 2, and 5) in respiratory secretions or stool does not, however, indicate clinical adenovirus infection because these viruses may be excreted chronically and asymptomatically. In these instances, discovery of a coincident rise in antibody by complement fixation (group specific) or neutralization or hemagglutination inhibition (type specific) is helpful in assigning a specific adenovirus type to disease. Adenovirus infection may also be considered etiologic if a rise in antibody is found between sera drawn in the acute stage and in convalescence from a patient with an appropriate illness. Adenovirus infection often results in a high erythrocyte sedimentation rate and white blood cell count.

TREATMENT.

There are at present no recognized antiviral agents that are effective in treating adenovirus infections. Ribavirin can inhibit viral growth of some strains in vitro, but evidence of its clinical efficacy is lacking.

PREVENTION.

Vaccines that contain either killed or live virus have been developed to prevent type 4 and 7 infections in military recruits. These vaccines have not, however, been used in children.

Infectious mononucleosis (Filatov's disease) is an acute feverish viral disease, being spread by air-droplet route. It is characterized by polyadenitis (especially cervical one), acute membranous tonsillitis, enlarged liver and spleen, leukocytosis, limphocytosis, presence of atypical lymphocytes. The pathogen of the disease is Epstein-Barr virus (EBV), which contains DNA. EBV is isolated in other diseases: such as Burkitt's lymphoma and nasopharyngeal carcinoma.

The sources of infection are infected individuals and virus carriers. Morbidity has sporadic nature. Contagiousness of the patients is not high. EBV has tropism to lymphoid and reticular tissues. That is why lymph nodes, liver, spleen, kidneys, bone marrow are affected. At present infectious mononucleosis is

considered to be a disease of immune system. The virus can persist in B-cells. It does not destroy them, but it stimulates their proliferation. Fixation of the virus on the B-cell membranes causes activation of circulating antibodies to a superficial antigen. The main way the destroying of EBV infected cells is producing specific cytotoxic T-killer cells.

When destroying B-cells, the substances, which cause fever, and have a toxic effect on liver, are produced. Viral antigens cause common allergic reaction. Activation of T-suppressors, depressing the B-cell reproduction and differentiation is typical.

In infectious mononucleosis the incubative period is 6–18 days (sometimes 30–40 days). The disease has an acute onset. The patients complain of fever (38°–40°C), weakness, headache, sore throat, anorexia, myalgia, joint pain. Fever, tonsillitis, enlarged lymph nodes, liver and spleen, difficulty of nasal breathing are typical clinical manifestations of the disease. They appear during the first 3–5 days after the onset of the disease. The patient's appearance is typical: edematous eyelids, congested nose, hoarse breathing, visibl enlarged lymph nodes. Fever may be lengthy, remittent, or irregular, sometimes it may be undulating.

Duration of the disease may be from 4–5 days till 2–4 weeks and over. Lymphadenopathy is the most permanent symptom. Cervical lymph nodes get enlarged on the onset. They become visible if the head is turned aside. Their size is to 1–3 cm. They are elastic, moderately painful and movable on touch. The skin over the lymph nodes does not change. Edema of the adipose tissue may be present at the same time. Clinical manifestations of tonsillitis are also present in lymphadenopathy. Catarrhal, follicular, lacunar, ulceronecrotic tonsillitis may be observed. White or cream-colored patch appears. Sometimes the patch may be fibrinous, like a diphtheritic one. The permanent symptoms of mononucleosis are enlarged liver and spleen.

Enlarged spleen is observed starting from the first days of the disease. Normalization of spleen size occurs the on 2nd–3rd week after the onset of the disease. The liver becomes enlarged on the 4th–6th day after the onset of the

disease. Sometimes moderate jaundice and liver dysfunction may be present. Some patients may have spotted, spotted-papular, urticaria, hemorrhagic rash. The rash may appear at different time after the onset of the disease. It remains for 1–3 days and disappears without a trace.

Hematologic disorders are typical for infectious mononucleosis. Considerable leukocytosis (10–25x10^9 per L) with lymphocytes and monocytosis are present. ESR is 15–30 mm/h. Presence of atypical mononuclear cells (lymphocytes, which similar monocytes) is a typical symptom of the disease. They are mature, atypical, mononuclear cells. Their protoplasm is wide in form and basophilic. Their quantity may reach 20 % and over. Atypical mononuclear cells appear on the 2nd–3rd day after the onset of the disease and they may be observed in blood for 3–4 weeks, sometimes — up to 2 months and longer.

In babies infectious mononucleosis has some clinical peculiarities: considerable coryza, edema of the eyelids and the face. Often membranous tonsillitis, neutrophilic leukocytosis may be present.

The main symptoms of clinical diagnosis of infectious mononucleosis are fever, acute tonsillitis, polyadenitis, hepatosplenomegaly, lymphocytosis, monocytosis, atypical mononuclear cells. Serologic test may be used in clearing up the doubtful cases. There are different modifications of hemagglutination test (the Paul — Bunnel test in modification of Davidson). Diagnostic titer is over 1:32 and higher.

Biologically the active virus can be isolated from saliva, peripheral blood or lymphoid tissue, by means of its ability to damage cultured human lymphocytes, usually from umbilical cord blood. Occasionally lymphoid cell lines can be grown directly from blood or lymph nodes. This assay is time consuming (6 to 8 weeks) and requires specialized tissue-culture facilities that are not generally available.
The most specific method of demonstrating EBV in pathologic material is polymerase chain reaction (PCR). The PCR is highly sensitive, it can detect approximately 100 genomes or less, therefore in most cases of acute infectious

mononucleosis Epstein — Barr virus DNA can be detected in the blood by PCR. The PCR can be used as a rapid assay for salivary excretion of EBV.

The is no specific **treatment** of infectious. Antibiotics should be prescribed if fever maintains longer than 6–7 days; symptoms of tonsillitis are very severe and accompanied by considerable lymphoadenitis. In severe cases glucocorticoids may be prescribed. Detoxication, desensitization, symptomatic therapy should be administered.

VI. Planning of the lesson

Table 2

	The main stages of a lesson, their contents	**The methods of control**	**Methodical equipment**	**Time in % from total time of a lesson**
1	Organization stage			**10-20 %**
2	Purposes of a lesson		Relevance of the Theme. Tutorial goals of a lesson	1-3min
3	Basic knowledge and skills control	Control questions	The list of control questions	10-15 min
4	Etiology, epidemiology, classification of disease	Test-control (first grade)	Tests of the first level	
5	Manifestations in connection with	Methods of the second grade: Individual	Questions Clinical cases (tests	

	pathogenesis	questioning in oral and writing form. Standard task's solution. Second grade test-control	of the second grade) Theory tasks for writing answers. Second grade tests	
6	Treatment	Methods of the third grade: 1. Solution of complicated tasks. 2.Third grade test-control	Third grade questions and tasks Third grade tests	
7	Prevention			
8	Professional skills formation		Patients with studied disease and similar diseases, patient's histories, medical cases.	**70-80 %**
9	To master the skills of: a) Diagnosis b)Laboratory confirmation c) Treatment		Laboratory data of the patients, antibacterial drugs and drugs for supportive care	

10	Independent work with patients		Patients, patient's histories, medical cases.	
11	Differential diagnosis		Drawing schemes of pathogenesis and clinical course of disease; making up a differential diagnosis table and list of prescriptions for intensive care.	
12	Teacher's control, recommendations, the task for the next lesson			**10 %** 10-15 min

Students' self-study program.

1. Objectives for students' self-studies.

You should prepare for the practical class using the available textbook and lectures. Special attention should be paid to the following:

Differential diagnosis infections with tonsillitis

Table 3

Signs	Scarlet fever	Diphtheria	Infectious Mononucleosis
Initial symptoms	Fever, malaise, sore throat, vomiting	Fever, fatigue, headache, decrease appetite, sometimes vomiting	Fever, sore throat, lymph nodes enlargement, labored nasal breathing
Tonsilitis	Permanent symptom (catarrhal, follicular, lacunar, necrotic)	Usually (islet, more seldom scarious, desseminated)	Develops in most cases (catarrhal, follicular, lacunar, necrotic)
Rashe	Typical symptom (small point-like, bright red colour, mainly on bending surfaces of limbs, down the abdomen, lumbar region, face, lateral surfaces of the trunk, pale nose-labial triangle)	Not typical	Macular-papular rash can develop, especially after usage of amino-penicillin antibiotics (ampicillin, amoxicillin). Sometimes the rash has hemorrhagic elements.
Lymphadenopathy	Enlargement of regional lymph nodes (submandibular),	Enlargement of regional lymph nodes	General lymphadenopathy is typical

	sometimes purulent lymphadenitis as complication		
Tongue and orophryngeal mucous membranes	Restricted hyperemia of oropharyngeal mucosa. In some patients on the background of hyperemia enanthema appears, which looks like pointed hemorrhages. On the first day of the disease tongue has white covering, since the 2nd till the 4th—5th day it gradually clears. Its clean surface becomes bright purple, enlarged papillae appear ("strawberry tongue")	Oral mucosa is hyperemic with cyanotic tint; tonsils enlarged due to edema, tonsilar surfase is covered by whitish-yellowish or grey pseudomembranes with even surface tightly connected to underlying tissue	Widespread hyperemia of oropharyngeal mucosa lisseen, palatine tonsils are enlarged due to edema and infiltration
Enlargement of liver and spleen	Not typical	Not typical	By the end of the first week of the disease the spleen and liver are enlarged, reaching their maximum by the 7th—10thday from disease onset.
Abdominal pain	Sometimes is odserved	In toxic form	Sometimes is odserved as

	as a symptom of general intoxication		a symptom of mesadenitis and hepatosplenomegaly
Catarrhal symptoms	Not typical	Not typical	Sometimes at the onset of the disease
Joint involvement	Possible as a complication after disease.	Not typical	Not typical
Intoxication	Intoxication presents with fever, headache, malaise, vomiting during prodromal period and acute phase of the disease.	Intoxication increase with duration of disease	Intoxication presents in most cases but sometimes not so prominent
Other symptoms	Involvement of cardiovascular system which are caused by imbalance of vegetative nervous system but not by direct heart damage	Myocarditis, nephritis, polyneuropathies, toxic shock	Voicenasality, adenoiditis, hepatits, encephalitis and other neurological disorders
Laboratory criteria	Leucocytosis, shift to the left, neutrophilosis, increased ESR, in pharyngeal, nasal	Leucocytosis, shift to the left, high ESR, bacterioscopia and bacteriological	Leukocytosis (more seldom leukopenia), lymphocytosis, monocytosis and atypical

	swabs - streptococci	investigations of nasal and pharyngeal secretions, ELISA, PCR, Reaction of direct hemagglutination of blood	mononuclears (virocytes) in the amount of 10 – 60 %, determination of EBV VCA IgM, EA IgG, EBV DNA in blood and salivary PCR

Tests for self-control

1.Causative agent of diphtheria belongs to:

A. Listeria

B. Corynebacteria

C. Neisseria

D. Protozoa

E. Viruses

2. Main mechanism of diphtheria transmission is:

A. Airborne

B. Fecal-oral

C. Transplacental

D. Transmissible

E. Contact

3. Main pathogenetic mechanism at tonsillar diphtheria:

A. Bacteremia

B. Toxinemia

C. Autoimmune mechanism

D. Necrotic processes

E. Hypoxia

4. At the place of diphtheria penetration the following process develops:

A. Serous inflammation

B. Purulent inflammation

C. Ulcerous necrotic process

D. Fibrinous inflammation

E. All the answers are correct

5. At localized croup the covers are situated on:

A. Larynx

B. Trachea

C. Bronchi

D. Nasopharynx

E. Oropharynx

6. For severe form of tonsillar diphtheria it is typical:

A. Spread of inflammatory process within oropharynx

B. Edema of palate tonsils and paratonsillar tissues

C. Edema of neck subcutaneous tissue

D. Prominent general intoxication

E. All the answers are correct

7. For diphtheria laryngotracheitis it is typical:

A. Gradual onset

B. Cyclic course

C. Moderate intoxication

D. Aphonia

E. All the answers are correct

8. Methods of laboratory diagnosis of diphtheria:

A. Direct bacterioscopy of smears

B. Bacteriologic examination

C. Toxin determination n blood

D. Reaction of direct hemagglutination

E. All the answers are correct

9. The remedy for diphtheria specific therapy is:

A. Antibiotic

B. Diphtherial anatoxin

C. Antidiphtherial serum

D. Bacteriophage

E. All the answers are correct

10. The remedy of diphtheria specific prophylaxis is:

A. Antibiotic

B. Diphtherial anatoxin

C. Antidiphtherial serum

D. Bacteriophage

E. All the answers are correct

Testanswers

1-B; 2-A; 3-B; 4-D; 5-A; 6-E; 7-E; 8-E; 9-C; 10-B.

Self-study

Signs	Scarlet fever	Diphtheria	Infectious Mononucleosis
1	2	3	4
Initial symptoms			
Tonsilitis			
Rashe			
Lymphadenopathy			
Tongue and orophryngeal mucous membranes			
Enlargement of liver and spleen			
Abdominal pain			
Catarrhal symptoms			
Joint involvement			
Intoxication			
Other symptoms			
Laboratory criteria			

Tasks for self-control:

1. To draw a scheme of clinical manifestations of pharyngeal diphtheria.
2. To make up a table of differential diagnosis of pharyngeal diphtheria with streptococcal and staphylococcal tonsillitis, Vincent´s angina, infectious mononucleosis.
3. To make up a table of differential diagnosis of laryngeal diphtheria with viral laryngitis.
4.To administer treatment for patients with various forms of pharyngeal diphtheria and laryngeal diphtheria (the list of intensive care).

Important terms. **Croup** – subglottic obstruction signs because of laryngitis, laryngotracheobronchitis (diphtheric in adults or viral). The patient has rapid and labored breathing. With each inspiration, there is stridor and retraction of suprasternal notch and supraclavicular areas. Cyanosis of the lips and nail beds becomes evident. **" Bull neck"** – distortion of normal contour of the submental and cervical area caused by oedema in toxic diphtheria.

Case 1

A 9 year old girl has a fever, lymphadenopathy, dysphagia, and pharyngitis with an adherent pseudomembrane covering the tonsils and portions of the oral pharyngeal mucosa. Gramstains of the orophahryngeal exudates how gram-positive pleomorphic rods arrange in palisades. The pharyngeal exudate show gram-positive pleomorphic rods arrange in palisades. The pharyngeal exudate is cultured on potassium tellurite agar, and numerous black colonies develop. Despite the initiation of penicillin therapy, systemic toxemia develops and the girl dies.

What is the diagnosis? Which therapy is appropriate in this case? Which substance is responsible for the exudate development?

Case 2

Girl, 10 years old, acutely developed a disease: malaise, headache, throat pain when swallowing, body temperature 38,2-39,4°C, vomitedtwice. On the 1st day of the disease rash appeared: small bright red papules on hyperemic skin. Oropharyngoscopy: purplered hyperemia of oropharyngeal mucosa, edematous tonsils covered with yellowish-white coating. Lymphnodes are markedly enlarged and moderately painful.

Your preliminary diagnosis? Laboratory tests for diagnosis confirmation? What are the pathognomonic signs of this disease?

Case 3

A girl 10 year old presented fever $38,4^0$C, sorethroat and difficulty in swallowing. She go till 2 days before. On the admission: moderate condition, pale skin, congestive hyperemia of throat, slight edema of pharynx with grey tightly attached membrane which covered both tonsilla's. CBC: Hb 114 g/L, WBC 9.800 $x10^6$, E 5%, B 12%, PMN 59%, LC 18%, M 6%, ESR 35 mm/hr. Throat culture was negative. Urinalysis: protein 0.66 g/L, epithelial cells 15-20, L 20, RBC 10. What is the most likely suspected bacteria which might be isolated from a swab throat? Interpretate the laboratory data. Which clinical signs in this patient are typical for this disease?

Aids and material tools: Charts "Diphtheria", "Tonsillitis: viral, bacterial, fungal", "Viral Croup", Diphtherial Croup"

Student's practical activities:

I. To perform the diagnosis:

1. Ask complaints, anamnesis and life history.
2. Examine the patients, find clinical features of disease
3. Make diagnose due to clinical and laboratory dates.

II Provide the treatment of croup syndrome and prevention of diseases that may be complicated by croup syndrome.

Students must know :

1. Etiology, epidemiology and pathogenesis of diphtheria, tonsillitis, viral croup, diphtheria croup.

2. Clinical diagnostic features of diseases.
3. Laboratory data in patient with croup syndrome.
4. Differential diagnosis of croup syndrome in children.
5. Main treatment of croup syndrome.
6. Prevention of diseases that may be complicated by croup syndrome.

Student should be able to

1. Separate anamnesis data, which told us about risk factors of croup syndrome.
2. Find diagnostic clinical criterions of croup syndrome during examination of patients.
3. To perform differential diagnosis among diseases which have the same clinical features.
4. To learn main tendentions of the croup syndrome treatment.
5. To perform prevention of diseases that may be complicated by croup syndrome.

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