

FEVER AND SORE THROAT (Diphtheria & IMN)

- Prof. Baha D Moohy Alosy//DCH ,FICMSP
- The Departments of Pediatrics- TOCUM.

objective

- Understand the etiology of Diphtheria & IMN.
- Identify clinical manifestation of Diphtheria & IMN
- Know the treatment for Diphtheria & IMN.

- **Tonsillitis** is inflammation of the tonsils most commonly caused by a viral or bacterial infection.
- Group A β -hemolytic streptococcus (GABHS), which causes strep throat. Less common bacterial causes include: Staphylococcus aureus (including methicillin resistant Staphylococcus aureus or MRSA), The most common causes of tonsillitis are adenovirus, rhinovirus, influenza, coronavirus, and respiratory syncytial virus. Epstein-Barr virus, herpes simplex virus, cytomegalovirus

Corynebacterium diphtheriae ➤

(Leffler rod)

Etiology

- Grampositive, nonmotile not forms spores and capsules
- Coloured by Neisser in brown-yellow color
- Cultural-biochemical types of *C. diphtheriae* - mitis, gravis, intermedius
- Production of very strong exotoxin (gene tox +) /Structure of exotoxin - dermanecrotoxin, hemolysin, neuraminidase, hyaluronidase
- Firm to low temperature, long save on a dry surfaces; high responsive to heating and disinfection solutions

Epidemiology➤

- Source – sick person or carrier (convalescent or health) of toxicogenic strains
- Ways of transmission - airborne, contact - household (occasionally)
- Sensibility is high, adults more often become sick (80 %)
- Case rate sporadic, outbreaks are possible
- Immunodefence antitoxic, postvaccine
- Seasonal character - autumn - winter

Pathogenesis➤

- Penetration of the agent through entrance gate (mucous of upper respiratory tract, sometimes conjunctivas, skin)
- Production of exotoxin
- Local and systemic effects of the toxin:
- Dermonecrototoxin - necrosis of a surface epithelium, retardation of blood stream, rising of a permeability of vessels, their fragility, transuding of plasma in ambient tissues, formation of a fibrinous film, edema of tissues; downstroke of pain sensitivity

Pathogenesis➤

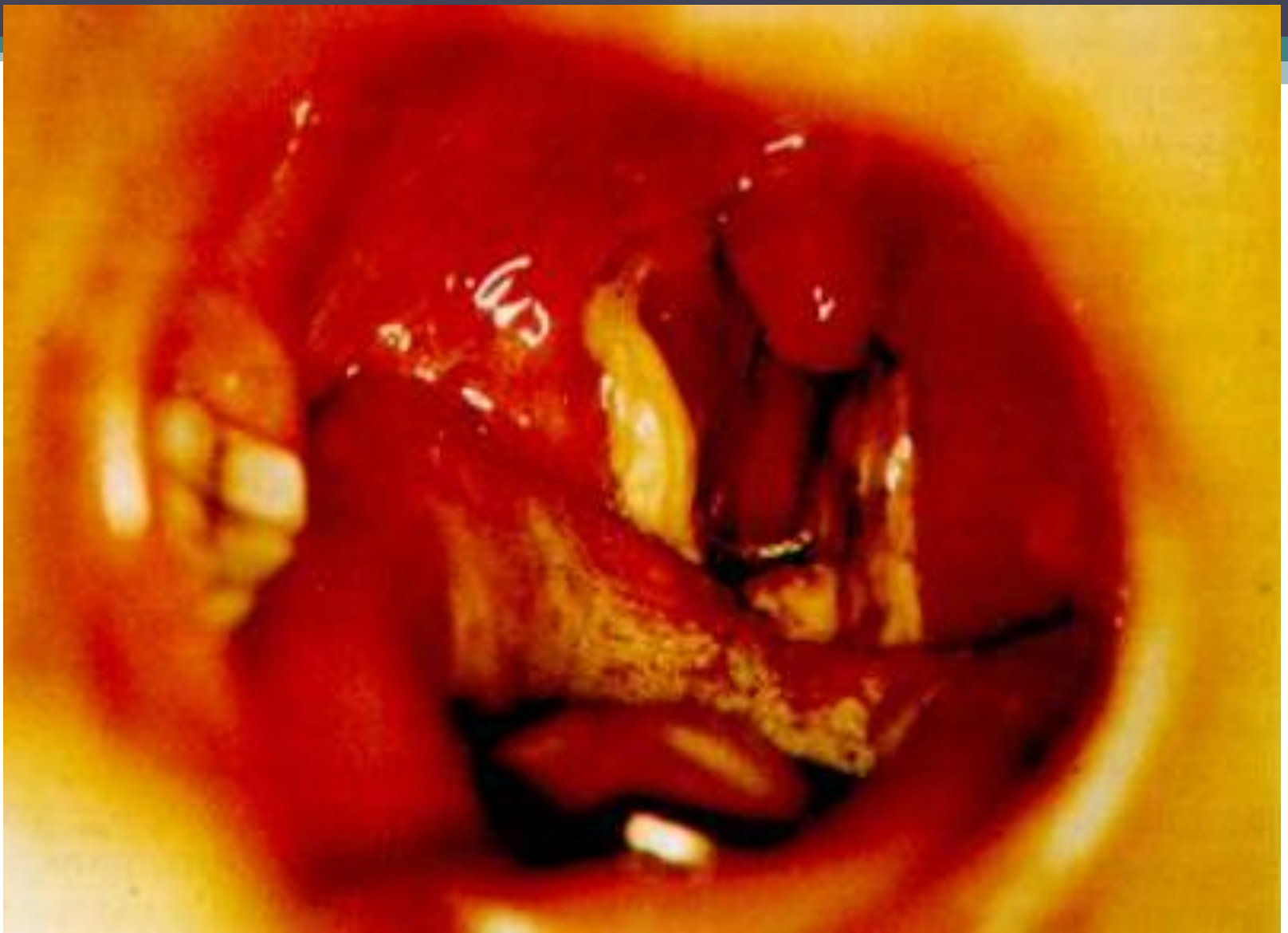
- Neuraminidase - replacement of cytochrome, disturbances a function of organs and tissues (central and peripheric nervous system, cardiovascular system, kidneys)
- Hyaluronidase - destruction of a stroma of a connecting tissue (rising of permeability of vessels, edema of tissues)
- Hemolysin - hemorrhagic set of symptoms

Classification➤

- Localization - otopharynx, nose, larynx, trachea and bronchi; rare localizations (skin, eye)
- Degree of severity - mild, moderate, severe, hemorrhagic, hypertoxic
- Form - localized, wide-spread, combined
- Nature of process - catarrhal, island-like, paleaceous
- Complications - myocarditis, neuritis, nephritis (early and late)
- Subclinical (carriering)

Clinical manifestation➤

- **Incubation period – 2-10 days**
- Phenomena of intoxication (high fever, malaise, general weakness, headache)
- Pharyngalgia - moderate
- Changes of a throat mucous - soft hyperemia, edema of tonsills, covers on their surface (grey colour, dense, hard to remove with bleeding, slime), spread out of tonsills limits (palatopharyngeal arches, uvula, soft palate)
- Augmentation and moderate morbidness of regional lymph nodes
- Edema of a hypodermic fat of a neck



Peculiarities of diphtheria covers



Diphtheria of the nose ➤

Features of diphtheria toxicosis➤

- (In wide-spread, combined, hypertoxical, hemorrhagic forms)
toxicosis I, II, III
- Edema of the neck hypodermic tissues
- Paleness of skin
- Cyanosis of lips
- Decreasing of arterial pressure
- Tachycardia
- Decreasing of a body temperature

Diphtheria of larynx➤

- Real croup (stenosis of a larynx)
- I (catarrhal) - labored inspiration, retraction of intercostal spaces, rasping "dog barking" cough, "horse" voice
- II (stenosis) - noisy respiration, inspiratory dyspnea with an elongated inspiration, participation in respiration of auxiliary muscles, aphonia
- III (asphyxia) - acute oxygen insufficiency, sleepiness, cyanosis, cold sweat, cramps, paradoxical sphygmus



Complications➤

- Infectious-toxic shock
- Intra vessels disseminated syndrome
- Myocarditis (early, late)
- Polyradiculoneuritis (early, late)
- Nephrosonephritis etc.

Treatment➤

- Immediate hospitalization
- Bed regimen (at localized forms - 10 days, at toxic - not less than 35-45 days)
- Specific treatment - introducing of antitoxic antidiphtherial Serum (from 30-50 thousand IU at the localized forms up to 100-120 thousand IU at toxic, by Bezredka method)
- Glucocorticoids (in toxic forms and croup)
- Antibiotics (penicilini, tetracyclini, erythromycini)
- Strychninum (in toxic forms)
- In case of croup - inhalations, broncholitics, diuretics, glucocorticoids, antibiotics, antihistamine, lytic admixture; under the indications - intubation, tracheotomy

Prophylaxis➤

- Plan immunization (vaccination in 3, 4, 5 months. With АРДТ vaccine, revaccination in 18 months; 6, 11, 14, 18 years and adults every 10 years with АДТ-М vaccine)
- In the focus –
 - 7 days medical observation after contact persons
 - Bacteriological examination
 - Sanation of detected carriers
 - Final disinfection
 - Revaccination

Epstein-Barr Virus (EBV)

- ❑ Spread through oral transmission
- ❑ Cause of ***Infectious Mononucleosis.***
- ❑ **Other Diseases include:**
 - ❑ African or Burkitt's lymphoma
 - ❑ Nasopharyngeal carcinoma
 - ❑ B cell lymphoma

Infectious Mononucleosis

- ❑ 4 to 7 week incubation
- ❑ Acute self-limiting infection of the RE system
- ❑ Enlarged lymph nodes in the neck.
- ❑ Sore throat, fever, rash
- ❑ Malaise, lethargy, extreme tiredness
- ❑ Liver and spleen involvement and enlargement
- ❑ Hematology: High WBC, over 20% atypical reactive lymphocytes also known as Downey cells.

Pathophysiology

- ❑ EBV is transmitted via intimate contact with body secretions, primarily oropharyngeal secretions.
- ❑ EBV infects the B cells in the oropharyngeal epithelium. On rare occasion, EBV is spread via blood transfusion.
- ❑ Circulating B cells spread the infection throughout the entire reticular endothelial system (RES), ie, liver, spleen, and peripheral lymph nodes.
- ❑ The humoral immune response **directed against EBV structural proteins.**
- ❑ the T-lymphocyte response is essential in the control of EBV infection; natural killer (NK) cells and predominantly CD8+ cytotoxic T cells **control proliferating** B lymphocytes infected with EBV.

Clinical features

- ❑ CNS : fatigue , loss of appetite , headache, fever
- ❑ Eye : photophobia
- ❑ Throat : reddening , soreness
- ❑ Tonsils : reddening , swelling , white patches
- ❑ Lymph nodes : generalized swelling
- ❑ Respiratory : cough
- ❑ Spleen : enlargement
- ❑ G.I.T : nausea , abdominal pain
- ❑ Maculapapular rashes

- ❑ Lab investigation
- ❑ Confirmed by blood tests : - Early in the course of the mono, blood tests lymphocytosis.
- ❑ More specific blood tests :
- ❑ Monospot and
- ❑ heterophile antibody tests (Ig M)
- ❑ Liver enzyme : raised
- ❑ Culture
- ❑ Complications
- ❑ Respiratory : pneumonia , severe airway obstruction

- ❑ Neurological : convulsion , aseptic meningitis , G – B syndrome

- ❑ Hematological : hemolytic anemia , thrombocytopenia , hemorrhage

- ❑ Splenic rupture

- ❑ Others : hepatitis , myocarditis , glomerulonephritis , orchitis

□ Treatment

- It is self-limiting disease
- Only symptomatic and/or supportive treatments are used.
- Rest during the acute phase of the infection,
- Heavy physical activity and contact sports should be avoided (risk of splenic rupture)
- Paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) (to reduce fever and pain).
- Intravenous corticosteroids (hydrocortisone or dexamethasone), useful if there is a risk of airway obstruction, severe thrombocytopenia, or hemolytic anemia .
- **Antiviral** drug **valacyclovir** (lower or eliminate the presence of the Epstein-Barr virus in patient with acute mononucleosis and decrease in the severity of symptoms).
- **Antibiotics** :
 - Are not used as they are ineffective against viral infections.
 - Ampicillin and amoxicillin are **contraindicated** in the case of any coinciding bacterial infections during mononucleosis because their use precipitates a non-allergic rash
 - With streptococcal infection in the throat and tonsils (strep throat) ---- **Penicillin** or other antibiotics (with the exception of the two mentioned above) should be administered to treat the strep throat.
- Opioid analgesics are also relatively **contraindicated** due to risk of respiratory depression.

• References

Diphtheria

- Centers for Disease Control and Prevention. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) in pregnant women and persons who have or anticipate having close contact with an infant aged MMWR Morb Mortal Wkly Rep</i>. 2011 Oct 21. 60(41):1424-6. [\[Medline\]](#).
- Center for Disease Control and Prevention. CDC Advisory Committee for Immunization Practices Recommends Tdap Immunization for Pregnant Women. Available at http://www.cdc.gov/media/releases/2012/a1024_Tdap_immunization.html. Accessed: November 19, 2012.
- Dajani NA, Scheifele D. How long can we expect pertussis protection to last after the adolescent booster dose of tetanus-diphtheria-pertussis (Tdap) vaccines?. *Paediatr Child Health*. 2007 Dec. 12(10):873-4. [\[Medline\]](#). [\[Full Text\]](#).
- Bronson-Lowe D, Anderson SM. Effects of a minimum interval immunization schedule for diphtheria and tetanus toxoids and acellular pertussis vaccination during a pertussis outbreak. *Arch Pediatr Adolesc Med*. 2009 May. 163(5):417-21. [\[Medline\]](#).
- Jayashree M, Shruthi N, Singhi S. Predictors of outcome in patients with diphtheria receiving intensive care. *Indian Pediatr*. 2006 Feb. 43(2):155-60. [\[Medline\]](#).
- Lurie P, Stafford H, Tran P. Fatal respiratory diphtheria in a U.S. traveler to Haiti--Pennsylvania, 2003. *MMWR Morb Mortal Wkly Rep*. 2004 Jan 9. 52(53):1285-6. [\[Medline\]](#).
- Maksimova NM, Markina SS, Iatskovskii KA, Cherkasova VV, Lazikova GF, Koshkina NA. [Immunization of adult population of Russia against diphtheria in 2006-2007]. *Zh Mikrobiol Epidemiol Immunobiol*. 2008 Nov-Dec. 27-31. [\[Medline\]](#).
- Prasad KC, Karthik S, Prasad SC. A comprehensive study on lesions of the pinna. *Am J Otolaryngol*. 2005 Jan-Feb. 26(1):1-6. [\[Medline\]](#).
- Zasada AA, Zaleska M, Podlasin RB, Seferynska I. The first case of septicemia due to nontoxigenic *Corynebacterium diphtheriae* in Poland: case report. *Ann Clin Microbiol Antimicrob*. 2005 May 5. 4:8. [\[Medline\]](#).

IMN

- Dunmire SK, Hogquist KA, Balfour HH. Infectious Mononucleosis. *Curr Top Microbiol Immunol*. 2015. 390 (Pt 1):211-40. [\[Medline\]](#). [\[Full Text\]](#).
- Ali AS, Al-Shraim M, Al-Hakami AM, Jones IM. Epstein- Barr Virus: Clinical and Epidemiological Revisits and Genetic Basis of Oncogenesis. *Open Virol J*. 2015 Nov 3. 9:7-28. [\[Medline\]](#). [\[Full Text\]](#).
- Epstein MA. Virus particles in cultured lymphoblasts from Burkitt's lymphoma. *Lancet*. 1964. 1:702.
- Henle G, Henle W, Diehl V. Relation of Burkitt's tumor-associated herpes-ytpe virus to infectious mononucleosis. *Proc Natl Acad Sci U S A*. 1968 Jan. 59(1):94-101. [\[Medline\]](#).
- Sawyer RN, Evans AS, Niederman JC, McCollum RW. Prospective studies of a group of Yale University freshmen. I. Occurrence of infectious mononucleosis. *J Infect Dis*. 1971 Mar. 123(3):263-70. [\[Medline\]](#).
- Rostgaard K, Wohlfahrt J, Hjalgrim H. A genetic basis for infectious mononucleosis: evidence from a family study of hospitalized cases in Denmark. *Clin Infect Dis*. 2014 Jun. 58(12):1684-9. [\[Medline\]](#).
- Langer-Gould A, Wu J, Lucas R, Smith J, Gonzales E, Amezcua L, et al. Epstein-Barr virus, cytomegalovirus, and multiple sclerosis susceptibility: A multiethnic study. *Neurology*. 2017 Sep 26. 89 (13):1330-1337. [\[Medline\]](#).
- Flavell JR, Baumforth KR, Wood VH, et al. Down-regulation of the TGF-beta target gene, PTPRK, by the Epstein-Barr virus encoded EBNA1 contributes to the growth and survival of Hodgkin lymphoma cells. *Blood*. 2008 Jan 1. 111(1):292-301. [\[Medline\]](#). [\[Full Text\]](#).
- Baumforth KR, Birgersdotter A, Reynolds GM, et al. Expression of the Epstein-Barr virus-encoded Epstein-Barr virus nuclear antigen 1 in Hodgkin's lymphoma cells mediates Up-regulation of CCL20 and the migration of regulatory T cells. *Am J Pathol*. 2008 Jul. 173(1):195-204. [\[Medline\]](#). [\[Full Text\]](#).
- Chaganti S, Ma CS, Bell AI, et al. Epstein-Barr virus persistence in the absence of conventional memory B cells: IgM+IgD+CD27+ B cells harbor the virus in X-linked lymphoproliferative disease patients. *Blood*. 2008 Aug 1. 112(3):672-9. [\[Medline\]](#).
- Domachowske JB. Infectious triggers of hemophagocytic syndrome in children. *Pediatr Infect Dis J*. 2006 Nov. 25(11):1067-8. [\[Medline\]](#).
- Lung ML, Chang GC, Miller TR, Wara WM, Phillips TL. Genotypic analysis of Epstein-Barr virus isolates associated with nasopharyngeal carcinoma in Chinese immigrants to the United States. *Int J Cancer*. 1994 Dec 15. 59(6):743-6. [\[Medline\]](#).