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ОСТРЫЕ РЕСПИРАТОРНЫЕ ИНФЕКЦИИ В АМБУЛАТОРНОЙ ПРАКТИКЕ

ACUTE RESPIRATORY TRACT INFECTIONS IN OUTPATIENT PRACTICE

Учебно-методическое пособие

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ABBREVIATIONS

ACP — American College of Physicians
AS(L)O — anti-streptolysin O
AS(L)OT — anti-streptolysin O Titre
ASA — acetylsalicylic acid
BP — blood pressure
C&S — culture and sensitivity
C3 — complement component 3
C4 — complement component 4
CHF — congestive heart failure
CMV — cytomegalovirus
COPD — Chronic obstructive pulmonary disease
CRP — C-reactive protein
CT — computed tomography
CXR — chest X-Ray
EBM — Epstein–Barr mononucleosis
EBN-A — Epstein–Barr nuclear antigen
EBV — Epstein–Barr virus
ECG — electrocardiogram
ENT — ear, nose and throat
EOM — extraocular muscles
ESR — erythrocyte sedimentation rate
EUA — examination under anaesthetic (anaesthesia)
FBC, CBC — fool blood count, common blood count
GABHS — group A β-hemolytic Streptococcus
GAS — group A streptococcus
GBM — glomerular basement membrane
GP — general practitioner
HFM — hand, foot and mouth disease
HHV-5 — human herpesvirus 5
HIV — human immunodeficiency virus
HR — heart rate
ICD-10 — International Classification of Diseases, 10th Revision
ICD-11 — International Classification of Diseases, 11th Revision
IgE — immunoglobulin E
IgG — immunoglobulin G
IgM — immunoglobulin M
IM — intramuscular
IV — intravenous
L(R)TI(s) — lower respiratory (tract) infection(s)
LUQ — left upper quadrant
MR — mitral regurgitation
MRI — magnetic resonance imaging

NICE — National Institute for Health and Care Excellence
NSAIDs — nonsteroidal anti-inflammatory drugs
PANDAS — paediatric autoimmune neuropsychiatric disorders associated with strep infections
PCR — polymerase chain reaction
PO — per os
PTA — peritonsillar abscess.
QOL — quality of life
RBC — red blood cell(s)
RR — respiratory rate
RSV — respiratory syncytial virus
RTI(s) — respiratory tract infection(s)
SpO_2 — peripheral capillary oxygen saturation
TMP/SM — trimethoprim/sulfamethoxazole
U(R)TI(s) — upper respiratory (tract) infection(s)
VAS — visual analogue scale
VCA — viral capsule
WBC — white blood cell(s)

BASIC ANATOMY REVIEW

The knowledge of relevant anatomy is of vital importance for understanding and managing respiratory tract infections. Basic anatomy review is illustrated in fig. 1–3. It may be a good idea to return to this chapter from time to time while reading. More precise anatomic details are given in the relevant chapters below.

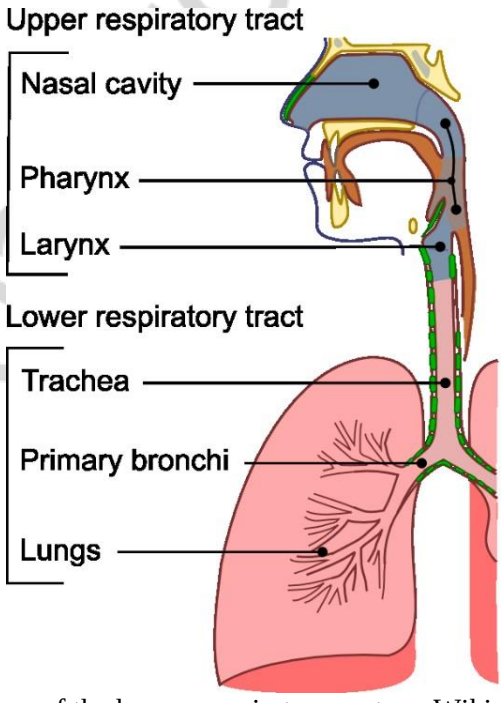

Fig. 1. Conducting passages of the human respiratory system. Wikimedia. File and and author information available from https://commons.wikimedia.org/wiki/File:Illu_conducting_passages.svg

Note: sometimes trachea is considered to be a part of the upper respiratory tract (e. g. tracheatis is classified as upper respiratory tract infection according to ICD-10 and ICD-11).

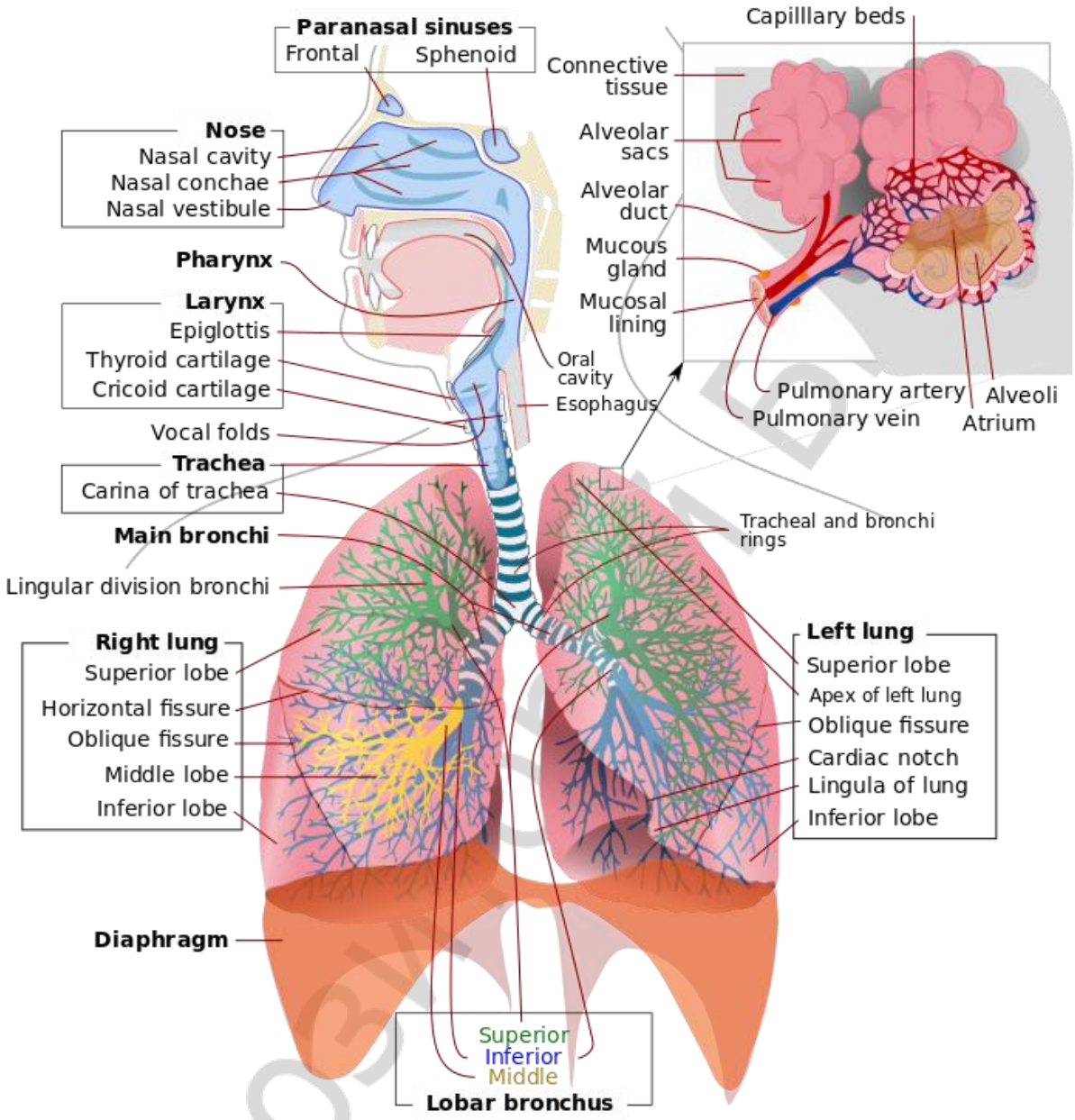

Fig. 2. Respiratory system. Mariana Ruiz Villarreal/ Wikimedia. https://commons.wikimedia.org/wiki/File:Respiratory_system_complete_en.svg

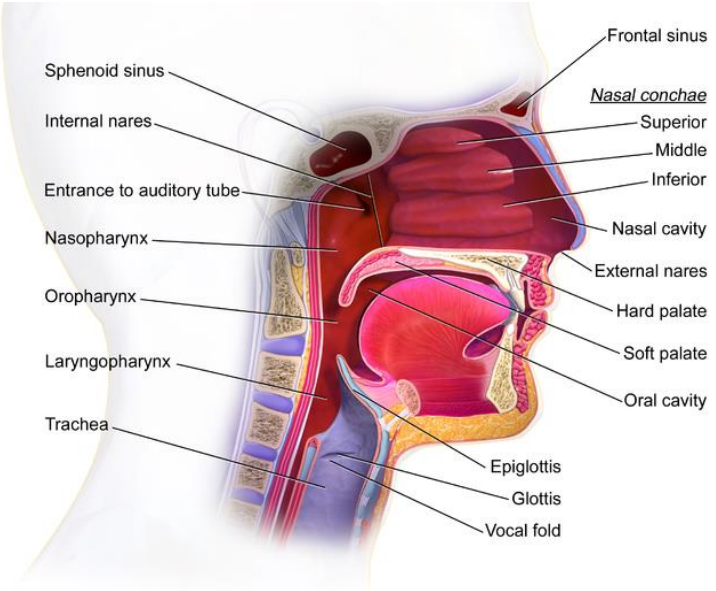

Fig. 3. Upper respiratory system. Blausen.com staff (2014). «Medical gallery of Blausen Medical 2014». *WikiJournal of Medicine* **1** (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436. https://commons.wikimedia.org/wiki/File:Blausen_0872_UpperRespiratorySystem.png

Note: Nasopharynx: spreads from the base of the skull to the soft palate.

Oropharynx: spreads from the soft palate to the hyoid bone (bony structure in front of the epiglottis in fig. 3).

Laryngopharynx: spreads from the hyoid bone to the inferior cricoid cartilage.

Glottis: vocal folds and the opening between them (which is called the rimma glottidis).

INTRODUCTION

Acute respiratory tract infections (RTIs) refer to any of acute infections that involve respiratory tract and cause inflammation.

RTI range from mild self-limited conditions that actually comprise most of them (such as common cold) to serious life-threatening conditions such as epiglottitis, bacterial tracheitis and pneumonia. Respiratory tract may also be involved in case of serious systemic conditions — such as lymphoma, HIV, vasculatidis, sarcoidosis and many more, even coronary heart disease — and presentation may be very similar to RTIs, and sometimes this may be the only (initial) presentation of such conditions, making RTIs *not that trivial* as one may think but an entity that should make one alert.

One of the main tasks of the clinician in acute RTI is to differentiate self limiting cases requiring no specific measures from conditions and cases requiring serious attention and specific management.

EPIDEMIOLOGY, DEFINITIONS AND CLASSIFICATION(S)

RTIs are usually further classified (see details below) as upper respiratory (tract) infections and lower respiratory (tract) infections — UR(T)Is and LR(T)Is respectively.

Usually the term RTI assumes that infection is acute.

URTIs are those involving the upper airways — nasal airways to the larynx (or to the trachea), while LRTIs affect lower airways — trachea and downwards.

Also there are respiratory infections that involve both upper and lower respiratory tract — combined URTIs and LRTIs, which include influenza, whooping cough, laryngotracheobronchitis, measles and some others.

Various data from all parts of the world concordate and suggest that RTIs, especially upper respiratory tract infections, are the leading reason why people miss work and school accounting for roughly 20 % of all time lost from work and 55–60 % of time lost from school thus making them really important.

Lower respiratory tract infections are the leading cause of death of ***all infectious diseases*** (fig. 4).

Recent data suggest that respiratory infection can act as a trigger for a heart attack.

Most RTIs, especially URTIs, are caused by viruses and are self-limited. Respiratory tract viruses mainly include rhinovirus, coronovirus, adenovirus, respiratory syncytial virus (RSV). They are transmitted by direct contact, infected fomites and airborne aerosole droplets. It should be noted though that it is not only those respiratory viruses that affect respiratory tract.

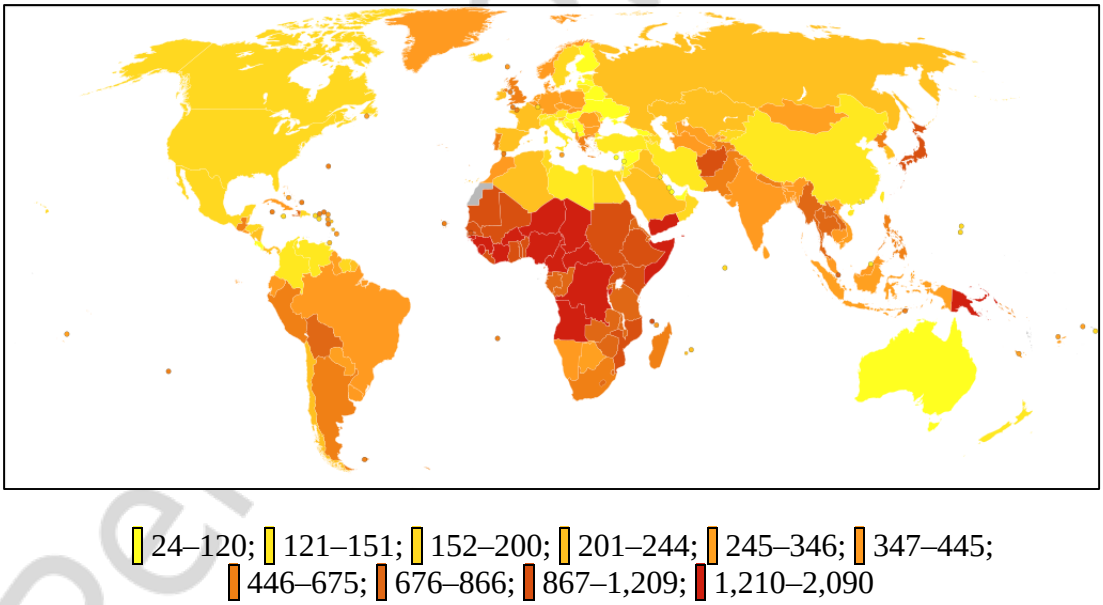

Fig. 4. Deaths from respiratory infections in 2012 per million persons. Chris55. Distributed under the Creative Commons Attribution-Share Alike 4.0 International license (https://creativecommons.org/licenses/by-sa/4.0/deed.en). Data from World Health Organization Estimated Deaths 2012. https://commons.wikimedia.org/wiki/File:Respiratory_infections_world_map-Deaths_per_million_persons-WHO2012.svg

RTI RISK FACTORS

Sick contacts (including URTI presence in a household), contacts with small children who attend school or daycare settings and have contacts with many other small children, traveling (possibly because of increase in contacts in closed settings), smoking (passive and active) through changing mucosal resistance, oversized immune response, alcohol abuse, inflammatory respiratory tract changes — e. g. allergic rhinitis, asthma, decrease in immune function, anatomical changes like polyps and inborn and aquired, e. g. posttraumatic, abnormalities, older age (people aged ≥ 65 years), presence of comorbid conditions, such as chronic respiratory diseases (COPD, asthma, cystic fibrosis and others) and cardiovascular diseases, cerebrovascular disease, Parkinson's disease, epilepsy, dementia, dysphagia, HIV or chronic renal or liver disease all increase risk of different RTIs. This is further described in the corresponding chapters.

Cold weather and cold exposure itself is not a risk factor for common cold (though one hypothesis suggests that cold exposure may precipitate an onset of clinical symptoms but in yet already infected asymptomatic individuals through impairment of local immune defenses), during cold weather people are more likely to stay inside and crowd, and this increasing number of contacts may be responsible for increased cold incidence in winter months. The same mechanism happens in rainy season in countries with no winter – people tend to stay inside more and crowd in rainy weather.

DEFINITIONS AND CLASSIFICATION

URTIS

Rhinitis: inflammation of the nasal mucosa.

Rhinosinusitis or sinusitis: inflammation of the nares and paranasal sinuses (frontal, ethmoid, maxillary, and sphenoid).

Nasopharyngitis (rhinopharyngitis, coryza or the common cold): inflammation of the nares, pharynx, hypopharynx, uvula.

Pharyngitis: inflammation of the pharynx, hypopharynx, uvula without or with the involvement of tonsils.

Tonsillitis: inflammation of tonsils only.

Epiglottitis (supraglottitis): inflammation of the superior portion of the larynx and supraglottic area — of the epiglottis.

Laryngitis: inflammation of the larynx that involves vocal cords.

Laryngotracheitis: inflammation of the larynx, trachea, and subglottic area.

Tracheitis: inflammation of the trachea and subglottic area.

Acute upper respiratory infection, (site) unspecified — can serve as a common diagnosis for URTI, actually every URTI can be classified under this entry, but usually it is used to indicate a diagnosis of non-specific, not requiring special management (e. g. antibiotics) self-limiting URTI.

Acute otitis medii (media): inflammation of the middle ear – technically is not an URTI and is not classified under URTIs in ICD but is often referred to as one of URTIs or viewed together with them and is a common complication.

LRTIS

Bronchitis: inflammation of the bronchial tree.

Bronchiolitis: inflammation of the bronchioles.

Pneumonia: inflammation of the lung parenchyma.

Combined Both Upper and Lower RTIs

Influenza, laryngotracheobronchitis (also such infections as pertussis, measles, whooping cough and some others) involve both upper and lower respiratory tract.

ICD-10 and ICD-11 Classification

Classification of RTIs according do ICD is available here:

- ICD-10:

https://icd.who.int/browse10/2010/en#/X

- ICD-11:

https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who. int% 2ficd% 2fentity%2f197934298

There may be some differences in which infections should be listed under upper and which under lower respiratory tract infections, e. g. tracheitis is listed under URTIs in ICDs.

ANTIBIOTIC USE IN RTI

Antibiotics resistance is an area of concern, and in case of RTIs, especially URTIs, there is a significant area for improvement of use of antibiotics. Most cases of RTIs require no antibiotics (though some obviously require them, e.g. pneumonia or strep throat) and unneeded use of antibiotics can contribute to increased resistance and lead to adverse effects that could have been avoided. However, research shows that antibiotics are heavily overused in RTIs and some specialists say that overuse is extreme (our data show that antibiotics were prescribed in 84 % of patients with URTIs who didn't require them). Given the number of cases of the RTIs in the community this is a very serious issue on a global scale.

Below are summaries from some major guidelines for prescribing antibiotics in acute RTIs.

NICE GUIDELINE

Identifying those patients with RTIs who are likely to be at risk of developing complications:

An immediate antibiotic prescription and/or further appropriate investigation and management should only be offered to patients (both adults and children) in the following situations:

- if the patient is systemically very unwell;
- if the patient has symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital and intracranial complications);

- if the patient is at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely;
- if the patient is older than 65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following criteria:
  - ✓ hospitalisation in previous year;
  - ✓ type 1 or type 2 diabetes;
  - ✓ history of congestive heart failure;

For these patients, the no antibiotic prescribing strategy and the delayed antibiotic prescribing strategy should not be considered.

ACP says that healthy adults without chronic lung disease (such a cystic fibrosis, bronchiectasis, and chronic obstructive pulmonary disease) or immunocompromising conditions (congenital or acquired immunodeficiencies, HIV infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma, Hodgkin disease, generalized cancer, multiple myeloma, iatrogenic immunosuppression, or a history of solid organ transplantation) should not routinely receive antibiotics.

ACP High-Value Care Advice

High-Value Care Advice 1:

Clinicians should not perform testing or initiate antibiotic therapy in patients with bronchitis unless pneumonia is suspected (see next page).

High-Value Care Advice 2:

Clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis (for example, persistent fevers, anterior cervical adenitis, and tonsillopharyngeal exudates or other appropriate combination of symptoms) by rapid antigen detection test and/or culture for group A Streptococcus. Clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.

High-Value Care Advice 3:

Clinicians should reserve antibiotic treatment for acute rhinosinusitis for patients with persistent symptoms for more than 10 days, onset of severe symptoms or signs of high fever (> 39 °C) and purulent nasal discharge or facial pain lasting for at least 3 consecutive days, or onset of worsening symptoms following a typical viral illness that lasted 5 days that was initially improving (double sickening).

High-Value Care Advice 4:

Clinicians should not prescribe antibiotics for patients with the common cold.

SUSPICION OF PNEUMONIA AND BACTERIAL INFECTION IN A PATIENT WITH ACUTE RESPIRATORY ILLNESS AND INDICATIONS FOR CHEST X-RAY

How can one determine whether the patient with acute respiratory illness symptoms has a higher chance of having pneumonia? Good question, because symptoms of common cold and other non-specific RTIs may be very similar or the same as pneumonia symptoms.

Several studies were conducted to evaluate this and the need of X-Ray. Unfortunately no symptoms and signs can definitely rule in or rule out the diagnosis of pneumonia, but the below signs may aid this task.

Chest X-ray is less likely to show abnormalities if the patient has no signs described below:

- Temperature > 37,8 °C;
- Heart rate > 100 minute (for adult);
- Crackles;
- Decreased breath sounds;
- Absence of asthma;

(the above is also called the Heckerling rule, 2 signs increase the chance of patient having pneumonia significantly);

- Age > 60;
- Temperature > 38 °C;
- Oxygen saturation (SpO_2) < 90 %;
- Respiratory rate > 24 breaths/minute (for adults);
- History of alcohol abuse;
- History of tuberculosis;
- History of thromboembolic disease;
- Night sweats.

The patient does not necessary have to have the above-mentioned signs to have an X-Ray. Note that progression and worsening of symptoms after initial improvement of patient's symptoms (double illness) may be a sign of bacterial infection, including pneumonia. Immunocompromized patient is in higher risk of pneumonia, too. If patient has acute bronchitis and congestive heart failure — X-Ray should also be considered. Cough that lasts 3 or more weeks also suggests X-ray has to be done. Diagnosis of pneumonia in children is often made only by X-Ray.

Lung ultrasonography may also be used to diagnose pneumonia.

There is no evidence that the colour of sputum is related to bacterial colonisation or the efficacy of antibiotics in otherwise healthy patients.

INVESTIGATIONS

Non-specific RTIs usually do not require any tests. However, some specific cases and diseases require investigations, e. g. when management heavily depends on the results of the test (like in case of strep throat and other bacterials or mononucleosis, which prompts restrain of physical activity).

Nasopharyngeal swabs for culture and rapid antigen detection tests (positive test obliterate the need for culture) are taken to confirm the suspicion of strep throat. Swabs are also done to detect other bacterial infection (e. g. gonococcal, pertussis).

Monospot test is used to diagnose mononucleosis. FBC may show atypical mononuclears which are present in mononucleosis.

Bacterial sinusitis may require MRI or CT in case symptoms do not improve despite therapy and persist.

Rapid tests are used for pertussis diagnosis.

Cell culture and PCR are used for herpex simplex detection.

Rapid test may also be used for influenza diagnosis.

Some conditions may actually be a contraindication for some diagnostic methods — e. g. in suspected epiglottitis throat must not be examined in outpatient settings, as examination of the throat in this case may precipitate worsening and spasm, so this should only be done in hospital.

Serious infections like pneumonia and other bacterial complications require thorough investigations including imaging studies and blood chemistry and cultures. Very ill and immunocompromised patients also require thorough work-up.

UPPER RESPIRATORY TRACT INFECTIONS (URTIs)

Acute respiratory tract infections (RTIs) refer to any of a number of acute infections that involve respiratory tract and cause inflammation. URTIs are those involving the upper airways — nasal airways to the larynx, sometimes the trachea is also considered to be a part of the upper respiratory tract and tracheitis is considered an URTI.

The upper respiratory tract is the site for a large number of viral and bacterial infections. URTI is the commonest cause of diseases leading to patients' acute visits to doctors.

Most infections remain localized, but some may spread to adjacent systems (e. g. nasopharyngeal infection may spread and cause pneumonia, otitis, sinusitis, epiglottitis, laryngitis, tracheobronchitis) and some may be the cause of a generalized disease (e. g. mononucleosis).

URTIs have much in common in clinical presentation, most of them are caused by viruses and usually self-limited requiring only symptomatic treatment in immunocompetent adult patients. URTIs are often self-diagnosed and treated at home. It is important though to identify specific causes and/or cases where specific treatment is required (e.g. streptococcal pharyngitis, mononucleosis, etc).

COMMON COLD (NASOPHARYNGITIS, RHINOPHARYNGITIS, CORYZA)

Most URTIs have much in common with common cold in clinical presentation and are very similar to it having significant symptoms overlap (e. g. viral pharyngitis, which is the cause of most cases of pharyngitis, may occur as part of the presentation of the common cold), though may have some peculiarities (e. g. hoarse voice in case of laryngitis is also present, while otherwise presentation is like in common cold)

Most non-specific URTIs will have presentation similar to common cold and will require same management.

Definition, Epidemiology, Aetiology and Pathology

Common cold is a viral URTI with inflammation of the nares, pharynx, hypopharynx, uvula, and tonsils. This highly infectious URTI is often mistakenly referred to as «the flu».

Most common diagnosis in primary care/general practice (and probably the most common acute disease in the world), peaks in winter months.

Incidence: adults 2–4 times a year, children up to 6–10 times a year.

Causative organisms: mainly rhinoviruses (up to 30–35 % of all cases). Other organisms also include: coronavirus, adenovirus, RSV, influenza B, C, parainfuenza, Coxsackie virus and others.

Incubation period lasts 12 hours — 5 days. Transmission is person-person contact via secretions on skin and objects and by aerosol droplets and their contact with mucosa.

Risk factors include sick contacts, psychological stress, excessive fatigue, allergic nasopharyngeal disorders, smoking — see RTI risk factors chapter.

Clinical Features

General:

- mild fever;
- malaise, tiredness;
- headache, myalgias.

Local:

- sore throat;
- sore and runny nose, nasal congestion, clear to mucopurulent nasal secretions — the watery nasal discharge becomes thick and purulent in about 24 hours and persists for up to 7 days;
- sneezing;
- conjunctivitis (often a sing of adenovirus);
- cough;
- possible hoarsness (this assumes the presence of laryngitis);
- boggy and erythematous nasal and/or oropharyngeal mucosa (see non-specific pharyngitis topic for normal throat and erythematous throat);

- enlarged lymph nodes;
- normal chest examination — an important sign. This is an example showing that absence of pathology may also be an important sign.

Mind cerebrospinal fluid rhinorrhea (congenital or aquired)!
One patient was not diagnosed with it for 10 years, during this time he visited doctors several times but the diagnoses were mostly URTIs.

Diagnostic tests

Laboratory tests are ***not*** helpful in the diagnosis or management of colds: the clinical presentation itself is diagnostic, though diagnostic tests will be required if something other than common cold is suspected.

Possible Complications

Secondary bacterial infections (it is worth noting that secondary bacterial infections are usually uncommon): otitis media, sinusitis, bronchitis, pneumonia.

In patients with reactive airway disease, e. g. asthma or COPD, colds and other RTIs can precipitate exacerbation. Patients with asthma, including undiagnosed asthma, may also say that their colds usually «go to chest» which may be the reason to suspect asthma diagnosis. Patients often learn that they have asthma when they have URTI and visit their GP.

Differential Diagnosis

Allergic rhinitis, pharyngitis (here it means that it is important to recognize specific causes of pharyngitis like strep throat and others, not the non-specific viral pharyngitis, see pharyngitis chapter below), influenza, laryngitis, croup, sinusitis, bacterial infections. See also table 1 below.

Table 1

Differential diagnosis of common cold with influenza and allergic rhinitis

Symptom	Allergy	URTI	Influenza
Itchy, watery eyes	Common	Rare; adenovirus can cause conjunctivitis	Soreness behind eyes, sometimes conjunctivitis
Nasal congestion	Common	Common	Sometimes
Rhinitis, sneezing rhinorrhoea, nasal discharge	Very common	Very common	Not very common, often dry and clear nose
Sore throat	Sometimes (because of postnasal drip); itchy throat	Very common	Usually fine
Cough	Sometimes	Common, mild to moderate, can be hacking, appears later	Common, dry cough, can be severe, hacking
Headache	Sometimes, facial pain	Rare	Common

End tabl. 1

Symptom	Allergy	URTI	Influenza
Fever and chills	Almost never	Possible in children, sometimes seen in adults	Very common, 38–39 °C (100–102 °F) or higher (in young children), lasting 3–4 days; may have chills
Malaise	Sometimes	Sometimes	Very common
Fatigue, weakness	Sometimes	Sometimes	Very common, can last for weeks, extreme exhaustion early in course
Muscle aches	None	Slight	Common, can be severe
Onset of illness	Sudden (after contact with allergen)	Slow	Sudden
Appetite		Normal	Decreased
Incubation period	–	12 hours to 5 days	1–3 days
Toxaemia	–	–	+
Causes	Causative allergen	Rhinoviruses Parainfluenza Influenza B, C Coronavirus RSV	Influenza A Influenza B

Management
(These management principles also apply to all non-specific URTIs)

No antibiotics are indicated because of viral etiology, ***this should be explained to the patient.***

Patient education and reassurance:

- symptoms peak at 1–3 days and in most cases usually subside within 1 week;
- cough may persist for days to weeks after other symptoms disappear;
- secondary bacterial infection can present within 3–10 days after the onset of cold symptoms.

Symptomatic relief:

- adequate sleep and rest, hydration, gargling warm salt water, aspirin in water or lemon juice for a sore throat, steam inhalations for a blocked nose, nasal irrigation (spray/pot), analgesics and antipyretics per need: acetaminophen (paracetamol), ASA (not recommended in children up to 16 years of age because of the risk of Reye's syndrome);
- cough suppression: dextromethorphan or codeine if necessary (children under 6 years of age should not use any cough or cold (paracetamol may be used) medications), cough mixtures can be administered for a dry cough;
- decongestants (alfa-mimetics no more than 5 days — watch out for rebound effect), antihistamines if signs of allergy are present;

- zinc lozenge use may help to reduce the duration of cold symptoms but gastrointestinal tract side effects may occur, clinical trials of zinc lozengers and echinacea give contradictory results.

Patients with reactive airway disease (e. g. asthma) will very likely require increased use of bronchodilators and inhaled steroids.

Prevention

Frequent hand washing, avoidance of hand to mucus membrane contact – hands may carry nasal secretions, use of surface disinfectants.

ACUTE LARYNGITIS

Definition, Epidemiology, Aetiology and Pathology

Inflammatory changes in laryngeal mucosa of less than 14 days duration (14 days and more is considered chronic) (fig. 5).

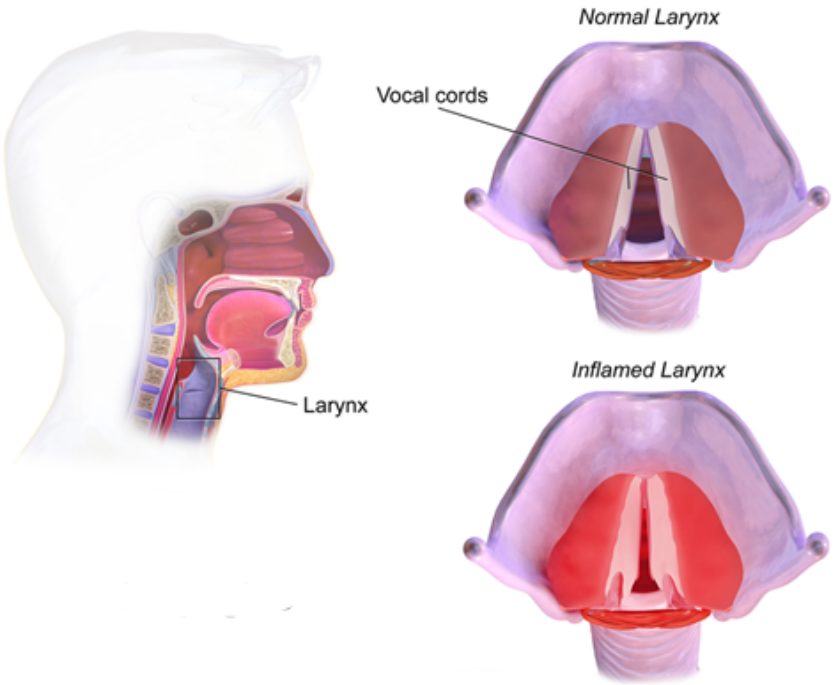

Fig. 5. Laryngitis. Blausen.com staff (2015). Wikimedia. https://commons.wikimedia.org/wiki/File:Laryngitis.png

Most cases are caused by viruses: rhinovirus, influenza, parainfluenza, Coxsackie virus, adenovirus and respiratory syncytial virus. Bacterial causes: be aware of Group A Streptococcus.

Mechanical causes: acute voice strain causes submucosal hemorrhage, which causes vocal cord oedema which results in hoarseness. Environmental causes: smoking, including passive, excessive alcohol drinking and exposure to irritants and pollutants, air-conditioning systems and very cold weather.

Clinical Features:

Hoarsness of more than 2 weeks in a smoking patient warrants exclusion of cancer.

- the infection usually is self-limited, resolves within about 1 week (3–14 days). More than 14 days is considered chronic, not acute process in this case;
- the main symptom is hoarseness, which usually persists for 3–14 days and leads to loss of voice. Even speaking can be painful;
- Other symptoms include aphonia, cough attacks, possibly even dyspnea in severe cases
- true vocal cords are erythematous/edematous with vascular injection, mobility remains normal.

Hoarseness implies one cord lesion, two cords lesion is more likely to result in voice pitch changes (or dyspnoea in severe cases) than in hoarsness.

Treatment:

- voice rest, avoid shouting, especially avoid whispering;
- humidification — hot, steamy showers may be of value (humidity helps), steam inhalations (e. g. 5–10 minutes, three times a day);
- hydration — drink ample fluids, water is preferred;
- avoid irritants (e. g. alcohol, smoking, including passive smoking);
- paracetamol or aspirin (aspirin — not in children yonger than 16) for throat discomfort;
- use antitussives if needed (not in children under 6 years), some advice mucolytic agents use;
- antibiotics are of no proven benefit unless bacterial infection (e. g. strep throat) is present. Treat with antibiotics **if there is evidence** of coexistent bacterial infection, e. g. strep pharyngitis (see Centor criteria in pharyngitis management chapter);
- possible use of corticosteroids (rarely used).

Prevention. See aetiology.

ACUTE LARYNGOTRACHEOBRONCHITIS (CROUP)

Definition, Epidemiology, Aetiology and Pathology

Infammation of tissues in the subglottic space and/or tracheobronchial tree which impairs normal function of ciliated mucous membrane causing swelling (oedema) of mucosal lining and associated with thick, viscous, mucopurulent exudate both of which (oedema and exudate) compromise upper airways (subglottic space is the narrowest portion of the upper airways).

Causes are viral: parainfuenzae (1 — most common type, 2, 3), respiratory syncytial virus (RSV), infuenza A and B, sometimes measles (rare).

Clinical Features:

- croup usually affects children aged 4–6 months to 5–6 years of age, peak incidence occurs in those aged 1–3 years but can be recurrent in older children with atopy (think also of subglottic stenosis if recurrent);
- usually follows self-limiting course, but not always;
- occurs in small local epidemics, more often in autumn and early winter;
- is preceded by URTI symptoms for about 2 days;
- generally occurs at night, usually 11 pm to 2 am;
- is characterized by croupy cough (due to obstruction in the laryngeal region) – characteristic harsh, brassy, loud cough, sounds like a dog or seal barking, with usually inspiratory (may be biphasic) stridor, with or without respiratory difficulty;
- inspiratory stridor confirmed by auscultation;
- stridor may appear if agitated;
- hoarseness;
- fever varies — in rare cases above 39 °C;
- patient appears less toxic than in epiglottitis;
- supraglottic area appears normal on examination;
- anteroposterior Neck X-ray: «steeple-sign» (fig. 6);
- classification: mild, moderate and severe, see below.

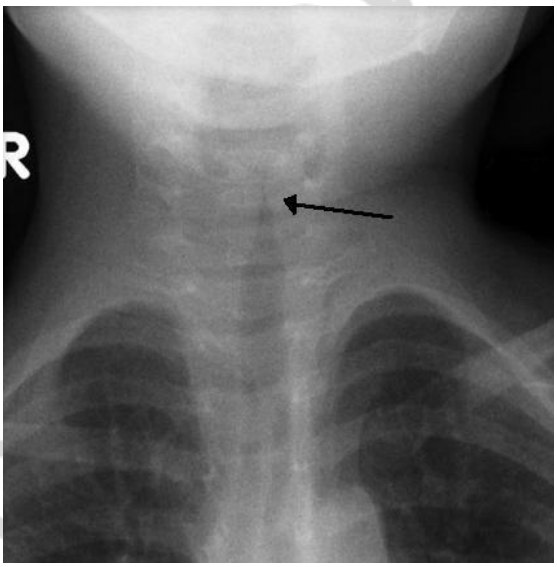

Fig. 6. Anteroposterior x-ray of the neck in a child with croup demonstrating the steeple sign — narrowing of the the trachea. Dr Frank Gaillard. Radiopaedia.org. Distributed under the licence GFDL 1.3 (https://www.gnu.org/licenses/fdl-1.3.html) and Creative Commons Attribution-Share-Alike 3.0 (https://creativecommons.org/licenses/by-sa/3.0/). https://commons.wikimedia.org/wiki/File:Croup_steeple_sign.jpg

Volume of stridor is a factor of flow; in severe disease, when subglottic space is very narrowed – stridor will actually be very soft.

Grade 1 croup: mild. No stridor or stridor at rest without chest retractions and no distress, barking cough, hoarseness, no cyanosis, alert child, good air entry.

Grade 2 croup: moderate. Stridor at rest with sternal and chest wall retractions.

Grade 3 croup: severe. Stridor at rest, sternal and chest wall retractions, restless and agitated child, marked respiratory distress: use of accessory muscles, pallor, cyanosis, tachycardia, tachypnoea and exhaustion (i.e. impending airway obstruction), altered consciousness level.

Croup score (Westley Croup Score) points may also be used to estimate severety, see for example here www.mdcalc.com).

Differential diagnosis. Rule out foreign body (not such a rare case in children) and subglottic stenosis, e. g. if recurrent croup, consider bronchoscopy several weeks after acute episode subsides.

In case of poor response to therapy bacterial tracheitis may be the cause.

Treatment and Management

Management is based on severety.

Grade 1 croup:

- may be managed at home (do not try this at home in case of signs of Grade 2 or 3 croup);
- keep patient calm and relaxed;
- provide adequate hydration;
- oral corticosteroids: dexamethasone 0.15–0.3 mg/kg statim or prednisolone 1 mg/kg if stridor and chest wall retraction develop. A randomised controlled trial found no benefit from mist (supersaturated air) therapy when coupled with oral corticosteroids (level II evidence).
- admit in case of poor response to steroids after 4 hours and persistent stridor at rest. If managed as an in-patient – keep interference to the minimal required, monitor life signs (temperature, SpO_2, HR, RR) carefully.

Grade 2 croup:

- admit to hospital;
- cool humidified air;
- provide adequate hydration;
- oral corticosteroids dexamethasone 0.6 mg/kg or prednisolone (tablets or oral solution)1 mg/kg, give 2–3 doses and/or (for children of 2 or more years of age) budesonide 100 mcg × 20 puffs or 2 mg nebulized;
- nebulised adrenaline if poor response to steroids — 1:1000 solution 0.4-0.5 mL/kg, up to 5mL;
- observe for at least 4 hours.

Grade 3 croup:

- admit to intensive care unit;
- adrenaline is first-line therapy;
- nebulised adrenaline 1 : 1000 solution 0.4–0.5 mL/kg, up to 5mL (there is a possibility of a rebound effect — the patient must be observed), do not dilute the

solution. Repeat this at 10–15 min if the response is poor; 4 ampoules of 1:1000 solution in a nebuliser run with oxygen 8 L/min may be used;

- oxygen;
- dexamethasone 0.2 mg/kg IV or 0.6 mg/kg IM followed by oral corticosteroids;
- adequate hydration;
- be prepared for artificial airway;
- endotracheal intubation may be required (if going into respiratory failure) for 48 hours, endotrachial tube 0.5–1 mm smaller than normal for age should be used (because of tissue oedema). Cough medicines or antibiotics unless bacterial infection, e. g. bacterial tracheitis, is present (see below), are strongly discoureged. Steaming methods are not recommended.

Failure to improve with the use of steroids/nebulized adrenaline may be a sign of **bacterial tracheitis**. This is defined by the presence of thick mucopurulent exudate and tracheal mucosal sloughing on laryngoscopy that is not cleared by coughing, and may lead to occlusion of the airways. There is often a history of a viral infection (such as croup) with an acute deterioration. Pronounced tracheal tenderness may be present.

ACUTE EPIGLOTTITIS

Acute epiglottitis is a medical emergency!

Definition, Epidemiology, Aetiology and Pathology

Acute epiglottitis is acute inflammation that causes swelling of supraglottic structures (e. g. epiglottis, fig. 7, hence the name) of the larynx without involvement of vocal cords.

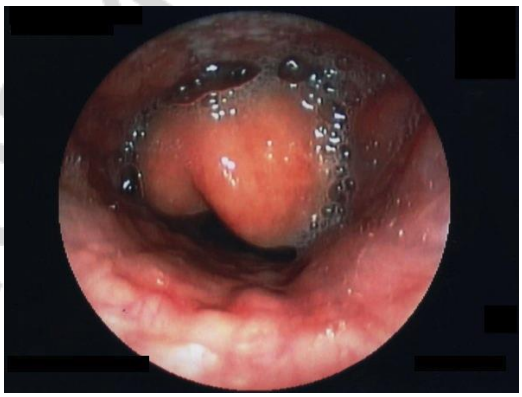

Fig. 7. Swollen epiglottis in laryngoscopy. Distributed under the Creative Commons Attribution-Share Alike 3.0 Unported license (https://creativecommons.org/licenses/by-sa/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Epiglottitis_endoscopy.jpg

It is caused mainly by Haemofilus influenzae type B infection. Relatively uncommon since Hib immunisation, so it may be wise to check patient's immunization

status if epiglottitis is suspected. Usually happens in children 1–6 years of age, but other age groups may be affected.

Clinical Features

Child with fever, drooling and stridor = probable epiglottitis

High temperature with sudden onset of expiratory stridor in a child raises suspicion of epiglottitis. In children this is a life-thereatening condition due to airway obstruction. In adults obstruction is much less likely (but this doesn't mean that this is not a severe infection, still hospitalization and parental antibiotics are required) and thus epiglottitis may be overlooked in them, the main complaints in this case usually are severe sore throat and dysphagia (though the throat looks normal on examination), tender neck, saliva drooling:

- acute epiglottitis is most common in children 1 to 6 years, but may happen at any age;
- toxic febrile illness;
- rapid onset, sudden onset of expiratory stridor (may be inspiratory stridor);
- in adults stridor and airway obstruction mostly absent;
- sore throat, dysphagia;
- possible neck tenderness;
- patient is pale, may be cyanotic, slow breathing;
- lungs are clear on auscultation, air entry is decreased;
- anorexia, restlessness;
- drooling, opened mouth, protruded tongue, child follows objects with his eyes movements only while keeping head and neck still (this protects the compromised airway).

Do not agitate the patient and do not examine the throat in outpatient facility (or elswhere out of the hospital without been prepared for intubation or tracheotomy)! This (as well as other investigations) may precipitate obstruction.

The initial diagnosis should be made based on history and the child's appearance.

Diagnosis is confirmed by a swollen, cherry-red epiglottis seen on nasopharynx examination.

See table 2 **Differential diagnosis** of bacterial tracheitis, croup and epiglottitis.

Table 2

Differential diagnosis of bacterial tracheitis, croup and epiglottitis

	Epiglottitis	Croup	Bacterial tracheitis
Anatomy	Supraglottic laryngitis	Subglottic laryngitis	Subglottic tracheitis
Epidemiology	Now uncommon — due to introduction of Hib vaccination. Check immunisation status! Age group: 1–6 years of age	Common in children 4–6 months to 5–6 years of age, peak incidence between 1–3 years. Common in autumn and winter	Rare. All age groups

End tabl. 2

	Epiglottitis	Croup	Bacterial tracheitis
Etiology	H. influenzae, GABHS	Parainfluenza (75 %), Influenza A and B, RSV, Adenovirus	S. aureus, H. influenzae, GABHS, Pneumococcus, Moraxella catarrhalis
Presentation	Toxic appearance, rapid progression 4 Ds: drooling, dysphagia, dysphonia, distress Stridor, «tripod» position, sternal recession, patient is anxious, fever (often > 39 C°)	Common prodrome (similar to common cold): rhinorrhea, pharyngitis, cough, ± low-grade fever. Symptoms: barking cough, hoarseness, stridor. Symptoms worse at night	Initially symptoms similar to croup but more rapid deterioration with high fever (> 39 C°) and toxic appearance. Does not respond to croup treatments — this should warrant suspicion of bacterial tracheitis
Investigations	Clinical diagnosis. Avoid outpatient throat examination — may induce airway compromise	Usually a clinical diagnosis. CXR if atypical presentation: subglottic narrowing causes «steeple sign», see **fig. 6**	Initially clinical diagnosis. Definitive diagnosis with endoscopy
Management	See corresponding chapters		

Investigations and Management

Thumb (thumbprint) sign: swollen cherry-shaped epiglottis seen on lateral neck X-Ray (fig. 8)

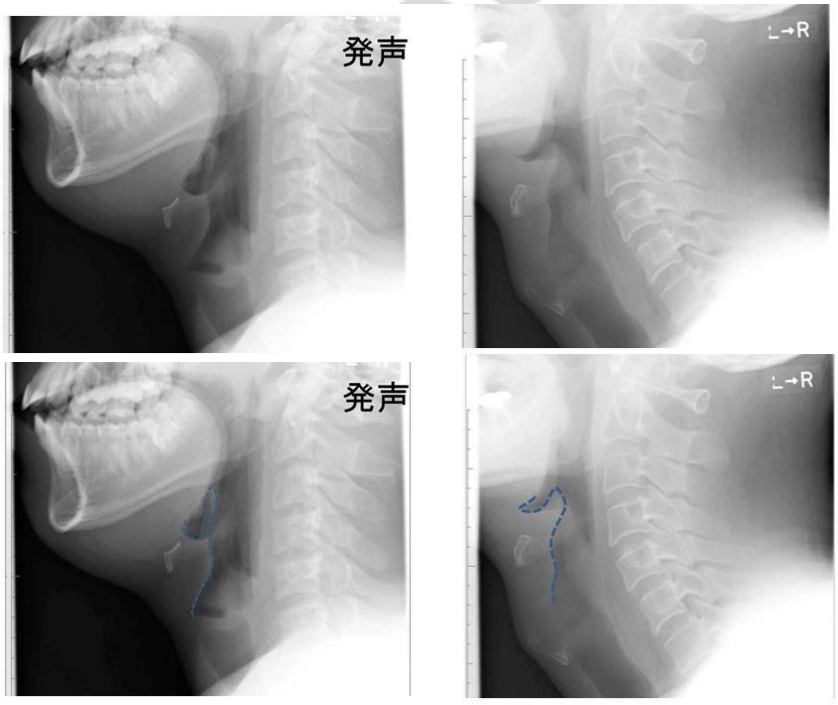

Fig. 8. Thumbprint sign. Left column: Normal epiglottis. Right column: Epiglottitis. Med Chaos. Distributed under the Creative Commons Attribution-Share Alike 3.0 Unported license (https://creativecommons.org/licenses/by-sa/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Compare_epiglottis.jpg

As already noted above investigations and physical examination and any manipulation may lead to complete obstruction of the airways, so do not attempt it if not prepared for intubation and tracheotomy and admit the patient (usually child) to hospital.

Ask for senior help from and stay in touch with an anaesthetist and ENT surgeon

- intubation (endotracheal tube of a smaller diameter than normal for that age may be needed): take the child to ICU and suck away profuse secretions and perform nasotracheal intubation, perform EUA if necessary. A tracheostomy may be required if complete obstruction occurs. Severe bacterial tracheitis also benefits from early intubation, allowing suctioning of respiratory secretions and improved ventilation.
- after intubation: FBC — elevated WBC, blood and pharyngeal cultures
- in a stable patient – lateral neck X-Ray
- antibiotics: IV cefotaxime 25 mg/kg up to 1 g for 5 days every 8 hour or ceftriaxone 25 mg/kg up to 1 g/day daily for 5 days
- IV access for hydration
- moist air
- hydrocortisone isn't of proven value, though it may be given
- extubation: when leak around tube occurs and the patient becomes afebrile.

Meningitis may develop so watch out for its signs

ACUTE TRACHEITIS INCLUDING ACUTE BACTERIAL TRACHEITIS

Acute viral tracheitis presentation is similar to common cold, but cough is more prominent and severe. Treatment is as in common cold.

Bacterial tracheitis is a bacterial inflammation of the subglottic part of the trachea. See tabl. 2. See fig. 9 for relevant anatomy. Treatment: intubation and IV antibiotics, as in epiglottitis.

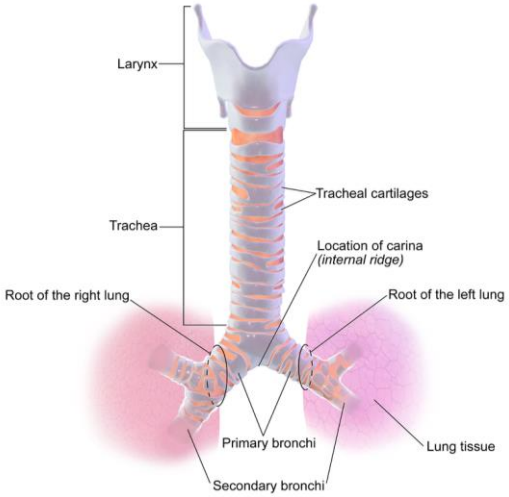

Fig. 9. Anatomy of the Trachea. Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". *WikiJournal of Medicine* 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436. https://commons.wikimedia.org/wiki/File:Blausen_0865_TracheaAnatomy.png

ACUTE PHARYNGITIS AND SORE THROAT — GENERAL FEATURES AND MAIN DIFFERENTIALS, COMPLICATIONS

Definition

Inflammation of the oropharynx, often referred to as «sore throat», though a sore throat is a much broader syndrome which also encompasses more complex and severe cases than just viral pharyngitis and common cold.

There are numerous potential pharyngitis-causing microorganisms. Most cases are of **viral origin and may occur as part of the presentation of a common cold**. Symptoms resolve in 40 % of cases within 3 days and within 1 week in 85 %.

A sore or painful throat is one of the commonest symptoms encountered in general practice. It may be caused by a wide range of infectious organisms, most of which produce a self-limited infection with no significant sequelae.

The terms «pharyngitis» and «sore throat», especially «acute sore throat», are often used interchangeably, but it's worth noting that a sore throat, however, is a broader concept which includes all the causes of discomfort in the throat including pharyngitis and other RTIs being the most common cause and systemic conditions manifesting also with throat symptoms and changes (these conditions are not limited to the throat only). Tests are available for many agents causing pharyngitis.

Aetiology

Some main causes of a sore throat mentioned here are described in detail in the following chapters.

Viral. Viruses is the most common cause (40–50 % to up to 90 % in adults). Viral pharyngitis occurs year round, may peak in winter months like common cold often being a part of its presentation. Viruses responsible: adenovirus (pharyngoconjunctival fever), rhinovirus and other upper respiratory tract viruses, enteroviruses, parainfluenza, influenza A and B virus, RSV, EBV, Coxsackie virus, herpes simplex virus, CMV, HIV, measles, Lassa (in ~80 % mild/asymptomatic, haemorrhage in ~20 %, variable mortality in different epidemics 25–80 %) and others.

Bacterial. Group A β-hemolytic Streptococcus, group C and G β-hemolytic Streptococcus, Neisseria gonorrheae, Chlamydia pneumoniae (the commonest chlamydial infection, person-to-person spread, often biphasic illness characterized by: pharyngitis, hoarseness, otitis, followed by pneumonia), Chlamydophila psittaci, Mycoplasma pneumoniae, Corynebacterium diphtheriae (especially if unvaccinated), Fusobacterium necrophorum (anaerobe causing Lemierre syndrome), mixed anaerobes, Arcanobacterium haemolyticum.

Fungal. Candida (oropharyngeal candidiasis) — common in infants and steroid inhalers; mucormycosis.

Other (rarer but it doesn't mean not serious) causes of sore throat:

- Haemophilus influenzae (causes epiglottitis);
- Moraxella catarrhalis (causes sinusitis);
- Staphylococcus aureus (rare);
- syphilis (rare);

- varicella (chicken pox);
- chronic sinusitis with postnasal drip;
- tonsilloliths;
- cricopharyngeal spasm;
- Kawasaki disease;
- chronic mouth breathing;
- thyroiditis;
- glossopharyngeal neuralgia;
- aphtous ulcers;
- peritonsillar abscess (quinsy);
- pharyngeal/retropharyngeal abscess;
- Vincent angina;
- trauma, foreign body (e. g. fish bone) – especially in children;
- scleroderma;
- Behçet disease;
- Sarcoidosis;
- malignant granuloma (granulomatosis with poliangitis — also known as Wegener's granulomatosis);
- tuberculosis;
- spinal problems (cervical spine);
- psychogenic causes — depression and/or anxiety;

Cardiovascular causes:

- angina (stable and unstable);
- myocardial infarction.

Neoplasia:

- cancer of oropharynx, tongue;
- blood dyscrasias (e. g. agranulocytosis, acute leukaemia).

Irritants:

- tobacco smoke, chemicals;
- antiseptic lozenges (oral use);
- reflux oesophagitis which may lead to pharyngolaryngitis.

The most usual cause is viral pharyngitis, which is self-limiting and usually requires only symptomatic treatment.

Red flags in patients with sore throat

- Persistence of symptoms longer than 1 week without improvement;
- Respiratory difficulty, particularly stridor (croup, etc.);
- Difficulty in handling secretions, drooling (peritonsillar abscess);
- Difficulty in swallowing (Ludwig's angina);
- Severe pain in the absence of erythema (supraglottitis/epiglottitis);
- Palpable mass (neoplasm);
- Blood in the pharynx or ear (trauma).

NON-SPECIFIC PHARYNGITIS

Definition, Epidemiology, Aetiology and Pathology

«Non-specific» here means pharyngitis which is self-limiting and usually requires only symptomatic treatment. Also see common cold chapter.

The cause is viral (respiratory viruses not causing generalized systemic illness, the same that are responsible for common cold), accounts for 50 % (in children) — to up to 90 % (in adults) of pharyngitis cases. Pharyngitis often occurs as a part of common cold presentation — pharyngitis associated with the common cold.

Clinical Presentation

It produces non-specific cold-like symptoms such as:

- fever (mild);
- mild to moderate pharyngeal discomfort: sore throat, scratchiness/irritation;
- cough;
- general malaise and myalgia;
- pharyngitis;
- conjunctivitis (especially if adenoviral — pharyngoconjunctival fever);
- often mimics bacterial infection;
- throat redness on examination and no exudates (fig. 10, 11);
- normal chest examimation.

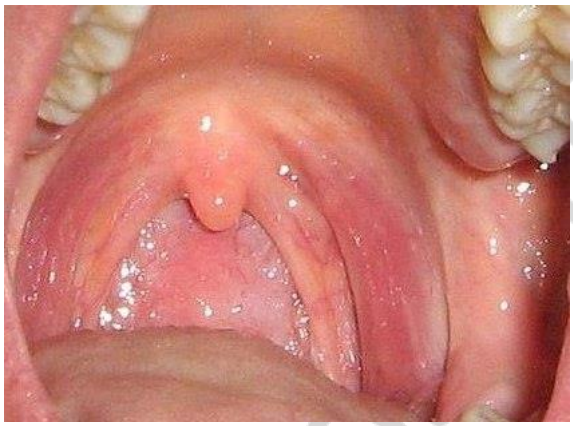

Fig. 10. Normal throat. James Heilman, MD. Cropped. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/ File:Amigdalas_(cropped).jpg

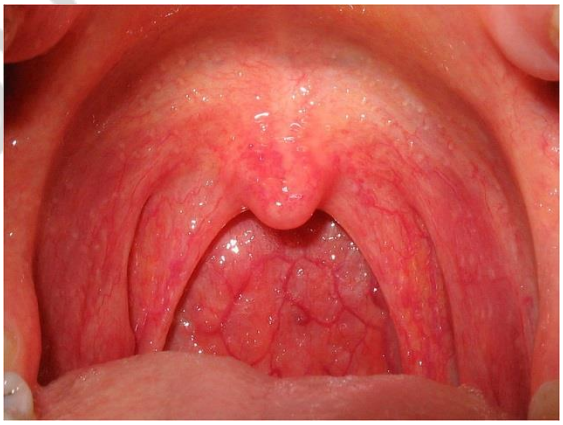

Fig. 11. Viral pharyngitis, the most common cause of a sore throat. Note the redness. Dake. Distributed under the Creative Commons Attribution-Share Alike 2.5 Generic license (https://creativecommons.org/licenses/by-sa/2.5/deed.en). https://commons.wikimedia.org/wiki/File:Pharyngitis.jpg

Management. See common cold chapter. Symptomatic treatment – paracetamol or NSAIDs for fever and muscle pain, decongestants. Antibiotics are not indicated.

STREPTOCOCCAL PHARYNGITIS AND TONSILLITIS (STREP THROAT)

Definition, epidemiology, aetiology

See definitions of tonsillitis and pharyngitis in definitions chapter from which it becomes clear that this infection may involve the pharynx only, the tonsils only or both tonsils and pharynx. May vary from mild to severe.

Streptococcal pharyngitis is caused by GABHS — also the most common cause of bacterial pharyngitis in general (bacterial pharyngitis is responsible for about 20 % of all cases of acute pharyngitis, it is responsible for up to 15 % of adult cases and up to 50 % of pediatric cases of acute pharyngitis). Tends to occur more often in late winter and early spring. Uncommon under 3 years or over 40–45 years – the peak incidence is 3–15 years of age.

Clinical presentation

The main diagnostic clinical features are (these are Modified Centor Criteria for GABHS, give one point for each feature present, see explanations in management section below):

- history of fever ≥ 38 °C;
- tender anterior cervical lymphadenopathy (enlarged lymph nodes);
- tonsillar exudate and/or swelling (fig. 12, 13);
- absence of cough;
- age 3–14 years (a point is subtracted if age is ≥ 45).

Note: these criteria are not applicable to patients < 3 years of age and during epidemic of GABHS-induced illness in the community.

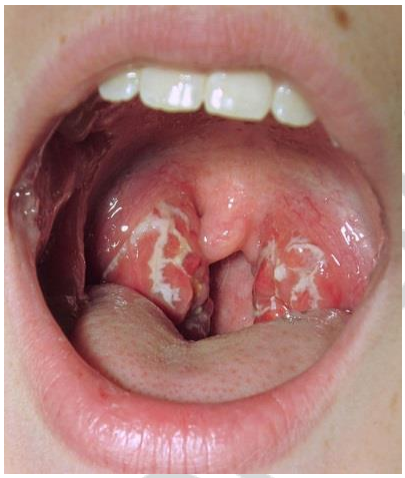

Fig. 12. A culture positive case of streptococcal pharyngitis with typical tonsillar exudate in a 16-year-old. James Heilman, MD. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en).https://commons.wikimedia.org/wiki/File:Pos_strep.jpg

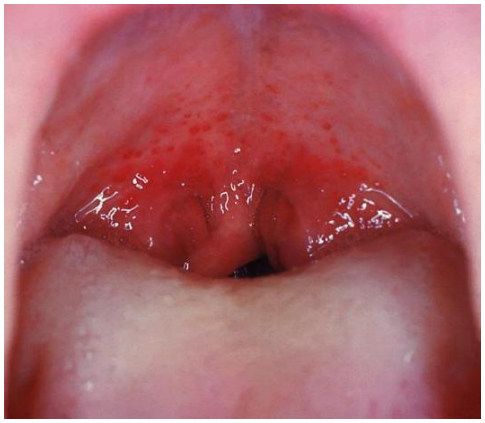

Fig. 13. Mouth wide open showing the throat. Note the petechiae, or small red spots, on the soft palate. This is an uncommon but highly specific finding in streptococcal pharyngitis. CDC/ Heinz F. Eichenwald, MD. https://phil.cdc.gov/details.aspx?pid=3183 https://commons.wikimedia.org/wiki/File:Streptococcal_pharyngitis.jpg

Other symptoms include:

- paharyngeal difficulty in swallowing, paharyngeal dyscomphort/pain on swallowing;
- significant local pain, including pain on talking;
- foul-smelling breath;
- malaise, headache;
- nausea, vomiting, abdominal pain — especially among children.

Treatment and Management

According to Modified Centor Criteria:

- **0–1 points**: no culture and no antibiotics are required;
- **2–3 points**: culture all patients, treat with antibiotics only if culture returns positive; it shoud be noted that treating with antibiotics in case 3 points are present is recommended by some authorities even without culture results;
- **4–5 points**: culture all patients, treat with antibiotics, discontinue antibiotics if culture returns negative.

Table 3

Antibiotic regimens recommended for GABHS pharyngiris

Antibiotic	Route	Dose	Duration
Phenoxymethyl penicillin (also known as penicillin V)	Oral	< 20 kg: 250 mg two times daily ≥ 20 kg: 500 mg two times daily	10 days
Amoxicillin*	Oral	25 mg/kg/dose (max 500 mg) twice daily or 50mg/kg (max 1g) once daily	10 days
Benzathin penicillin G**	IM	< 20kg: 450 mg (600,000 U) ≥ 20kg: 900 mg (1,200,000 U)	Single dose
For individuals with penicillin allergy, especially anaphylaxis			
Clindamycin	Oral	7 mg/kg/dose (max 300 mg) 3 times daily	10 days
Azithromycin***	Oral	Children: 12mg/kg/dose (max 500 mg) once daily Adults: 500 mg once daily	5 days
Clarithromycin***	Oral	7.5 mg/kg/dose (max 250 mg) twice daily	10 days

*Amoxicillin — second line therapy for improved compliance. Some authorities say that amoxicillin should be avoided in patients with tonsillitis because in case of infectious mononucleosis, which may look similar to streptococcal tonsillitis, it causes severe rash in 90 % of cases, see mononucleosis chapter. May consider it second line therapy for improved compliance in case given 1g once daily.

**Benzathine Penicillin G – useful in poorly compliant patients.

***Azithromycin, Clarithromycin — resistance of GABHS to these agents is well-known and varies geographically and temporally.

Antibiotic treatment of strep throat (table 3):

- decreases severity and shortens the duration of symptoms;
- reduces risk of transmission (after 24 hours of treatment) to close contacts (e. g. family members, classmates);
- reduces risk of rheumatic fever, delay in antibiotic treatment for up to 48 hours does not increase the incidence of rheumatic fever;

- may prevent development of suppurative complications;
- does not protect against glomerulonephritis.

Note: although most symptoms and signs usually disappear within 1–2 days after treatment is commenced, a full 10-day course of antibiotics should be given to provide an optimal chance of eradicating GABHS from the nasopharynx and thus minimising the risk of recurrence and/or complications such as rheumatic fever and suppurative complications.

Some studies indicate that 5–7 days may be sufficient and some recent recommedations say that antibiotics may not be necessary in many patients with suspected group A streptococcal pharyngitis and are mostly recommended for high-risk groups (those with personal or family history of rheumatic fever or rheumatic heart disease or some population groups, e. g. Indigenous Australians or immunocompromised) of children to prevent non-suppurative complications of GABHS infection.

Other than antibiotics the treatment is symptomatic, refer to Common Cold chapter again. Adequate hydration is important.

Complications. Scarlet fever, rheumatic fever, glomerulonephritis, suppurative complications (abscess, sinusitis, otitis media, cervical adenitis, pneumonia), meningitis, impetigo, cervical vein, e. g. jugular vein thrombosis — Lemierre syndrome).

Investigations.

1. In case of suspected GABHS:

- throat culture is a gold standard for diagnosis
- rapid test for streptococcal antigen may also be used: has high specificity (95 %) but low sensitivity (50–90 %).

A positive culture and a fourfold rise in the ASO titre are necessary for a precise diagnosis.

2. If suspicious for EBV (infectious mononucleosis):

- peripheral blood smear, heterophile antibody test (i.e. the latex agglutination assay or «monospot»). See also investigations chapter above.

Some recent guidelines say that throat cultures, though being the gold standard of diagnosis, generally are not necessary except to verify the presence of S. pyogenes, especially in closed institutions such as boarding schools, or if diphtheria is suspected in the non-immunised.

Follow-Up. Routine follow-up and/or post-treatment throat cultures are not required for most patients. They are usually recommended only for high-risk groups.

Main Differentials of Strep Throat. EBM, virals and diphtheria (see corresponding topics above and below).

JUGULAR VEIN THROMBOSIS (LEMIERRE SYNDROME)

Acute septicaemia and jugular vein thrombosis secondary to infection with Fusobacterium species + septic emboli (to lungs, bones, muscles, kidneys, liver). Rare but dangerous and possible complication.

SCARLET FEVER

Definition, Epidemiology, Aetiology and Pathology. Scarlet fever results when a Group A Streptococcus pyogenes organism produces erythrogenic toxin (delayed-type hypersensitivity reaction).

Clinical Presentation. The prodromal symptoms prior to acute exanthema (diffuse erythematous rash) comprise:

- sore throat
- fever (may be rigors)
- malaise
- Pastia lines (= Thompson's sign, see below)
- vomiting

A throat swab should be taken (fig. 14–16) if rash and symptoms present.

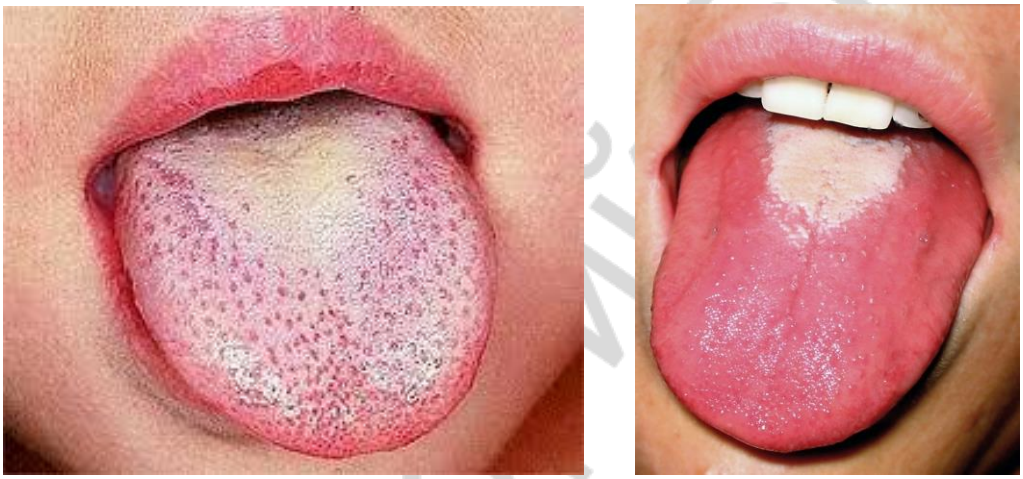

Fig. 14. Two examples of strawberry tongue which is a characteristic of scarlet fever. Afag Azizova. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Skarlatina.jpg Martin Kronawitter. Distributed under the Creative Commons Attribution-Share Alike 2.5 Generic license (https://creativecommons.org/licenses/by-sa/2.5/deed.en). https://commons.wikimedia.org/wiki/File:Scharlach.JPG

Features of the rash:

- appears 12–24 hours after the start of the fever;
- first appears on the neck;
- rapidly becomes generalized;
- punctate and red, a «boiled lobster» or sunburnt appearance;
- blanches on pressure;
- prominent on neck, in axillae, cubital fossa (Pastia lines), groin, skinfolds;
- absent or sparse on face, palms and soles;
- circumoral pallor (area around the mouth is spared from rash);
- feels like fine sandpaper;
- lasts about 5 days;
- fine desquamation.

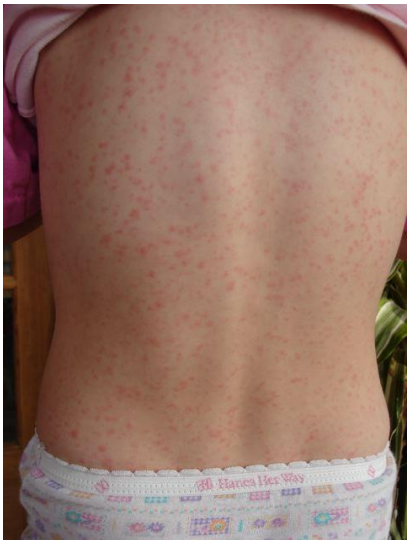

Fig. 15. The rash of scarlet fever. ToNToNi. Distributed under the Creative Commons Attribution-Share Alike 2.5 Generic license (https://creativecommons.org/licenses/by-sa/2.5/deed.en). https://commons.wikimedia.org/wiki/File:Scarlet_fever_2.jpg

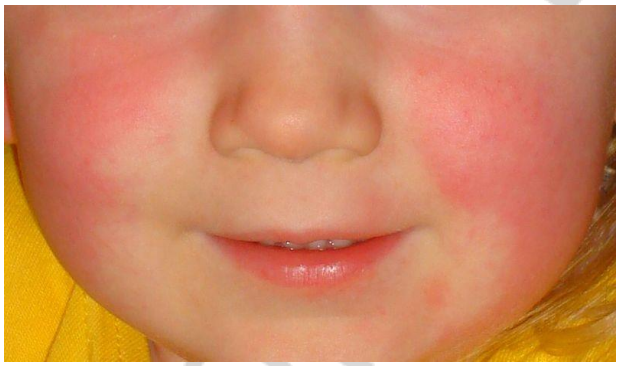

Fig. 16. Red cheeks and pale area around the mouth in scarlet fever (https://commons.wikimedia.org) Red cheeks and pale area around the mouth in scarlet fever. Alicia Williams. Distributed under the Creative Commons Attribution-Share Alike 4.0 International license (https://creativecommons.org/licenses/by-sa/4.0/).https://commons.wikimedia.org/wiki/File:Scarlet_fever_1.1.JPG

Treatment. Phenoxymethylpenicillin (dose according to age) for 10 days promotes rapid resolution of symptoms. Children can return to school 24 hours after starting taking antibiotics and feeling well.

ACUTE RHEUMATIC FEVER

***Definition, Epidemiology, Aetiology and Pathology*.** Rheumatic fever is a systemic inflammatory disorder that typically occurs in children and young adults following a group A Streptococcus pyogenes infection. It is common in developing countries and among some populations (e. g. Indigenous Australians have the highest prevalence in the world) but increasingly uncommon in first world countries. Affects ~1 : 10,000 children in the developed world; more prevalent in developing nations; peak incidence is observed at 5–15 years of age.

Tends to recur unless prevented. Pharyngeal infection with Lancefield group A beta-haemolytic streptococci may trigger rheumatic fever 2–4 weeks later, in the

susceptible 2% of the population. An antibody to the carbohydrate cell wall of the streptococcus cross-reacts (antibody cross-reactivity) with valve tissue (antigenic mimicry) and may cause permanent damage to the heart valves.

Clinical Presentation:

- young persons 5–15 years (can be older);
- acute-onset fever, joint pains, malaise;
- flitting (one joint settles as the other is affected) arthralgia mainly in the legs (knees, ankles) and arms (elbows and wrists);
- may follow a sore throat.

However, symptoms depend on the organs affected and arthritis may be absent. The diagnosis is based on clinical criteria — revised Jones criteria (may be over-rigorous): 2 or more major criteria or 1 major and 2 or more minor are required PLUS the presence of supporting evidence of preceding Group A streptococcal infection:

- positive throat culture (usually negative by the time RF symptoms appear);
- positive rapid streptococcal antigen test;
- elevated or rising streptococcal antibody titre (eg anti-streptolysin O (ASO) or DNase B titre);
- recent scarlet fever.

Major criteria:

- carditis: tachycardia, murmurs (mitral or aortic regurgitation, Carey Coombs' murmur), pericardial rub, CHF, cardiomegaly, conduction defects (45–70 %). An apical systolic murmur may be the only sign;
- arthritis: a migratory, «fleeting» polyarthritis; usually affects larger joints (75 %);
- subcutaneous nodules: small, mobile, painless nodules on extensor surfaces of joints and spine (2–20 %);
- erythema marginatum: see fig. 17, geographical-type rash with red, raised edges and clear centre; occurs mainly on trunk, thighs and arms.
- Sydenham's chorea (St Vitus' dance): occurs late in 10%. Unilateral or bilateral involuntary semi-purposeful movements. May be preceded by emotional lability and uncharacteristic behaviour.

Minor criteria:

- fever ($\geq$ 38 °C);
- raised ESR or CRP. ESR > 30 mm/hr or CRP > 30 mg/L;
- arthralgia (but not if arthritis happens to be one of the major criteria);
- prolonged ($\geq$ 200 ms) PR interval on ECG (but not if carditis is one of the major criteria);
- previous rheumatic fever.

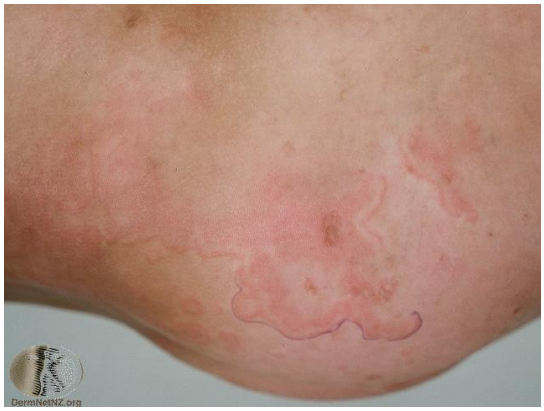

Fig. 17. Erythema marginatum. It occurs in less than 2-10% of patients with rheumatic fever, but is considered a major Jones criterion when it does occur. © DermNet New Zealand. Distributed under the licensing requirements of Creative Commons Attribution-NonCommercial-NoDerivs 3.0 (New Zealand) (https://creativecommons.org/licenses/by-nc-nd/3.0/nz/legalcode). https://www.dermnetnz.org/topics/rheumatic-fever/ https://www.dermnetnz.org/imagedetail/3284?copyright=&label

***Investigations*.** A selective combination of:

- FBC;
- throat swab;
- ESR;
- streptococcal ASOT;
- streptococcal anti-DNase B (repeated in 10–14 days);
- C-reactive protein;
- ECG and echocardiogram (if ECG shows increased PR interval) and CXR.

Complications. Acute: myocarditis, conduction system aberrations (sinus tachycardia, atrial fibrillation), valvulitis (acute MR), pericarditis.

Chronic: valvular heart disease — onset of symptoms usually after 10-20 year latency (mitral and/or aortic insufciency/stenosis), infectious endocarditis ± thromboembolic phenomenon

Prognosis. 60 % of patients with carditis develop chronic rheumatic heart disease. This correlates with the severity of the carditis. Acute attacks last an average of 3 months. Recurrence may be precipitated by further streptococcal infections, pregnancy, or use of the oral contraceptive pills. Cardiac sequelae affect mitral (70 %), aortic (40 %), tricuspid (10 %), and pulmonary (2 %) valves. Insufficiency lesions develop during the attack, valve stenoses occur years or even decades later.

Management:

- bed rest until CRP is normal for 2 weeks (may take up to 3 months).
- benzylpenicillin 0.6–1.2 g IV statim, then phenoxymethylpenicillin 250–500 mg 4 times daily PO for 10 days (if the patient is allergic to penicillin, give erythromycin or azithromycin for 10 days).
- analgesia for carditis/arthritis: aspirin 100 mg/kg/day PO in divided doses (mac 4–8 g/day) for 2 days, then 70 mg/kg/day for 6 weeks. Monitor salicylate level. Toxicity causes tinnitus, hyperventilation, and metabolic acidosis, mind also risk of Reye syndrome in children less than 16 years of age. Alternative: other NSAIDS.

If moderate-to-severe carditis is present (cardiomegaly, CHF or 3rd-degree heart block), add oral prednisolone to salicylate therapy. In case of heart failure, treat appropriately, surgery may be required in case of severe heart valve disease.

- immobilize joints in severe arthritis.
- haloperidol (0.5 mg/8 hours PO) or diazepam for the chorea.

Prevention. Primary*:* where incidence is high, this might be worthwhile, but might entail giving IM penicillin for sore throats, see strep throat part.

Secondary*:* Symptoms are often worse on recurrence of rheumatic fever—seen in 2.6 %. Prevent with phenoxymethylpenicillin 125 mg twice daily if < 6 years; 250 mg twice daily if > 6 years, though evidence to support long term antibiotics is poor. PANDAS *(*paediatric autoimmune neuropsychiatric disorders associated with strep infections*)* may be suspected in those with tics (or Tourette's syndrome) and obsessive–compulsive disorder. Anorexia nervosa may also be a feature. Antibiotics and risperidone may be tried.

PERITONSILLAR ABSCESS (QUINSY), PARAPHARYNGEAL ABSCESS

Definition, Epidemiology, Aetiology and Pathology.

Begins as cellulitis of peritonsillar area behind the tonsil (peritonsillitis) leading to abscess:

Usually caused by GABHS (up to 50% of cases) or anaerobes, occasionally by S. aureus, H. infuenzae.

Can develop from acute tonsillitis with infection spreading into peritonsillar area. Unilateral (though exceptions may exist).

Unlike tonsillitis, which is more common in the children, PTA has a more even age spread, from children to adults, most often happens in 15–30 year age group.

Clinical Features

Peritonsillar abscess follows follows a typical presentation of tonsillitis. Symptoms start appearing 2 to 8 days before the formation of an abscess.

- very sore throat;
- marked swelling of the peritonsillar area (peritonsillar bulge) with medial displacement of tonsillar tissue (but tonsil may appear normal) (fig. 18);
- trismus (due to irritation of the medial pterygoid muscle and which results in refex spasm) is the most reliable indicator of peritonsillar abscess;
- fever and dehydration;
- dysphagia and odynophagia;
- oedema of soft palate;
- muffled voice, dysphonia (oedema → failure to elevate the palate) secondary to CN X involvement («hot potato voice»);
- uvular deviation;
- unilateral referred otalgia;
- cervical lymphadenitis.

Quinsy Triad:

- Trismus;
- Uvular deviation;
- Dysphonia — «hot potato voice»

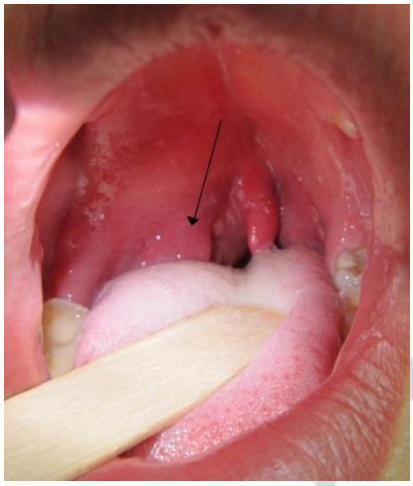

Fig. 18. Right sided peritonsillar abscess (https://creativecommons.org/licenses/by/3.0/deed.en) https://commons.wikimedia.org/wiki/File:PeritonsilarAbsess.jpg

Complications. Aspiration pneumonia secondary to spontaneous rupture of abscess, airway obstruction, lateral dissection into parapharyngeal and/or carotid space, bacteremia, retropharyngeal abscess.

Treatment:

- secure airways
- surgical drainage (incision or needle aspiration — preferred to surgical drainage) under local anaesthetic with C&S
- warm saline irrigation
- antibiotics: IV/ IM procaine penicillin (Oral penicillin treatment is likely to fail) for 10 days if cultures positive for GAS + add PO/IV metronidazole or clindamycin x 10 d if culture positive for Bacteroides.

Subsequent tonsillectomy may, but not always, be necessary — consider it afer second episode.

Parapharyngeal abscess. May occur standalone or as a complication (rare but serious) of peritonsillar abscess. Presents with diffuse swelling in the neck. Ultrasound is used to identify the site, than the abscess is incised and drained under general anaesthesia.

MONONUCLEOSIS AND EBM (EBSTEIN-BARR MONONUCLEOSIS)

Definition, Epidemiology, Aetiology and Pathology

This is a systemic viral infection caused by EBV (a member of herpesviridae) with multivisceral involvement; it is often called «the great imitator» because it can

mimic many diseases, including serious ones, such as HIV primary infection, streptococcal tonsillitis, viral hepatitis and acute lymphatic leukaemia. Other names include glandular fever, kissing disease.

Mononucleosis can also be caused by HHV-5(CMV), in this case monospot will be negative (see about monospot below).

EBM has an annual incidence of 4–5 new cases in a population of 2500. It may occur at any age but usually between 10 and 35 years; it is commonest in 15–25 year age group with the peak incidence being between 15–19 years. It is endemic in most countries, affecting over 95 % of the adult population worldwide.

EBV is excreted in oropharyngeal secretions during the illness and for some months (sometimes years) after the clinical infection, though the virus itself is never eliminated from the body. EBM has a low infectivity and isolation of the patient is not necessary. It is apparently transmitted only by close contact, such as kissing (hence is the name «kissing disease»), sharing drinking utensils and sexual activity (less commonly).

Progress of the primary infection is checked partly by specific antibodies (which might prevent cell-to-cell spread of the virus) and partly by a cellular immune response, involving cytotoxic T-cells (which are actually atypical mononuclear cells, not B lymphocytes affected by the EBV), which eliminate the infected cells. This response accounts for the clinical picture.

Second attacks and fatalities do occur and there is a possible association between EBM and lymphoma.

Risk factors include infectious contacts, being sexually active and multiple sexual partners in the past.

Clinical Features. Subclinical infection is common in young children — 50 % of children in developed countries have a primary EBV infection by 5 years, which is usually asymptomatic, < 10 % of children develop clinical infection, while about 50 % of adults develop classical (sore throat, fever, anorexia, lymphadenopathy and others) symptoms in case of primary infction.

The incubation period is at least 1 month (1–2 months) but the data are insufficient to define it accurately.

There are three forms: the febrile (with fever), the anginose (with a sore throat) and the glandular (with lymphadenopathy). The «clinical reality» though is not so precise and various combinations and overlaps of these presentations occur.

The prodrome is characterized by: 2–7 days of malaise, up to 6 weeks of slow-onset malaise.

Classic triad:
febrile temperature, generalized non-tender lymphadenopathy, sore throat with pharyngitis/tonsillitis (exudative, but not purulent, though looks like it)

Clinical features are:

- sore throat (85 %);
- malaise, fatigue, fever, myalgia;

- blocked nose which leads to mouth breathing;
- nasal quality to voice;
- headaches;
- nausea ± vomiting , dyspepsia, anorexia;
- rash — primary in 5 %;
- abdominal pain (often LUQ), probably because of spleen enlargement;
- periorbital oedema;
- exudative pharyngitis (84 %) (fig. 19);
- petechiae of the palate (not pathognomonic for EBM) (11 %);
- lymphadenopathy, especially posterior cervical (bull's neck appearance, see fig. 20);
- splenomegaly (50 %);
- jaundice ± hepatomegaly (5–10 %);
- clinical or biochemical evidence of hepatitis;
- any «-itis» (including arthritis, hepatitis, nephritis, myocarditis, meningitis, encephalitis, etc.);
- rash: maculopapular, can be urticarial or petechial – more common after inappropriate treatment with β-lactam antibiotics.

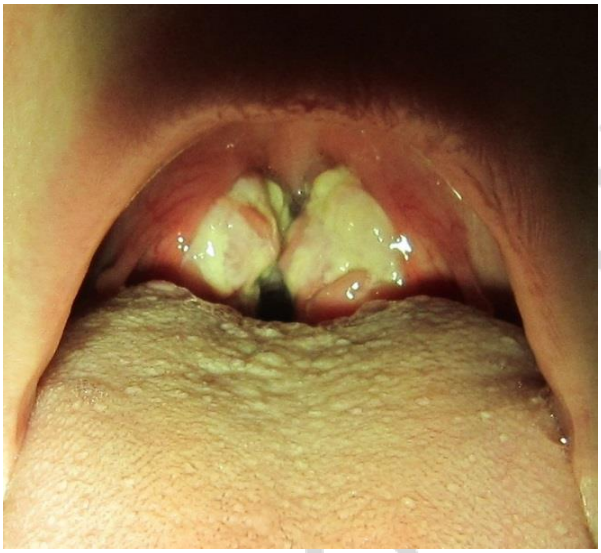

Fig. 19. Exudative pharyngitis in a person with infectious mononucleosis. Compare with streptococcal pharyngitis (see above). James Heilman, MD. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Mononucleosis.JPG

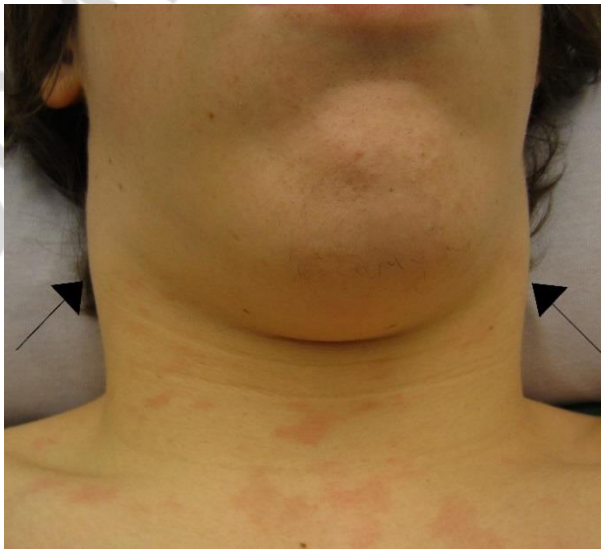

Fig. 20. Swollen lymph nodes in the neck of a person with infectious mononucleosis. James Heilman, MD. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Lymphadanopathy.JPG

The anginose form of EBM is a real trap and must be considered in patients aged 15–25 years (peak incidence) with a painful throat that takes about 7 days to reach its peak.

Clinical features include:

- sore throat;
- prodromal fever, malaise, lethargy;
- anorexia, myalgia;
- nasal quality to voice;
- skin rash;
- petechiae on palate (not pathognomonic);
- enlarged tonsils with or without white exudates (looks like, but isn't purulent);
- periorbital oedema;
- lymphadenopathy, especially posterior cervical lymphadenopathy;
- splenomegaly (50 %);
- jaundice ± hepatomegaly (5–10 %).

The rash of EBM is almost always related to antibiotics given for tonsillitis. The primary rash, most often non-specific, pinkish and maculopapular (similar to that of rubella), occurs in about 5 % of cases only. The secondary rash is most often precipitated by one of the penicillins, especially ampicillin or amoxycillin. About 90–100 % of patients prescribed ampicillin or amoxycillin will be affected; up to 50 % of those given penicillin will develop the rash. It can be extensive and sometimes has a purplish tinge. Macrolides shoud not cause rash. The beta-lactam related rash is not hypersensitivity — not an allergic rash, though looks very similar.

Investigations and Diagnosis. The following laboratory tests confirm the diagnosis of EBM:

- FBC: WCC shows absolute lymphocytosis
- blood film shows atypical lymphocytes — Downey cells (these are T, not B-lymphocytes (large, irregular nuclei), they also occur in other viral infections (CMV, HIV, parvovirus, dengue), toxoplasmosis, typhus, leukaemia, lymphoma, drug reactions, lead poisoning.
- Paul–Bunnell or Monospot test for heterophil antibody is positive (although positivity can be delayed or absent in 10% of cases). The test is 85-90% sensitive in adults and older children, but only 50% sensitive in children <4 years of age. False-positives for the Paul-Bunnell an Monospot may occur in case of HIV, SLE, lymphoma and other blood malignancies, rubella, parvovirus, pregnancy
- reverse transcriptase viral PCR
- throat culture to rule out streptococcal pharyngitis

The diagnosis is confirmed (if necessary) by EBV-specific antibodies, viral capsule antigen (VCA) antibodies—IgM in acute infection, IgG in case of previous infection (**G** if infection is **G**one) and EB nuclear antigen (EBN-A), but tests for specific viral antibodies and culture for EBV are not done routinely.

Management, Treatment:

- supportive measures (no specific treatment);
- rest (the best treatment) during the acute stage, preferably at home and indoors;

- NSAIDs or paracetamol to relieve discomfort, including throat discomfort;
- gargling the throat soluble aspirin, 30 % glucose or saline to soothe the throat;
- avoiding alcohol, fatty foods, continued activity, especially contact sports (risk of splenic rupture because of enlarged spleen — splenic enlargement is often not clinically apparent so all patients should avoid contact sports for 6–8 wk);
- ensuring adequate hydration;
- corticosteroids are not recommended for uncomplicated cases, reserved for: neurological involvement, thrombocytopenia, threatened airway obstruction — if airway obstruction secondary to nodal and/or tonsillar enlargement is present (especially in younger children) the patient is to be admitted for steroid therapy.

Acyclovir DOES NOT reduce duration of symptoms and DOES NOT result in earlier return to school/work.

Prognosis. EBM usually has an uncomplicated course over 6–8 weeks. Major symptoms subside within 1–3 weeks. Patients should be advised to take about 4 weeks off work.

Post-EBM malaise. Some young adults remain debilitated and depressed for some months. Lassitude and malaise may extend up to a year or so.

Complications. Early complications of EBV: splenic rupture, Guillain-Barré syndrome, antibiotic-induced skin rash. Common later complications are: prolonged debility (see above), hepatitis, depression.

Rare complications.

Cardiac: myocarditis, pericarditis.

Haematological: agranulocytosis, haemolytic anaemia, thrombocytopenia.

Respiratory tract: upper airway obstruction (lymphoid hypertrophy).

Neurological: cranial nerve palsies, especially facial palsy, meningoencephalitis, transverse myelitis.

HERPANGINA (HAND, FOOT AND MOUTH (HFM) DISEASE)

Definition and General Information. HFM diseases is a rather uncommon infection caused mainly by Coxsackievirus A16 or enterovirus 71, which is less common (suspect it in outbreaks with herpangina, meningitis, flaccid paralysis ± pulmonary oedema), sometimes coxsackievirus B. HFM disease affects both children and adults but typically children under the age of 10. Sometimes referred to as «crèche disease», it often occurs among groups of children in child care centres. Transmission is through respiratory secretions, touch contact with the blistered areas or faecooral transmission (hand washing after changing nappies is important to reduce transmission). HFM has seasonal pattern — primarily occurs in late summer and early autumn. This has nothing to do with the bovine form.

Clinical presentation:

- incubation period lasts 3–7 days;

- initially fever, headache and malaise, may be abdominal pain, nausea and vomiting;
- sore mouth and throat (pharyngitis);
- the rash appears after 1 or 2 days, starts as a red macule, then progresses to vesicles;
- vesicles rupture and ulcerate, lead to shallow ulcers on buccal mucosa, gums and tongue, soft palate, tonsils, pharynx. Ulcers are pale grey and several mm in diameter (fig. 21);
- ulcers and vesicles are greyish with surrounding erythema;
- vesicles and later ulcers may appear on hands, palms and soles (usually lateral borders);
- may appear on limbs especially buttocks and genitals;
- lesions resolve in 1–5 days;
- healing of lesions occurs without scarring;
- the virus is excreted in faeces and saliva for several weeks;
- children are infectious until the blisters have disappeared;
- diagnosis is clinical, investigations are usually unnecessary.

Management. The treatment of HFM is symptomatic:

- reassurance and explanation;
- careful hygiene;
- exclusion until blisters have dried up.

Transmission is through respiratory secretions, touch contact with the blistered areas or faecooral transmission — hand washing after changing nappies is important to reduce transmission.

HERPES SYMPLEX PHARYNGITIS

Clinical Presentation. In adults primary infection is similar to severe streptococcal pharyngitis: pharyngitis, tonsillar exudate, fever, lymphadenopathy, fatigue. Ulcers and vesicles appear but extend beyond the tonsils, looks like Coxsackie virus but ulcers are usually fewer and larger (fig. 21, 22).

Herpex simplex gingivostomatitis: fever, sore throat followed by tender oropharyngeal vesicles, also on gingives, palate.

Viruses multiply in epithelial cells of mucosal surface producing vesicles or ulcers. Lifelong latent infection occurs when virus enters sensory neurons at infection site. The virus can then reactivate, replicate, and infect surrounding tissue.

Treatment. Aciclovir decreases symptoms and viral load, will not prevent latent infection.

May cause herpes simplex virus encephalitis — so give empirical IV aciclovir as soon as HSV encephalitis is suspected!

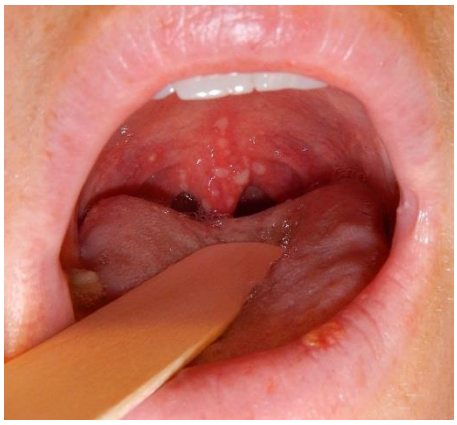

Fig. 21. An example of herpangina in a child. James Heilman, MD. Distributed under the Creative Commons Attribution-Share Alike 4.0 International license (https://creativecommons.org/licenses/by-sa/4.0/). https://commons.wikimedia.org/wiki/File:Herpangina2016.jpg

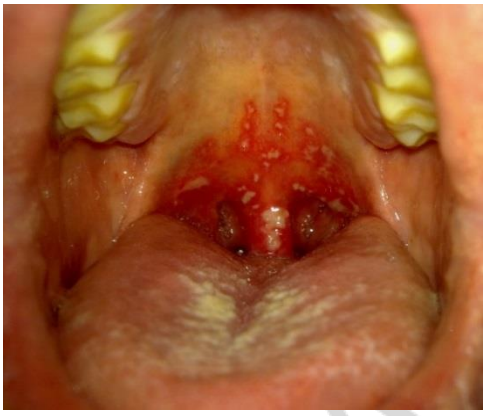

Fig. 22. Herpetic stomatitis (herpetic gingivostomatitis). Klaus D. Peter. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/ wiki/File:Stomatitis_herpetica.jpg

DIPHTHERIA

Definition and Aetiology. Diphtheria is caused by bacterium Corynebacterium diphtheriae, more precisely by the toxin of Corynebacterium diphtheriae, may be potentially fatal and such form of this disease almost always occurs in non-immunised people. Diphtheria is usually spread by direct contact or through the air.

Preventable with vaccine, although immunization does not give 100 % protection.

Risk of diphtheria is increased if the patient is homeless/refugee, aged 3–6 years old, in «asocial» families, if unvaccinated.

Clinical features. The clinical presentation may be modified by previous immunisation or by antibiotic treatment. It usually starts with tonsillitis ± a false membrane over the fauces. Diphtheria is carachterized by:

- insidious onset;
- mild to moderate fever;
- mild sore throat and dysphagia;
- muffled voice;
- patient looks pale and ill;
- enlarged tonsils;
- inflamed and oedematous pharynx;
- pseudomembrane (which can be of any colour but usually greyish–green) can spread beyond tonsils to the fauces, soft palate, lateral pharyngeal wall and downwards to involve the larynx (fig. 23);
- enlarged cervical lymph nodes;
- soft tissue swelling of the neck — «bull neck» appearance (fig. 24);
- airway obstruction preceded by a brassy cough (laryngotracheal diphtheria);
- nasal discharge with an excoriated upper lip (nasal diphtheria).

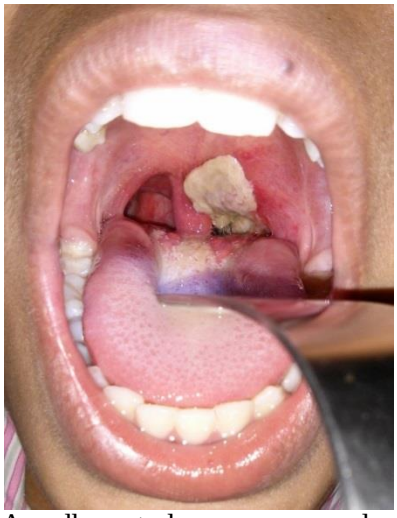

Fig. 23. An adherent, dense, grey pseudomembrane covering the tonsils is classically seen in diphtheria. Dileepunnikri. Distributed under the Creative Commons Attribution 3.0 Unported license https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Dirty_white_pseudomembrane_classically_seen_in_diphtheria_2013-07-06_11-07.jpg

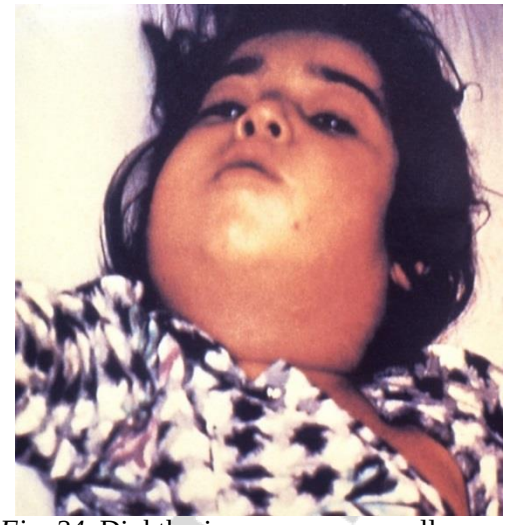

Fig. 24. Diphtheria can cause a swollen neck, sometimes referred to as a bull neck. CDC. https://phil.cdc.gov/details.aspx?pid=5325 https://commons.wikimedia.org/wiki/File:Diphtheria_bull_neck.5325_lores.jpg

Other signs: the toxin may cause polyneuritis which often starts with cranial nerves. Motor palatal paralysis also occurs causing fluids to escape from the nose on swallowing. Shock may occur from myocarditis, toxaemia, or cardiac conducting system involvement. Bronchopneumonia may happen.

If there is tachycardia out of proportion to fever, suspect toxin-induced myocarditis — do frequent ECGs.

Investigations and Diagnosis. Culture — throat swab (swab culture of material below pseudomembrane), toxin detection, PCR.

Treatment and Management:

- diphtheria antitoxin within 48 h 10 000–30 000U IM (any age; more if severe);
- penicillin or erythromycin (also syrup) 500 mg qid for 10 days, give contacts 7–10 days course of erythromycin syrup: < 2 years old 125 mg per 6 hours PO (500 mg per 6 hours if > 8 years) before swab results are known;
- isolate patient until 3 negative cultures separated by 48h.

LUDWIG'S ANGINA

Ludwig's angina is a medical emergency. It's a type of severe cellulitis which develops rapidly and involves the floor of the mouth (sublingual and submandibular spaces) without abscess formation (fig. 25). It is often caused by root canal infection — in up to 90 % of cases. Mandible fractures, oral ulcers and other oral cavity infections, immune deficiency states (diabetes, HIV) may also increase the risk of this condition.

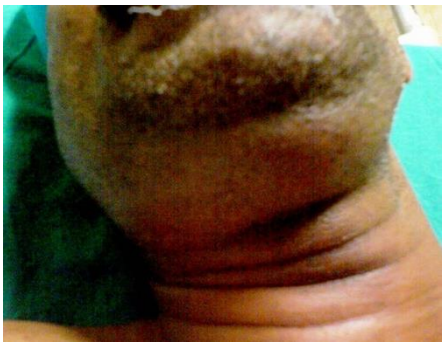

Fig. 25. Mouth floor swelling (swelling in the submandibular area) in a person with Ludwig's angina. Anand H. Kulkarni, Swarupa D. Pai, Basant Bhattarai, Sumesh T. Rao and M. Ambareesha. Distributed under the Creative Commons Attribution 2.0 Generic license (https://creativecommons.org/licenses/by/2.0/deed.en). https://casesjournal.biomedcentral.com/articles/10.1186/1757-1626-1-19 https://commons.wikimedia.org/wiki/File:Ludwig_angina.jpg

Early in the course of the disease the floor of the mouth is raised and there is difficulty swallowing saliva, which may run from the person's mouth. As the swelling increases and condition worsens, the airway may be compromised – this is potentially life-threatening. This condition resembles an abscess and should be treated accordingly.

Treatment: immediate specialist consult, test for culture and sensitivity, empiric antibiotics: IV amoxicillin + IV metronidazole.

POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

This is the commonest cause of nephritic syndrome in children. Usually seen in children 4–8 years of age, more frequently in males, usually occurs 1–3 weeks or sometimes up to 6 weeks after streptococcal infection, usually that of the throat, also skin, e. g. impetigo, skin sores, scabies (causes infected skin sores that carry streptococcus). Incidence of APSGN has decreased over last decades, but it is still may present a problem in socially disadvantaged populations.

Mechanism: complement activation mediated by immune complexes (antigen-antibody, in this case streptococcal antigen) — type 3 hypersensitivity reaction, complexes deposition along GBM and mesangium leads to inflammation.

Clinical features. Postreptococcal glomerulonephritis is a nephritic-spectrum glomerulonephritis, hence nephritic syndrome presentation, though not all features may be present and severity may vary – from almost asymptomatic subclinical cases to classical nephritic syndrome presentation:

- haematuria: microscopic and macroscopic («coca-cola urine», «coke» urine (fig. 26);
- urine output is decreased (usually resolves in 2–3 days);
- oedema, usually peri-orbital, better seen on waking, also legs, scrotum, abdomen, usually resolves in 5–10 days;
- oedema leading to weight gain;

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Fig. 26. Haematuria. James Heilman, MD. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:HematuriaTrauma.JPG

- hypertension (may lead to complications), usually resolves in 4 days but may last for several weeks. Remember that in children hypertension cut-off is age-adjusted;
- haematuria, hypertension and oedema are main symptoms;
- malaise, anorexia, fever, child is irritable, lethargic;
- possible abdominal pain;

Subclinical case — recent Group A streptococcal infection and blood on urinalysis — but no oedema and no swelling.

Investigations. Urinalysis: proteinuria, haematuria, RBC casts, oliguria.

Blood: increased createnine and urea, decreased C3 and C4 (consumed by immune complex formation so that blood concentration decreases).

Renal biopsy is not usually required.

Diagnosis requires confirmation of recent streptococcal infection – at least one of the following: positive group A streptococcal culture from skin or throat, elevated ASO titre, anti-DNase B.

The disease is usually is self-limitary and long-term prognosis is very good — complete recovery usually achieved within 2 weeks, its rate is 95 %, though 5 % of patients retain persistent haematuria.

A case of poststreptococcal glomerulonephritis requires notification of infection control authorities (check local guidelines). Everybody who was present in patient's house in 2 weeks that preceded the case should be examined including BP, dipstick urine, presence of skin sores, scabies, culture of skin lesions if any. Contacts aged 1 to 16 years should receive prophylactic bicillin (other antibiotics in case of penicillin allergy), all other contacts should receive it if found to have infected skin sores.

Treatment and Management. The treatment is supportive: admission to hospital, especially if elevated BP, bed rest, Na+ and fluid restriction, daily weight and

fluid balance control, antihypertensives and loop diuretics (e.g. frusemide) for hypertension and oedema (as necessary), check blood pressure frequently, low protein diet during oliguria.

Give penicillin for 10 days (oral route is also possible). Persons allergic to penicillin should receive appropriate alternative treatment such as oral roxithromycin, or erythromycin for 10 days or TMP/SM for 5 days.

Dialysis may be required in severe cases when kidney function is significantly impaired.

Follow-up: monitor blood pressure, kidney function – urea, creatinine, ions, urinalysis (microscopic haematuria may be present for years).

In **a subclinical case** admission may not be necessary but it requires notification. Follow-up within 12 weeks with BP measurement, C3 and C4 levels, urinalysis and kidney function tests.

RHINOSINUSITIS

Definition, Aetiology and Pathology. Sinusitis (also termed rhinosinusitis, sinus inflammation, sinus infection) is an inflammation of the mucosal lining of the paranasal sinuses and nasal passages. Viral rhinosinusitis actually occurs as part of the presentation of the common cold.

Most common cause of acute sinusitis is viral infection — viral rhinosinusitis; this in turn may cause bacterial infection — acute (and possibly later chronic) bacterial rhinosinusitis. Children are more prone to bacterial rhinosinusitis. Maxillary sinus is affected most commonly.

The causing agents:

- viral: rhinovirus, influenza, parainfluenza and others;
- bacterial: the most common being Streptococcus pneumoniae (35 %), Haemophilus influenzae (35 %), Moraxella catarrhalis; other: Staphylococcus aureus, anaerobes (if infection comes from dental root scource);
- fungi — rare cause, but must rule out fungal causes (e. g. mucormycosis, see below).

Fungi – rare cause of sinusitis (though fungi can be isolated from the sinuses of almost every patient), but fungal causes must be ruled out (e. g. mucormycosis) particularly in immunocompromised hosts (especially if painless, black or pale area of mucosa on examination, also on palate).

Paranasal sinuses (fig. 27) all drain to the same area located in the middle and upper meatus — this area is called the osteomeatal complex (or osteomeatal unit).

Children under 4 years have not well-developed sinuses.

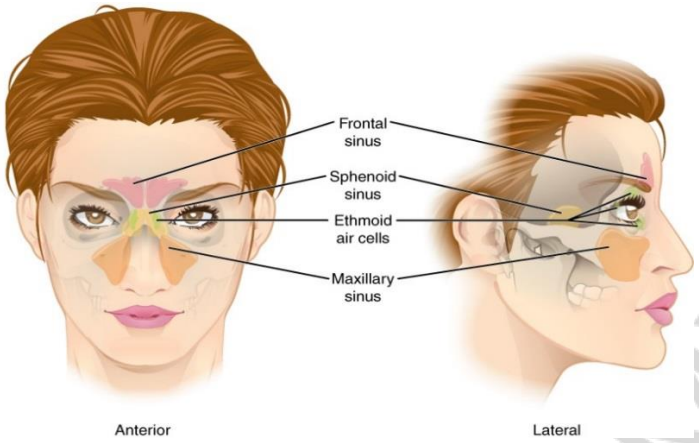

Fig. 27. Paranasal sinuses. OpenStax College. Anatomy & Physiology, Connexions Web site. Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). http://cnx.org/content/col11496/1.6/ https://commons.wikimedia.org/wiki/File:724_Paranasal_Sinuses.jpg

Epithelium which lines the nose and paranasal sinuses is ciliated and produces mucous. Mucous traps noxious particles and they get transported from the sinus to the nasopharynx by the action of the cilia — mucociliary clearance. Obstruction of sinuses drainage into the nasal cavity (which may occur relatively easily — e. g. maxillary sinus is the largest air-filled sinus in the body but its ostium diameter is only 2–3 mm) leads to impairment of mucociliary clearance, stagnantion of mucus and eventually infection and inflammation (most often in maxillary sinuses). One of the main targets of therapy in sinusitis is to restore this clearance.

Viral infection causes mucosal oedema and decreased cilia action thus impairing sinus drainage — so secondary bacterial infection may follow.

Other causes that may contribute to sinuses drainage obstruction and infection including bacterial infection are:

- allergy;
- some medications, e. g. prolonged and excessive use of nasal decongestants;
- anatomical odds and abnormalities: septum deviation, cleft palate, polyps (fig. 28), turbinate hypertrophy, large ethmoidal bulla, large uncinate process (ethmoid bone part that forms the lateral wall of the nasal cavity nearby osteomeatal complex), tumor, foreign body, adenoid hypertrophy and others;

Fig. 28. Nasal polyp in right nostril. MathieuMD/ Wikimedia Commons. Distributed under the Creative Commons Attribution 3.0 Unported license https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Polype_nasal.jpg

- direct spread of infection – infection from dental roots, swimming in infected water, nasal irrigations with unboiled water in improper way;
- immune causes: haematological malignancies, neutropenia, diabetic patients, HIV;
- iatrogenic causes: mechanical ventilation, prolonged horizontal position, nasogastric tube;
- some systemic diseases: Kartagener Syndrome (causes immobile cilia), cystic fibrosis;
- facial fractures;
- biofilms (organisms anchored to sinus mucosa interfearing with cilia function).

Clinical Features (Acute Sinusitis). Acute sinusitis is typically a clinical diagnosis.

It is very important for management to distinguish bacterial and viral sinusitis, timely recognize dangerous complications of sinusitis and specific serious causes and infections which may look like sinusitis at first.

One of the below is required for diagnosis:

- nasal congestion/obstruction;
- nasal discharge (may be anterior and/or posterior – posterior nasal drip), clear or purulent.

Other symptoms and signs:

- facial pain and tenderness (e. g. on palapation, percussion) over sinuses, may worsen when bowing head;
- hyposmia or anosmia;
- maxillary toothache;
- headache;
- cough (often worse at night), cough is especially relevant symptom in children;
- elevated temperature, fever;
- epistaxis;
- ear pain/fullness;
- sore throat;
- fatigue;
- speculum exam: erythematous mucosa, oedema/mucosal obstruction primarily in middle meatus, mucopurulent discharge, pus originating from the middle meatus.

Diagnostc criteria from The European Position Paper on Rhinosinusitus and Nasal Polyps.

Rhinosinusitis in **adults** is defined as:

- inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):

- ± facial pain/pressure
- ± reduction or loss of smell

and either

- endoscopic signs of:

- nasal polyps, and/or
- mucopurulent discharge primarily from middle meatus and/or
- oedema/mucosal obstruction primarily in middle meatus

and/or

- CT changes:

-mucosal changes within the ostiomeatal complex and/or sinuses

Rhinosinusitis in **children** is defined as:

- inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):

- ± facial pain/pressure
- ± **cough**

and either

- endoscopic signs of:

- nasal polyps, and/or
- mucopurulent discharge primarily from middle meatus and/or
- oedema/mucosal obstruction primarily in middle meatus

and/or

- CT changes:

- mucosal changes within the ostiomeatal complex and/or sinuses

Duration of the disease:

Acute: < 12 weeks, sudden onset, with complete resolution of symptoms (symptom free intervals if the problem is recurrent); with validation by telephone or interview.

Chronic: ≥12 weeks symptoms without complete resolution of symptoms (may also be subject to exacerbations)

Common cold/acute viral rhinosinusits is defined as: duration of symptoms for less than 10 days. Acute post-viral rhinosinusitis is defined as: increase of symptoms after 5 days or persistent symptoms after 10 days with less than 12 weeks duration.

To evaluate the total severity of acute rhinosinusitus the patient is asked to indicate on a VAS (visual analogue scale) the answer to the question: How troublesome are your symptoms of rhinosinusitis? Scale ranges from 1 to 10: not troublesome – 1, worst thinkable troublesome – 10. A VAS > 5 affects the patient QOL. The disease can be divided into MILD, MODERATE and SEVERE based on VAS score (0–10 cm):

MILD = VAS 0 – 3
MODERATE = VAS 4 – 7
SEVERE = VAS 8 – 10

Some vasculitidis, e. g. granulomatosis with polyangitis (Wegener granulomatosis) and others may manifest as sinusitis at first.

Sinus tenderness – tips for diagnosis.

Diagnosing sinus tenderness is important for diagnosis of sinusitis. It should be tried to be elicited not only over sinus bones, e. g. also over zigomaticus and temporal bones, they can be palpated before and after sinus bones during examination.

It should be noted that bone tenderness may be caused not only by sinusitis (e. g. by cancer) and may be seen not only in sinus bones.

Presence of fluid in sinuses may be assessed using illumination (in those over 9 years of age). This method is used primarily for maxillary sinus and to some extent for frontal sinus. This is done in a dark room, diminished illumination of the sinus indicates decreased pneumatization of that sinus.

How to tell that sinusitis is bacterial?

Acute bacterial rhinosinusitis:

At least 3 of the following should be present:

- discoloured, purulent nasal discharge with unilateral predominance and purulent secretion in the nasal cavity;
- severe, localised pain (with unilateral predominance);
- fever > 38 °C;
- elevated erythrocyte sedimentation rate/C-reactive protein;
- double sickening — worsening of symptoms within 5 days after initial improvement.

Less than 2 % of episodes of viral upper respiratory tract infections are complicated by bacterial transformation, but primary care physicians prescribe antibiotics for > 85 % of presentations of sinusitis.

Also: Bacterial infection is more likely if symptoms persist for more than 7–10 days, and with high fever and purulent nasal discharge.

Complications. Complications of sinusitis are rather rare, 1 in 12 000 episodes in children and 1 in 32 000 episodes in adults. Orbital complications occur twice as often as intracranial complications; osseus complications are less common but they can cause very severe consequencies if left untreated, so immediate ENT referral is warranted.

Complications include: preorbital (preseptal) and orbital (postseptal) cellulitis (fig. 29), orbital abscess, cavernous sinus thrombosis, meningitis, encephalitis, brain abscess, sinus bones osteolitis, osteomyelitis, usually frontal, subperiostal abscess – Pott's puffy tumor, infected mucocoeles (espesially in frontal sinus) — pyocoeles.

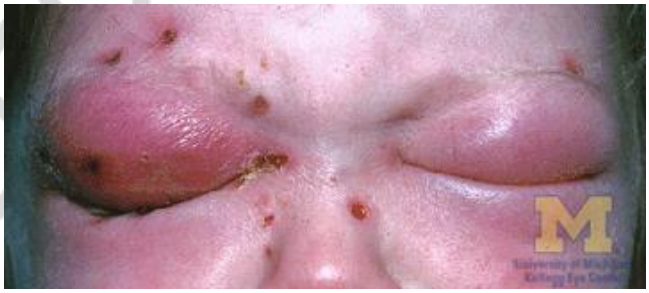

Fig. 29. Orbital cellulitis. Jonathan Trobe, M.D. - University of Michigan Kellogg Eye Center (http://kellogg.umich.edu/theeyeshaveit/). Distributed under the Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). https://commons.wikimedia.org/wiki/File:Orbital_cellulitis.jpg

Red Flags for rhinosinusitis — actually clinical features of its complications — **require urgent referral**:

- periorbital and/or eyelid oedema/redness
- frontal oedema
- headache (generalized, not only above sinuses)
- meningeal signs
- changes in mental status
- systemic toxicity
- visual changes or EOM (cranial nerves lesions) signs
- hard (meaning localizable to a specific brain area) neurological findings

Periorbital oedema and redness may be signs of orbital complications (cellulitis, Pott's puffy tumor).

Headache, meningeal irritation signs, altered mental status and systemic toxity may indicate intracranial complications – meningitis, encephalitis, brain abscess, intracranial abscess (Pott's puffy tumor may spread inwards).

Visual changes (blurred vision, loss of aquity, loss of coloured vision — green/red colour differentiation loss may be the first sign of decreased visual acuity, so Ishihara plates should be used) and EOM and cranial nerve signs — double vision, unequal pupils, abnormal eyes position and movement, as well as extraocular muscles themselves may be affected) may indicate cavernous sinus thrombosis (fig. 30), upper orbital fissure syndrome.

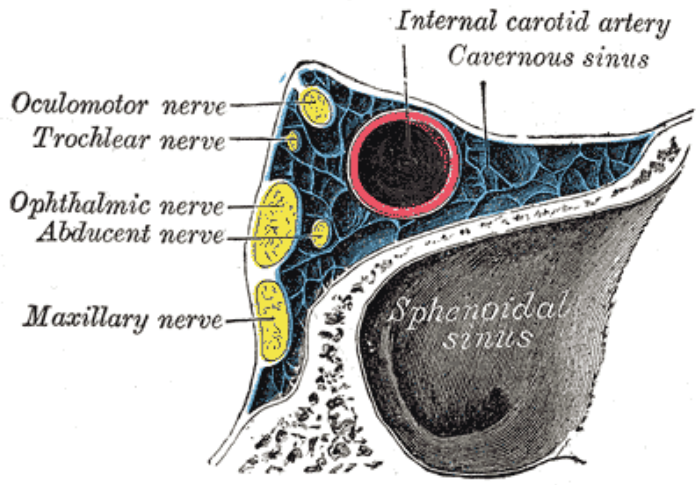

Fig. 30. Cavernous sinus anatomy. Henry Gray (1918) Anatomy of the Human Body/ Wikimedia. https://commons.wikimedia.org/wiki/File:Gray571.png

Investigations. A CT scan is the imaging modality of choice (MRI may be alternative), may visualize mucosal thickening with or without fluid levels, though these findings are non-specific. CT is not done routinely but may be considered if initial management failed, if complications are suspected or if surgical management is being considered.

Sinus puncture for culture and sensitivity is useful but invasive and painful and is not performed routinely.

Plain X-Ray usually is not useful and is usually not indicated.

Management. Principles: help restore adequate sinus drainage and use antibiotics where appropriate. Viral rhinosinusitis treatment is actually the same as common cold treatment (refer to that chapter), it is actually a part of its presentation. Suspected bacterial sinusitis is treated mainly with antibiotics.

- analgesics (if required, may provide pain relief – paracetamol, NSAIDs);
- decongestants – nasal (drops or sprays), possibly oral, for no more than 5–7 days only if congestion;
- nasal inhalations (by some considered a very important adjunct, but controversial);
- nasal saline irrigations;

Check the patient's technique of using nasal preparations — they may be using it incorrectly! Also educate about saline irrigations – water should be boiled before use (then cooled to adequate temperature) to prevent serious infectious complications.

- intranasal corticosteroids – if acute bacterial sinusitis is suspected and if decongestion is required for more than 5-7 days. Also may be used for nasal decongestion in post-viral sinusitis;
- antibiotics — if suspected bacterial sinusitis it is its main treatment (adjust doses for age if necessary):
  - first-line: amoxycillin 500 mg three times daily for 5–7 days;
  - amoxycillin/clavulanate 875/125 mg three/two times daily for 7–14 days, if patient has had amoxycillin in the last month and also if poor response to the above regimen (indicates resistant H. influenzae);
  - (if penicillin-allergic) doxycycline 100 mg twice daily for 7 days;
  - cefalexin 500 mg twice daily, cefaclor 500 mg three times daily for 7 days
- in complicated (see complications above) or severe disease, use intravenous cephalosporins (e. g. ceftriaxone) + flucloxacillin.

Antihistamines and mucolytics are of no proven value. They may thicken secretions and complicate drainage.

Invasive methods: surgery is rearly needed, drainage may be necessary by atrial lavage or frontal sinus trephine. In patients who have no evidence of sinus disease on CT or endoscopy surgery produces poor results.

When to refer: if complications are present (refer immifiately), if there is no improvement after 48-72 hours of antibiotic therapy or second-line therapy failure, structural abnormalities present, more then 4 cases per year.

Chronic Sinusitis. The most common complication of acute sinusitis. In chronic sinusitis symptoms last for 12 and more weeks without completely symptoms-free intervals. Can occur with or without nasal polyps (anterior rhinoscopy

should be performed). More likely to be associated with sinus drainage impairing factors (e. g. polyps, fig. 28). Presence of allergic symptoms should be explored.

Also facial pain is associated with sinusitis, it is not commonly occurs in it (roughly in 16% of patients). So in any case of chronic sinusitis, including those with facial pain, consider alternative diagnoses: different types of headaches including migrane, neuralgias and dental infection.

Examination includes nasal endoscopy, culture, IgE test, CT (MRI is an alternative).

Cancer of the paranasal sinuses.

Suspect it in those who presents with chronic sinusitis not in young age.

Nasal obstruction, recurrent nasal bleeding, blood-stained discharge from nose may be present. Later signs include local swelling and displacement of the contents of the orbit—upwards for maxillary, laterally for the ethmoids and downwards for the frontal mass (may be caused not only by tumors, e. g. mucocele)

Imaging – CT/MRI±PET and nasal endoscopy with biopsy. X-Ray is not very helpful.

Management. In general the same medications as for acute sinusitis are used.

- long-term nasal corticosteroids, nasal saline irrigation
- if symptoms are severe – long term antibiotics, up to 3-6, even 12 and more weeks, especially if IgE is not elevated in chronic sinusitis with nasal polyps.
- saline sinus irrigation and/or surgery if the above treatment fails.
- in general, acute exacerbations of chronic sinusitis should be treated like acute rhinosinusitis, but for prolonged period.
- referral for ENT consultation is an option, also refer urgently if treatmemt fails or if complications (see above) develop.

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