Pharyngitis

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49.1 Introduction

Pharyngitis is inflammation of pharyngeal tissue, which mainly affects the oropharyngeal part. Tissues of pharynx prone to frequent inflammation because of the prominent presence of lymphoid tissue and the communication with the external environment during breathing [1]. Sore throat which is one of the most commonly encountered complaints to physicians [2]. Pharyngitis can be classified into infectious and noninfectious or to acute and chronic pharyngitis. A viral infection is the most common cause of pharyngitis in both children and adults. Bacterial infection represents only 30–40% of pediatric pharyngitis, while it is even less in adults with a rate of 5–15% [3]. The differential diagnosis of pharyngitis is summarized in Table 49.1.

Knowledge of the pharyngeal anatomy and the deep neck spaces is important for a successful diagnosis and understanding the clinical manifestations of the pharyngitis. The pharynx is a 12–14 cm musculo-membranous tube. It has three interior sections: the nasopharynx, oropharynx, and hypopharynx. The nasopharynx extends from the base of the skull superiorly to the pharyngeal isthmus (back of the soft palate and posterior pharyngeal wall) inferiorly, bounded by the nasal cavity and choanae anteriorly, and clivus posteriorly. The oropharynx extends from undersurface of the soft palate to the upper border of the epiglottis bounded by the circumvallate

| Table 49.1 | Differential diagnosis of pharyngitis |
|-------------|--------------------------------------|
| **Bacterial** | GABHS (S. pyogenes), Staphylococcus aureus, C. diphtheriae, N. gonorrhea, A. haemolyticum, T. pallidum (Syphilis), others |
| **Infectious** | Rhinovirus, coronavirus, adenovirus, parainfluenza virus, measles, respiratory syncytial virus, Coxsackie virus, EBV, CMV, HSV, HIV |
| **Fungal** | C. albicans, other organisms—C. glabrata, C. tropicalis, C. dubliniensis, C. rugosa, and C. krusei |
| **Noninfectious** | Inflammatory/autoimmune acute pharyngitis: PFAPA, Kawasaki disease, PTLD, Oral mucocutaneous diseases |
| | Inflammatory chronic pharyngitis: Reflux pharyngitis, postnasal drip, granulomatous disease |
| | Membranous Pharyngitis: Agranulocytosis, aphthous ulcers, traumatic ulcer |
| | Malignancy: Tonsillar malignancy, leukemia, lymphoma |
| | Radiation pharyngitis |
| | Keratosis pharyngitis |

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papillae anteriorly, and by the palatopharyngeal arch and palatine tonsils laterally. The hypopharynx extends from the superior border of epiglottis to the inferior border of the cricoid cartilage, contains the pyriform sinuses, post-cricoid region, and posterior pharyngeal wall.

The pharynx contains the Waldeyer’s tonsillar ring (pharyngeal lymphoid ring), which consists of the pharyngeal tonsil (adenoids), tubal tonsils (Gerlach tonsil), palatine tonsils (commonly called “the tonsils”), and lingual tonsil. The superior, middle, and inferior constrictor muscles from the external open-tubed structure of the pharynx, and fuse in the posterior midline at the pharyngeal raphe. The pharyngeal wall is surrounded via fascial layers and deep neck spaces. From anterior to posterior these are the buccopharyngeal fascia, retropharyngeal space, alar fascia, danger space, and the prevertebral fascia.

49.2 Infectious Pharyngitis

49.2.1 Bacterial Infection

In children, bacterial pharyngitis accounts for 30–40% of cases while in adults it accounts for only 5–15% [3]. Most cases of bacterial pharyngitis are caused by group A beta-hemolytic streptococcal (GABHS) pyogenes [4].

49.2.1.1 Streptococcal Infection

*Group A beta-hemolytic streptococcal (GABHS), also known as Streptococcus pyogenes is the most common cause of acute bacterial tonsillitis pharyngitis. GABHS are Gram-positive cocci. Spread mainly through aerosolized microdroplets. It is a precursor of two serious conditions acute rheumatic fever and poststreptococcal glomerulonephritis.*

**Clinical Features**

- The disease often affects age group of 5–15 years, especially the early school years, but it can affect any age. The incubation period is 1–4 days. Considered contagious during the acute illness and one week after, it becomes noncontagious after 24 h of antibiotics use [1].

| Symptoms          | Signs                                      |
|-------------------|--------------------------------------------|
| Sore throat       | Acute membranous tonsillitis: erythematous swollen tonsils with yellowish spots hyperemia of pillars, soft palate and uvula, that can be easily removed with a swab |
| Dysphagia, odynophagia | Halitosis                                |
| Fever             | Tender enlarged jugulodigastric lymph nodes |
| Earache           | Other symptoms: headache, myalgia, fatigue and abdominal symptoms, such as vomiting |

- Note that cough, coryza, and nasal congestion are not suggestive of bacterial pharyngitis [5].

**Diagnosis**

- Diagnosis of GABHS depends on clinical judgment and laboratory testing.
- *Rapid strep test (rapid antigen detection test, RADJ): detects antigen (group-A streptococcal) from a swab. It is highly specific but less sensitive than culture and allows for immediate antibiotic treatment of a positive result. Carriers of GABHS, are around 5–10%, and they will have positive strep testing without acute symptoms [6].

**Throat culture**: The gold standard laboratory test with the sensitivity of 90–95% [6].

**Treatment**

- Supportive treatment including analgesics, antipyretics, bed rest, and hydration. Noting that GABHS is usually self-limited and resolved within 3–10 days.
- Antibiotics: avoid the overuse of antibiotics in case of other pathogens, especially in the case of viral pharyngitis. Penicillin or amoxicillin is the drug of choice for 7–10 days. If suspect resistance uses amoxicillin + clavulanic acid or clindamycin. Corticosteroids have not been proven to have benefit in acute streptococcal pharyngitis. The major aim of antibiotic use is
to reduce the rate of rheumatic fever, rheumatic heart disease, suppurative complications, and abscess formation. Noting that antibiotic therapy does not prevent poststreptococcal glomerulonephritis [7].

- Tonsillectomy in case of recurrent infections, despite appropriate antimicrobial therapy.

Complications
- Suppurative complications such as peritonsillar, retro or parapharyngeal abscess, lymphadenopathy with abscess, bacteremia, and sepsis.
- Scarlet fever.
- Rheumatic fever: occur in 3% of untreated GABHS patients, risk can be reduced to 0.3% with the use of antibiotics [1].
- Rheumatic heart disease.
- Poststreptococcal glomerulonephritis.
- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal (PANDAS) infections: tonsillectomy in these patients can resolute the neuropsychiatric symptoms [8].

### 49.2.1.2 Corynebacterium Diphtheriae

This condition caused by gram-positive rod-shaped *Corynebacterium diphtheriae*. A significant reduction in the incidence happened after the introduction of the Diphtheria vaccine [9]. The incubation period for diphtheria pharyngitis is 2–6 days. Spread mainly through infected secretions from the nose, throat, eyes, or skin lesions.

**Clinical Features**
- The disease often affects children. The patients usually appear ill and toxemic.
- Exotoxin leads to systemic cardiotoxicity and neurotoxicity which account for many of the infection consequences.

| Symptoms          | Signs                                      |
|-------------------|--------------------------------------------|
| Sore throat       | Pseudomembrane tonsillitis: adherent greyish-white membrane extends to the uvula, soft palate and can reach the larynx causing asphyxia, it bleeds on removal |

**Diagnosis**
- Diagnosis is usually based on the clinical picture.
- It is confirmed with the culture of the pseudomembrane on Loeffler or tellurite medium. The growth shows “Chinese character” appearance. Treatment should be starting without wasting of time [1].
- Note that identifying GABHS does not rule out the possibility of diphtheria, as 30% of Diphtheria cases shows positive GABHS [10].
- Serial electrocardiograms: for early detection of cardiac complications.

**Treatment**
- Treatment consists of antitoxin and antibiotics; penicillin or erythromycin are the recommended antibiotics [1].
- Early administration of medication specially antitoxin significantly affect the outcome.
- In rare cases, with extended pseudomembrane to upper airway intubation or tracheostomy is needed to secure the airway and avoid aspiration.
- Confirm eradication of the disease by having two negative cultures after completion of the treatment.
- Diphtheria toxoid booster injection is recommended every 10 years in adults.

**Complications**
- Diphtheria exotoxin is toxic to heart and nerves that can occur up to the second or third week of infection.
- Heart involvement includes; myocarditis, arrhythmia, and acute heart failure. It can improve at 2 weeks after onset [7].
• Neurological involvement affects mainly the motor nerves. Commonly affects the soft palate and pharyngeal muscles, other muscles like the diaphragm and ocular muscles can be affected. It can improve from 3 to 7 weeks later [7].
• Other organs can be involved; the larynx with airway obstruction, the kidney can lead to acute tubular necrosis.
• Death can occur due to cardiac or neurological involvement, or from asphyxiation from membranous pharyngitis.

49.2.1.3 Other Bacterial Pharyngitis
• Vincent’s Angina: ulcerative lesion on the tonsils, mainly unilateral. covered by a slough which may extend to beyond pharyngeal tissues. Came with a characteristic fishy odor. On microbiology, it shows a fusiform bacillus and spirochete. Treatment: penicillin or erythromycin.
• Others: Mycoplasma pneumoniae, Neisseria gonorrhoeae, Treponema pallidum, Chlamydia pneumoniae, Mycobacterium tuberculosis, Yersinia enterocolitica.

49.2.2 Viral Infection
A viral infection is the most common cause of infectious pharyngitis in both pediatrics and adults [3]. The most common viruses causing the infection are rhinovirus followed by coronavirus and parainfluenza [4]. It comes with gradual onset, as part of the common cold, symptoms typically include rhinorrhea, cough, and diarrhea, and usually, it is self-limited. Presence of pharyngitis with conjunctivitis, coryza, hoarseness, and cough suggest a viral etiology. Spread is by direct contact and inhalation/ingestion of respiratory secretions. Determining the virologic agent is unnecessary as it does not affect the management. Different viral pharyngitis has been described including the following:

49.2.2.1 Infectious Mononucleosis (Glandular Fever)
Epstein-Barr virus (EBV) is a common cause of acute sore throat in adolescents and young adults. 80–90% of adults are seropositive for EBV [11]. EBV has been associated with nasopharyngeal undifferentiated carcinoma, Burkitt lymphoma, and posttransplant lymphoproliferative disease (PTLD) [7]. It has an incubation period of 3–7 weeks.

Clinical Features
• Affects mainly older children and young adults. The classic triad of sore throat, fever, and lymphadenopathy.

| Symptoms     | Signs                                    |
|--------------|------------------------------------------|
| Sore throat  | Exudative pharyngitis enlarged congested membranous tonsils |
| Severe odynophagia | Lymphadenopathy with enlarged Lymph nodes mainly in the posterior triangle of neck |
| Fever        | Others: nasal cavity can also be affected |
| Myalgia      | Hepatosplenomegaly                        |

• Splenomegaly can be found in (50%), while hepatomegaly (10–15%) [11].
• Characteristic feature: Petechiae at the junction of hard and soft palate typically 1–2 mm in diameter, although these are not diagnostic.

Diagnosis
• Diagnosis is usually based on the clinical picture.
• Blood test showed near normal white cell count with increment in lymphocytes, of which 10% are atypical on the blood smear.
• Serological tests: Monospot and Paul Bunnell or Ox-cell. Hemolysis test shows high titers of heterophil antibody. When the Monospot test is negative, but still infectious mononucleosis is highly suspected, EBV-specific antibody studies (to viral capsid antigen) can confirm the diagnosis [11].

Treatment
• Symptomatic treatment including rest, analgesics, antipyretics, and hydration.
• A single dose of dexamethasone during acute symptoms can relieve the symptoms. The steroid also is recommended for complicated infections with upper airway obstruction,
severe hemolytic anemia, severe thrombocytopenia, or persistent severe disease [1, 12].

- Antibiotics: has no role except in secondary bacterial infection. Amoxicillin or ampicillin should be avoided as they can cause a maculopapular rash (salmon-colored rash) in 95% of the patients [12].
- Management of upper airway obstruction: nasopharyngeal airway, high dose steroids, tonsillectomy, endotracheal intubation or a tracheostomy (rarely necessary).
- Recovery from acute phase may take 2–3 weeks. While feelings of malaise may persist for weeks or months. Avoid contact sports to decrease the risk of splenic rupture and hemorrhage until ultrasound examination confirms the resolution of splenomegaly.

Complications
- Secondary bacterial infection up to 30% [7].
- Hemolytic anemia, thrombocytopenia (25–50%).
- Hyperplasia and severe tonsillitis which may cause upper airway obstruction occurs in fewer than 5% [7].
- Splenic rupture, elevated hepatic enzymes.
- Severe neurologic complications occur in 1–5% [7].

49.2.2.2 Coxsackie virus infections (Herpangina)

Mostly it affects children 3–10 years of age. Characterized by a painful vesicular eruption (enanthem) in the palatal and anterior tonsillar pillars area. Treatment is symptomatic, spontaneously resolve in 1 week.

49.2.2.3 Cytomegalovirus

Most infections are asymptomatic, except in immunosuppressed patients, especially post-transplant patients. Infectious mononucleosis-like illnesses but heterophil antibody test is negative. Monoclonal antibodies against CMV is diagnostic. Treatment is symptomatic.

49.2.2.4 Others

Adenovirus (pharyngoconjunctival fever), measles, Herpes simplex virus (HSV).

49.2.3 Fungal Infection

49.2.3.1 Oropharyngeal Candidiasis (Thrush)

Mainly occur in immunosuppressed and chronically debilitated patients as an opportunistic infection [7]. Different Candida species are isolated in oropharyngeal fungal infection. Candida albicans is the most common isolated organism [13].

Clinical Features
- It can occur in any age group with immunocompromised status. It is more common in adults, but neonates can be affected as well in 2–5%, which is typically self-limited [1].
- Isolated patches on the pharyngeal mucosa and larynx may be due to inhaled steroids from asthma treatment.

| Symptoms       | Signs                                           |
|----------------|-------------------------------------------------|
| Sore throat    | Mucosal pseudomembranous: characteristic white, cheesy, which can be scraped off to expose an erythematous underlying mucosa |
| Odynophagia    |                                                |
| Change in taste and burning sensation |                                                |
| Myalgia        |                                                |

Diagnosis
- The diagnosis of oral candidiasis is essentially clinical and is based on the recognition of the lesions.
- KOH preparation and microscopic examination. Staining (10% KOH) and culture (Sabouraud dextrose agar).

Treatment
- Topical fluconazole or nystatin are the first line drugs.
- Itraconazole is used for fluconazole-resistant strains, which should be suspected for patients without a clinical resolution after 14 days course of fluconazole.
• Recurrent infections and those with a high risk of systemic infection treated with systemic antifungal therapy [14].
• Prophylactic fluconazole is generally not recommended due to the risk of resistance. May be used with high risk patients for invasive fungal infections.

49.3 Noninfectious Pharyngitis

• Inflammatory/autoimmune acute pharyngitis:

| Disease | Description |
|---------|-------------|
| PFAPA (Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenitis) syndrome | • Unknown etiology  
• Affect children <5 years of age  
• PFAPA is a diagnosis of exclusion (described as regular (clockwork) episodes of high fevers (>39 °C) and oral/neck manifestations every 2–8 weeks and last for 2–7 days with no symptoms between episodes)  
• Steroids can be used during acute episodes and it mainly reduces the fever episodes  
• For prevention cimetidine and colchicine can be used  
• Spontaneous resolution is expected in such pathology, but tonsillectomy has been described to decrease the episodes and possible resolution of PFAPA |
| Kawasaki disease | • Systemic medium-sized vasculitis of unknown etiology  
• Treatment focus on Gamma globulin infusion and aspirin to avoid the long-term complications of coronary artery aneurysms and sudden death |
| Caustic ingestion | • Leads to inflammation or necrosis of the pharynx and upper GI tract |
| Posttransplant Lymphoproliferative Disorder (PTLD) | • Can present with non-Hodgkin lymphoma  
• Diagnosis requires a biopsy from Waldeyer’s tonsil region  
• Treatment includes a reduction in immunosuppressive therapy, antivirals, and rituximab if EBV titers are high |

• Membranous Pharyngitis-Tonsillitis: pharyngitis with exudative membrane can also occur in cases of agranulocytosis appears as ulcerative necrotic lesions in the oropharynx, leukemia, aphthous ulcers, tonsillar malignancy, traumatic ulcer.

• Radiation Pharyngitis: head and neck radiation therapy are known to cause unavoidable acute and long-term pharyngeal inflammation and changes. Starting at an exposure of 20 Gy, and the severity is dose dependent. The acute stage presents with edema, erythema, odynophagia, ulceration, and mucosis. Note that mucositis is worsened in patients with concomitant chemoradiation therapy. Management focuses on symptomatic and superinfection treatments including oral hygiene, topical (analgnesia, mouth wash, and antifungals) with or without systemic (analgnesia, antibiotics, and antifungal). Healing of acute stage can take around 3–4 weeks or even more [1, 15].

• Inflammatory chronic pharyngitis:
  – Reflux pharyngitis (laryngopharyngitis): presents with gastroesophageal reflux disease (GERD), laryngopharyngeal reflux (LPR), and hiatal hernia. Manifestations include chronic throat pain, burning sensation, sour taste, halitosis, chronic dry cough, hoarseness, globus sensation, and habitual throat clearing. Note that many patients with LPR do not show typical symptoms of GERD of heartburn or indigestion. Clinical exam findings include oropharyngeal erythema, posterior pharyngeal wall cobblestoning, laryngeal edema, contact ulcers and pachydermia on the interarytenoid. The diagnosis is confirmed by a pH probe monitoring study. Treatment using empiric therapy via lifestyle modifi-
cations and proton pump inhibitors or H2-blockers [1].

- **Postnasal drip**: most commonly from allergic rhinitis. Manifestations include globus pharyngeus, chronic cough, and sore throat (irritative pharyngitis). The associate nasal obstruction leads to a habit of mouth breathing which is an important predisposing cause of chronic pharyngitis. Treatment for rhinitis with nasal saline, nasal steroids, and humidification [1].

- **Granulomatous disease**: includes pathologies that induce granulomas, such as tuberculosis (TB), Grahn’s disease, foreign body granulomas, iatrogenic (e.g., suture), or as a reaction to hair or keratin debris [1].

- **Malignancy**: Chronic inflammation of the pharynx may hide underlying malignancy in the oral cavity or pharynx.

- **Keratosis Pharyngis**: It is a benign condition, characterized with white/yellow horny keratin outgrowths on the surface of tonsils, pharyngeal wall or lingual tonsils, which is firmly adherent and cannot be removed easily. No accompanying inflammation. No specific treatment is required as usually, it goes into spontaneous regression, the patient needs only reassurance.

**Take Home Messages**

- Viral infection is the most common cause of pharyngitis in children and adults. Rhinovirus is the most common etiologic agent.

- Bacterial pharyngitis in adults (~10%) is less common than in children (~40%).

- Group A beta-hemolytic streptococci: It is the most common cause of bacterial pharyngitis and can be complicated with deep neck abscess, rheumatic fever, and poststreptococcal glomerulonephritis.

- Poststreptococcal glomerulonephritis risk does not decrease with the use of antibiotics.

- Candidal pharyngitis is common in immunocompromised patients and post-radiotherapy patients.

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