Pathology

Diseases of the Oral Cavity and the Oropharynx

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Our mouth is the gateway to our body. Food, allergens, the air we breathe - everything finds its way through our mouth into our body. Our immune system in this area defends us against some of the seasonally occurring cold pathogens. Lymphoid cells located just under the epithelial mucous membranes, which line the oral cavity and oropharynx, serve this purpose. What is the function of these cells in the immune response and what happens when they are overwhelmed and can no longer fulfil their task? The answers will be outlined for you in this article!

Function and Location of the Tonsils
Oral cavity is an important area for the processes of digestion and contain the tonsils that participate in the defense of the body.

Tonsils are also commonly known as ‘almonds’. They are located in the upper pharynx and are part of the human immune defense system.

In total, six tonsils comprise the pharyngeal lymphoid ring (Waldeyer’s tonsillar ring): The paired palatine tonsils (tonsils, located between the palatoglossal and palatopharyngeal arches), the tubal tonsil (eustachian tonsil, associated with the pharyngeal opening of the auditory tube), the unpaired lingual tonsils (lingual tonsils, located on the floor of the oropharyngeal passageway, at the root of the tongue) and the pharyngeal tonsils (adenoid tonsils, located in the roof and the posterior wall of the nasopharynx, also called polyps).

Located at the entrance to the epi- and mesopharynx, their task is to act as filters for ingested or inhaled antigens and to render them harmless.

**Histology of the tonsils**

The tonsils are accumulations of lymphoid tissue, located just beneath the mucosal epithelial lining of the respiratory and digestive systems. Accordingly, they form part of the **mucosa-associated lymphoid tissue** (MALT) and are referred to as lympho-
epithelial organs.

Lymphoid tissue is located just beneath the epithelium, assuring direct contact of lymphocytes with epithelial cells, facilitating protection against pathogens that may enter the body via the mucosa.

When using a compound microscope to study tonsil histology, a characteristic tonsillar surface structure is visible: The epithelium is characterized by invaginations, forming deep tonsillar crypts, which markedly increase the surface area and thus, enhance antigen uptake.

**Note:** MALT is a diffuse system of small concentrations of lymphoid tissue that is strategically positioned along epithelial mucosal linings in the human body. It basically consists of a T-zone, which is located between B-cell follicles and of a reticular fibre network. In addition to the tonsils, examples for MALT are Peyer's patches (aggregate nodules associated with the gut) and lymphoid nodules in the vermiform appendix. The palatine tonsils and the lingual tonsil are covered by stratified squamous non-keratinised epithelium. The palatine tonsils are located in the isthmus of the fauces, between the palatoglossal arch and the palatopharyngeal arch of the soft palate. This area is called tonsillar fossa. The lingual tonsil is located in the lamina propria on the dorsal surface of the root of the tongue.

Approximately 20 tonsillar crypts extend through to and almost reaching the base of the tonsil. Excretory ducts of mucous glands open into the bases of the tonsillar crypts. The lymphatic epithelium is diffuse and forms an open meshwork of cells interspersed with free cells (dendritic cells, lymphocytes).

The basal lamina is often disrupted, which facilitates the infiltration of the epithelium by lymphocytes and macrophages and the migration of antigens to the underlying secondary lymphoid follicles (B zone). Their cap-shaped surface points towards the surface and oral cavity. It remains unclear to date as to how antigens enter healthy tonsils with stratified squamous epithelium.

Tonsillar invaginations respectively crypts often contain oral detritus composed of degenerating cells and deposited material. The crypts of the lingual tonsil are less deep than those of the palatine tonsil.

**Pharyngeal tonsils** are located in the upper posterior part of the throat, more specifically in the mucosa of the posterior wall of the nasopharynx. Their surface consists of irregular folds and they are covered by respiratory epithelium. In school children these tonsils are most active, which changes with age. In adults, they are usually atrophic.
Tubal tonsils are an accumulation of lymphoid follicles located close to the torus tubarius, posterior to where the auditory tubes open into the throat (pharyngeal opening of auditory tube; pharyngeal ostium).

Although all tonsils belong to the lymphatic system, they are not directly located along the routes of afferent and efferent lymphatic vessels in the body. It is important to note, that tonsils have no afferent and only small efferent lymphatic vessels, which pass via the submandibular lymph nodes and drain into the superior deep cervical lymph nodes.

Tonsillar Hyperplasia and Tonsillitis
When tonsils are inflamed (tonsillitis), submandibular lymph nodes are palpable and pressure sensitive. Because of their location at the back of the mouth, where they are guarding the entrance to the digestive and respiratory systems, many germs and components of food come into contact with the tonsils.

Physiologically they are rendered harmless, but often contact of viral (up to 60% of cases) and bacterial pathogens (up to 15 to 30%) with the lymphoid tissue induces humoral and cell-mediated immune responses. These lead to inflammation accompanied by symptoms, such as fever, odynophagia, swelling and redness of the tonsils and discharge of yellow or white pus from the tonsillar crypts.
Among children younger than 3 years, the most common pathogens are viruses
(adenovirus, Epstein-Barr virus, coxackie virus, rhinovirus, coronavirus and influenza
virus). Between older than 5 years and adults, the most frequent germs are bacteria, and
especially group A beta-hemolytic streptococcus (Streptococcus pyogenes or SBHGA)
(almost 40% of all cases).

The exposure of the immune system to pathogens particularly in children leads, as part of
the inflammatory response, to an enlargement of the tonsils (tonsillar hyperplasia or
adenoids). Hypertrophic tonsils are tightly packed with enlarged secondary follicles,
which indicate that the immune system is ‘ready for battle’.

Especially among children, swollen adenoids (adenoids are also called polyps) can cause
nasal obstruction (alveolar hypoventilation) and hearing impairment, due to a lack of
ventilation of the tympanic cavity via the eustachian tube. If left untreated, this may
cause serious speech or language development delays.

Treatment of tonsillar hyperplasia is based on the severity of the clinical symptoms and
accordingly may involve partial (tonsillotomy, TT) or complete removal (tonsillectomy, TE)
of the tonsils.

Treatment is based on antibiotics with penicillin or macrolides for bacterial infections, but
in some cases the surgery is indicated.

Indications for a tonsillectomy are chronically inflamed tonsils with focal infection (spread
of pathogens from the foci of infection), prevention of recurrent or persistent ENT
infections (sinusitis, etc.), abnormal craniofacial (tooth) development due to chronic
airway obstruction, articulation errors, pathological daytime sleepiness and severe
dysphagia.

According to scientific studies, in 70 % of all cases chronic tonsillitis is the main indication
Interesting facts on the suitability for surgery and on the surgical procedure of a tonsillectomy and a tonsillotomy

A tonsillectomy is performed under a general anesthetic and takes about 20 minutes.

Surgery should only be performed when the child, adolescent or adult is physically healthy and at least one week in advance was neither suffering from fever or a cold.

The surgical procedure in children under one year remains controversial, as the immune system of these children is still maturing. Equally a decrease in certain blood cells of the immune system (agranulocytes) or cancer of white blood cells (leukaemia) constitute contraindications to surgery.

Before surgery, a conversation with the anesthetist and consultant takes place. If a patient is high-risk for a general anesthetic, it is also recommended to refrain from surgery. Patients on regular medication, for example anticoagulants, have to discontinue their medication in consultation with the doctor before surgery. Within about two weeks before surgery vaccines should not be administered anymore.

Tonsillotomy is a procedure frequently performed in children aged between 3 to 6 years, during which the tonsils are partially removed. Strong indication for this procedure is tonsillar hyperplasia associated with severe airway obstruction or dysphagia.

Most importantly, the main indication for a TT, in contrast to a TE, is tonsillar hyperplasia, that is not a sign or consequence of acute or chronic recurrent tonsillitis. During tonsillotomy part of the tonsil is removed on an outpatient basis using a laser or by radiofrequency. Thus, the tonsil remains a lymphatic and immunologically active rudiment, which is particularly relevant for children.

Tonsillectomy is a procedure during which the tonsils are completely removed and the scar is coagulated. The less heat is produced during surgery, the better for the wound, and the less damage occurs in the surrounding tissue.

The following different methods differ in the degree of heat applied. First, the tonsil is
grasped by tonsil-holding forceps, an incision is made in the mucous membrane using a surgical scalpel and in addition to the tonsil, and often also parts of the palatal arch are removed from the tonsillar fossa. The following tonsillectomy techniques and instruments can be used:

1. Periosteal Elevator (raspatory) or rugine
2. Harmonic scalpel method: tissue removal by means of ultrasound and subsequent obliteration
3. Bipolar radiofrequency dissection: The tonsil is dissected by a highly focused plasma field and the tissue is coagulated.
4. Carbon dioxide/diode lasers: Laser-assisted serial tonsillectomy (LAST)

For the removal of the vascular pedicle, which is adjacent to the lower palatopharyngeal arch, a loop is used. Haemostasis is achieved with bipolar electric tweezers. After successful surgical procedure an approximately 2 cm wide wound area can be seen between the posterior and anterior palatine arches, which in the following days will be covered in white scab (fibrin).

After about a week the initial scab is repelled and bleeding may occur. Subsequently, the process of scar healing begins.

**Complications and risks of surgery**

Due to the direct proximity of major blood vessels leading to the brain, rupture of these vessels during surgery is probably one of the most feared scenarios, which at the same time, is the least likely. The most common post-tonsillectomy complication is haemorrhage, which can occur during the healing process, if the scab from the wound is dislodged too soon, due to the consistent physiological act of swallowing. Therefore, a long healing period is required.

Risk of bleeding from those wounds is highest in the first 24 hours after surgery, which is
why a postoperative inpatient observation period is generally recommended. Especially after a TE, extensive postoperative haemorrhage may occur. These cases sometimes need to be treated with surgery or require a blood transfusion, which is why the demand for an outpatient surgical procedure should be rejected.

Overall, according to the Austrian tonsil study 2009/2006 (Sarny S, G Ossimitz, Habermann W, Stammberger H (2012) The Austrian tonsil study 2010. Laryngo-Rhino-Otology 91: 16-21 [PubMed] [CrossRef]) the acquisition of 1,000,000 patient records indicated in only 2.7 % of all cases, post-tonsillectomy haemorrhage required follow-up treatment and care. In a group of patients who had been treated by a TT, the post-surgical risk for bleeding was 2.7 % of which only 0.8 % needed a reintervention.

**Note:**

1. The pharyngeal tonsil is a lymphatic organ and should therefore not be removed without strong indication.
2. Conservative drug treatment includes a 7-day course of penicillin.
3. The main indications for a TE currently include obstructive tonsillar hyperplasia, recurrent and chronic inflammation, and suspected malignancy.
4. The main indication for a TT is tonsillar hyperplasia, which is not a sign or consequence of acute or chronic recurrent tonsillitis.
5. Post-tonsillectomy haemorrhage straight after surgery or about a week later, when scabs begin sloughing off from the surgical sites, represent the highest risk of this procedure. The likelihood of bleeding after a tonsillotomy is much lower.

**Pharyngitis**

Pharyngitis commonly presents with the abrupt onset of a sore throat, caused by the inflammation of the pharyngeal mucosa. Additional symptoms may be fever and the general feeling of having flu and dysphonia. If the inflammation includes tonsillitis, it may be called pharyngotonsillitis. Pharyngitis is much more common in children than adults.

**What is the cause of pharyngitis?**

Pharyngitis may be caused by bacterial or viral infections; however, most frequently pharyngitis is caused by the most common cold viruses (up to 60% of cases). These include parainfluenza-, adeno-, rhino- and coronaviruses. Once the mucosa of the throat is disrupted by a virus infection, the tissue is susceptible to secondary bacterial infections, which may increase inflammation.

The most common bacteria causing oral stomatitis are streptococci belonging to serogroup A (Streptococcus pyogenes). The mechanism that causes this disease is very simple and typical for diseases occurring in winter months: Mucous membranes are getting irritated and dry out when exposed to cold and dry air outdoors and heated air indoors, causing compromised host defense mechanisms.

Pharyngitis can also be triggered by chronic mucosal dysfunction caused by physico-chemical factors, such as smoking cigarettes and contact with hazardous irritants, as well as by the menopause with its hormonal changes. Transmission of the disease occurs via airborne droplets.
Approach to diagnosis and treatment of pharyngitis

In order to be able to exclude other conditions and confirm the clinical diagnosis of pharyngitis, the patient’s vaccination certificate should be presented to the physician. With regular successful vaccinations against diphtheria, at least the differential diagnosis of diphtheria can be excluded with certainty.

The identification of the bacterial pathogen involves swabbing the throat (known as pharyngeal exudate) and targeted antibiotic treatment. Causal treatment of pharyngitis is not possible and also not necessary, since the disease subsides in most cases within a week, if the patient rests sufficiently and follows medical advice.

Squamous Cell Carcinoma of the Floor of the Mouth

Squamous cell carcinoma of the floor of the mouth is a malignant disease that has developed in the squamous epithelium of the base of the tongue and affects cells of the oral mucosa. Includes up to 90% of all cases of oral cancer. Is 4 times more common in women than men, reaching peak prevalence between 50 to 59 years. The size of the affected tissue area varies, depending on the time of diagnosis.

In advanced stages, even the muscles forming the floor of the oral cavity, and later also the cervical lymph nodes may be affected. In eight out of ten cases, affected patients regularly use alcohol and tobacco (cigarettes, chewing and snuff tobacco).

The effect of smoking on this carcinogenic disease is easily explained: Carcinogenic components of cigarette smoke accumulate under the tongue in the saliva. There, they have enough time to exert their harmful effect on the cells. Additional, regular, heavy alcohol consumption increases the risk of oral cancer even further. Poor oral hygiene and a diet low in vitamins, particularly a lack of vitamin A and C, can be harmful as well.

On average, men are three times more likely to be affected than women. Floor of the mouth cancer accounts for 6% of all cancers affecting patients, and ranks as the 6th most prevalent malignancy worldwide.

In most cases, cancers of the floor of the mouth are associated with preceding an oral precancerous lesion, which means that even before malignant transformation, stages of precancerous oral epithelial changes are detectable. So called facultative precancerous lesions rarely lead to cancer, while obligate precancerous lesions have a high probability to turn into early stage carcinoma.

Oral leukoplakia, a small, predominantly white patch, is the most common facultative precancerous lesion of the oral mucosa and can be easily overlooked as it can be quite small. Dentists should remain vigilant for signs of potentially malignant disorders and oral cancer whilst performing routine oral examinations of patients from the age of 50.

Leukoplakia is often localized in the buccal mucosa or the corners of the mouth. Obligate precancerous lesions, for example Bowen’s disease, can occur on the oral mucosa or the sides of the tongue. Frequently, at the time of discovery, these lesions have undergone malignant transformation.

Morphology and prognosis of the squamous cell
Different histopathological variants of squamous cell carcinoma have been identified, each of them having a different prognosis: The conventional, ulcerated form is characterized by invasive growth and occurs in 99% of the cases affected by this cancer. Cancers originating in the tissue that lines the lips have a better prognosis when compared to other oral locations, as for example the root of the tongue.

The uncommon, verrucous variant of squamous cell carcinoma is an exophytic, clinically
slow-growing lesion, with potential to metastasize only in an advanced stage of the
disease. The spread of cancer to other parts of the body is called metastasis. Metastasis
of squamous cell carcinoma of the oral floor occurs via the lymphatic route to the
submandibular and, less common, to the submental lymph nodes. Cancer cells are not
disseminated via the bloodstream (hematogenous spread). Cancer of the oral mucosa
affects both parotid and pharyngeal lymph nodes. Diagnosis is based on a punch or
excisional biopsy.

Clinical symptoms and treatment options

The diagnosis of squamous cell carcinoma of the oral floor is challenging, as patients in
the initial stages of this disease frequently present with only vague symptoms (i.e.
painless lesions) and minimal physical findings. However, if cancer of the oral floor is
detected in the early stages, patients have a good chance of recovery. Many non-specific
symptoms, such as halitosis or the presence of phonetic speech disorders may be
indicative of early-stage oral floor cancer.

Diagnostic tests to confirm or exclude the diagnosis of oral cancer include computed
tomography or magnetic resonance imaging of the suspected area. At an advanced stage
of oral cancer (from T3), also organs potentially affected by metastasis of the primary
tumor, for example the liver or the kidneys, must be examined.

Treatment of oral cancer usually requires a combination of surgery and radiotherapy. To
adequately remove a tumor from the floor of the mouth, approximately 1 cm of normal
tissue should surround the tumor. Floor of the mouth resection is usually the first
treatment of choice. If the cancer is already more advanced, segmental mandibular
resection is necessary.

Also the removal of involved lymph nodes in the neck (‘neck dissection’), which can be
performed as a prophylactic measure, is a treatment option. Radiation therapy can be
used in the treatment of small tumors. If the cancer is very aggressive, a combination of
surgical and radiological therapy is also possible.

Carcinoma of the Tongue
How do I recognize carcinoma of the tongue?

Carcinomas of the tongue and of the oral floor are equally difficult to diagnose, based on clinical signs and symptoms. Early signs of tongue cancer may be a sore throat, dysphagia, excessive salivation or in an advanced stage, slurred pronunciation and a foreign body sensation in the neck and throat. White to yellow plaques on the oral mucosa, which cannot be wiped or scraped off, may be indicative of oral cancer. Symptoms of advanced stage tongue cancer include different degrees of impairment of tongue movement, depending on the location and extent of the tumor.
Movement disorders of the tongue occur only in advanced stages and have different strengths depending on the location and extent of the tumor. A definite diagnosis can be obtained by taking a biopsy, performing CT scans or magnetic resonance tomography.

**Tongue cancer treatment**

Lesions are treated surgically where possible. If the cancer is so severe that a large part of the muscles of the tongue has to be removed, surgery may be performed only on a small portion, complemented by radiotherapy. Otherwise, moving the muscles of the tongue and mouth properly to produce speech would no longer be possible.

Chemotherapy is also recommended if the cancer has spread. Abstaining from smoking tobacco and excessive alcohol consumption reduces the risk of recurrent cancer of the tongue or indeed carcinogenesis in the first place.

**Note:** In histopathology the five ‘S’s’ of smoking, spirits, syphilis and septic teeth have been associated with the emergence of head and neck squamous cell cancer. Further to the known causes of oral cancer, such as smoking, alcohol consumption and poor oral hygiene, also sexual practices and associated infections with high-risk types of human papillomavirus have been linked to oral cancer.
Dentures: A cause for cancer of the tongue?

Determining the cause of tongue cancer in non-smoking patients is difficult. This type of cancer usually develops most commonly after the fifth decade of life, when many patients have been fitted with bridges, dentures or crowns. This leads to the assumption that dentures, particularly ill-fitting dentures, may predispose tissues to malignant change. However, so far a significant relationship between the use of dentures and the incidence of cancer of the tongue has not been established.

Hypopharyngeal Cancer

Hypopharyngeal cancer is a term used for tumors characterized by the malignant degeneration of epithelial cells in the lower part of the throat. Most important risk factors include smoking, heavy use of alcohol, poor dental hygiene affecting the composition of saliva and work-related contact with metal dusts. Cancers of the hypopharynx usually are, like cancers of the tongue and of the oral floor, squamous cell carcinomas.

Hypopharynx cancer constitutes between 12 and 15% of SCC of head and neck, is characterized as being one of those cancer with bad prognosis, with an overall survival in 5 years between 10 and 35%.

Localization and symptoms

The three most common sites of origin of hypopharyngeal carcinoma include the pyriform sinus, the postcricoid pharynx and the posterior pharyngeal wall. The most
common symptoms include dysphagia (difficulty swallowing), foreign body sensation in the throat or stabbing pain radiating towards the ear.

If the tumor has spread to the larynx, it will cause symptoms such as hoarseness and hyperventilation due to shortness of breath (dyspnoea). Enlarged lymph nodes behind the ear and below the angle of the jaw are palpable.

**Popular Exam Questions on Oral Disease**

The correct answers can be found below the references.

1. **Which structure is not part of the ‘Waldeyer’s tonsillar ring’?**
   - A. Palatine tonsil
   - B. Thymus
   - C. Pharyngeal tonsil
   - D. Tubal tonsil

2. **What are the indications for a tonsillectomy?**
   - A. Chronically inflamed tonsils
   - B. A collection of pus on palatine tonsils
   - C. Significantly elevated inflammation markers in blood test results
   - D. Tonsillar hyperplasia in children

3. **Which diagnostic tool is not useful in the diagnosis of oropharyngeal disorders?**
   - A. Computer Tomography
   - B. Palpation with the thumb and forefinger
   - C. Magnetic Resonance Imaging
   - D. Biopsy

**References**

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Entstehung, Behandlung und Prävention von Mundhöhlenkrebs via Fanconi-Anämie

Endspurt Histologie, Thieme Verlag

Duale Reihe Anatomie, 2. Auflage, Thieme Verlag

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**Correct answers:** 1B, 2D, 3B