Chapter

Oral Microbiota from the Stomatology Perspective

Andrea Stašková, Radomíra Nemcová, Stanislav Lauko and Andrej Jenča

Abstract

Besides the properties typical of body cavities, the oral cavity exhibits many differentiating features that allow it to occupy position of an autonomous functional and biological unit, a characteristic ecosystem. An appropriate homeostasis of oral biocenosis and balanced conditions for microorganisms concerning proportions of physiological and pathogenic or potentially pathogenic microbiota play an important role with regard to the oral cavity health and eventually the overall health of an individual. The oral cavity is a constantly changing habitat. The current market offers a number of relevant preparations supporting oral health, and alternative approaches serving these purposes are also available. Results of the studies that focused on microbiocenosis of the dental plaque and interactions between individual bacterial species indicate a probiotic potential of some oral bacteria and their prospective use in prevention of oral cavity diseases. This chapter deals with the state of physiological microbiota found in oral biofilms, with the most important infections of the oral cavity and the potential use of probiotics as a prospective alternative approach to prevention and therapy of oral cavity diseases.

Keywords: oral cavity, microbiome, biofilm, focal infection, probiotics

1. Introduction

Microbiological analysis of oral microbiota is still a challenge the science has to face. Up to this day, we have knowledge of only a portion of microorganisms living in the oral cavity. Their research is very important from the point of view of prevention, diagnostic and treatment of oral and general diseases [1]. Dental caries is the most common chronic disease in the world affecting people regardless of sex, age and ethnic origin, although it affects more the individuals with low social-economic status. *Streptococcus mutans* was identified as the causative agent of this disease. Presented were also results indicating participation of acidogenic bacteria in the process of its development [1]. These bacteria are generally called cariogenic bacteria. However, no pathogen is the direct and only cause of the development of dental caries or periodontitis. More profound knowledge of microbial composition of the oral biofilm of humans on the surface of teeth or in the subgingival space can help to understand better the complexity of pathogenesis of the development of dental diseases, and find new ways how to affect positively the oral health through balanced, physiologically beneficial microbiota [2]. The oral cavity is a constantly changing habitat. Traditional methods intended for the studies of diversity of mirobiocenoses are based

on conventional isolation of bacteria by cultivation, their morphology and identification by means of their biochemical properties. These methods do not suffice to ensure concise characterisation and quantification of microbiota, are time demanding, provide results not earlier than after 48 hours and involve only cultivable bacteria. High percentage of bacteria is cultivated only with difficulties due to unknown requirements on their growth [2]. Currently, a number of genetic techniques intended for quantification, identification and characterisation of bacterial communities are available. The study of the external influence on oral cavity microbiocenosis is inevitable due to high incidence and prevalence of dental caries or periodontopathies, despite the current widespread use of oral hygiene preparations [3]. Today's market offers a multitude of such preparations, and also, alternative approaches for the improvement of oral health are available. Scientific studies presented interesting knowledge about beneficial bacteria capable of inhibiting the growth of pathogenic bacteria by their bioactive products. This concerns, for example, the proof of the suppression of oral pathogens by *Streptococcus salivarius* K12 probiotic bacteria, or their bioactive compounds can serve as a basis for the development of new strategies contributing to prevention and treatment of oral diseases [4].

2. Oral cavity microbiome

Immediately after birth, the sterile mouth cavity of the newborn individual mediates the contact between the internal and external environments and, at this time, also its colonisation by microorganisms commences. After several days, the microbiota characteristic of the oral cavity becomes stabilised [5]. In the process of colonisation of the mouth cavity of newborns, streptococci are acquired the first. Over time, the diversity of populating microorganisms grows until the individual acquires certain microbiota the stability of which depends on compensation mechanisms ensuring suitable conditions in the mouth cavity. Mucosa and teeth in the oral cavity come into constant contact with the exogenous microbiota, and the health state of dentition is also affected by proportions of individual groups of microorganisms. Some factors, for example unsuitable diet, can irreversibly affect the homeostasis of the oral ecosystem and subsequently lead to propagation of pathological changes in the oral cavity [6].

Although the oral microbiota contains bacteria, fungi, viruses and archaea, research has focused mostly on oral bacterial populations present in the highest numbers [7]. Fungi as one of the components of the oral microbiota were identified by pyrosequencing with focus on RNA, which exhibits high species variability. Peterson et al. [8] reported that the number of fungal species in the oral microbiota ranges from 9 to 23.

Molecular microbiology techniques based on 16S rRNA allowed scientists to describe more than 700 bacterial species present in the oral cavity of humans. More than 50% of bacterial species were not cultivated and thus their role in the oral microbial ecology has not been explained. It was assessed that approximately 1000 bacterial species are capable of stable existence in the mouth of humans, while each man can harbour 50–200 species of this diverse spectrum [9]. Many species are found temporarily in the saliva or as a part of biofilms formed on teeth or mucosa. Analysis of biodiversity in the mouth cavity showed that the number of oral phylotypes is considerably undervalued. Quantification of oral microbiota of humans was performed by metagenomics of unique phylotypes using pyrosequencing 454 and sequencing by Ilumina technology. This quantification method confirmed 668 bacterial phylotypes in microbiota of one plaque, which is considerably more than the numbers published in the previous studies. Similar sequencing technique detected

3621 phylotypes in the saliva and 6888 phylotypes in a subgingival plaque [7]. Oral cavity bacteria identified by modern sequencing methods are classified in various strains the majority of which belongs to strains (phyla) *Firmicutes*, *Fusobacteria*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, *Spirochaetes* and *Synergistetes*.

In addition to its principal function—intake of food and water—the mouth cavity fulfils a number of other important functions that include the primary protective function against microorganisms entering the gastrointestinal tract and various functions involving discrimination of taste, temperature and pressure [10]. In addition to properties typical of body cavities, the oral cavity possesses many differentiation features owing to which it acquires a position of separate functional and biological unit, a characteristic ecosystem [11].

Microbiota of the oral cavity is not uniform and changes according to anatomical and physiological conditions; it is different at the orifices of salivary glands, on the surface of teeth, in sulcus gingivalis, on the tongue, at tonsils or at the buccal mucosa [12]. The growth of oral microorganisms depends on temperature, pH, oxidation-reduction potential, availability of nutrients and water, morphology of oral structures, flow of saliva and the presence of antimicrobial compounds. Each of these factors puts a selection pressure on the oral ecosystem and helps to maintain balance between populations of microorganisms (**Figure 1**).

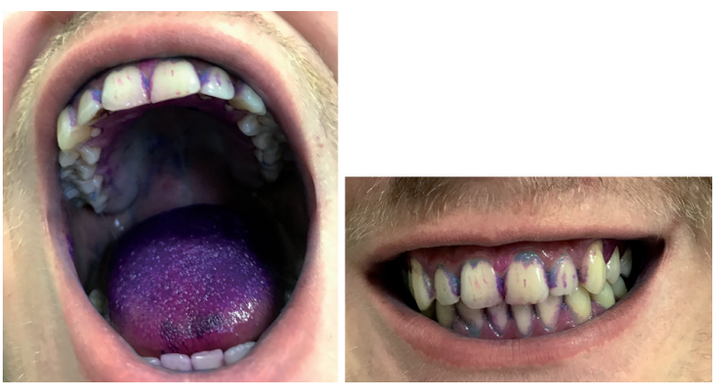

Figure 1.
Detection of oral biofilm by means of a plaque-finder, the new dental plague is coloured red, the older one is coloured blue.

2.1 Oral microbiota in sulcus gingivalis

Sulcus gingivalis is one of the sites where the microorganisms from the external environment begin to act as first. The total count of cultivable bacteria in sulcus gingivalis of healthy people is relatively low and amounts to about 103–106 CFU (colony forming units) per gingival slit. Sulcus gingivalis supplies nutrients to bacteria, exhibits low redox potential and thus is colonised mostly by obligate anaerobic rods. The subgingival plaque is also dominated by *Actinomyces* and streptococci that belong among Gram-positive microorganisms. It has been assumed that microbiota of sulcus gingivalis is related to the composition of the supragingival plaque with frequent occurrence of black-pigmented rods of *Porphyromonas gingivalis*, *Porphyromonas endodontalis*, *Prevotella melaninogenica*, *Prevotella intermedia*, *Prevotella loescheii* and *Prevotella denticola*.

The most frequent bacterial populations in the sulcus gingivalis are the following: *Streptococcus sanguis*, *Streptococcus mitis*, *Staphylococcus epidermidis*, *Micrococcus* spp., *Mycoplasma* spp., *Trichomonas tenax*, *Entamoeba gingivalis*, *Streptococcus intermedius*, *Veillonella parvula*, *Streptococcus mobillorum*, *Streptococcus constellatus*, *Peptostreptococcus micros*, *Lactobacillus casei*, *Lactobacillus acidophilus*, *Eubacterium*

lentum, *Propionibacterium acnes*, *Catonella* spp., *Johnsonella* spp., *Rothia dentocariosa*, *Actinomyces viscosus*, *Actinomyces odontolyticus*, *Actinomyces naeslundii*, *Capnocytophaga gingivalis*, *Capnocytophaga ochracea*, *Prevotella oralis*, *Prevotella denticola*, *Bacteroides melaninogenicus*, *Fusobacterium nucleatum*, *Eikenella corrodens*, *Wolinella* spp., *Campylobacter sputorum*, *Selenomonas sputigena*, *Treponema* spp., and *Leptotrichia* spp., *Granulicatella* spp. [13]. Of the more noteworthy representatives, one should mention parasitic protozoa *Entamoeba gingivalis* and *Trichomonas tenax* [14].

2.2 Oral microbiota on the surface of teeth

Dental plaque consists of microorganisms producing a complex matrix composed of extracellular products of microorganisms and salivary components. Bacteria isolated from supragingival plaques include mostly Gram-positive, facultatively anaerobic species, particularly streptococci, and members of the genus *Actinomyces.* Bacteria of the genera *Veillonella*, *Haemophilus* and *Bacterioides* are usually isolated from deeper layers.

Formation of the dental plaque can be divided to several stages: formation of pellicle, initial bacterial adhesion, bacterial colonisation and plaque maturation and finally its mineralisation and calcification (**Figure 2**, **Figure 3**), i.e., formation of dental calculus (*calculus dentis*) [9].

Some bacteria are able to adhere to the tooth surface and by their factors of virulence and metabolic products are capable of causing dental caries or other bacterial diseases of additional parts of the oral cavity [15]. After disturbance of the balance between the original microbiota and the propagated potentially pathogenic microorganisms, various diseases frequently occur in the oral cavity. Therefore, these microorganisms may exhibit some pathogenicity, but only under certain conditions, and therefore, we refer to them as facultative or opportunistic pathogens [16]. From the surface of teeth, we may isolate *Streptococcus sanguis*, *Streptococcus mutans* and bacteria of the genera *Neisseria*, *Haemophilus*, *Lactobacillus*, *Propionibacterium*, *Actinomyces*, *Leptotrichia*, *Fusobacterium*, *Veillonella*, *Bacteroides* and *Bacterionema*, described in **Table 1**.

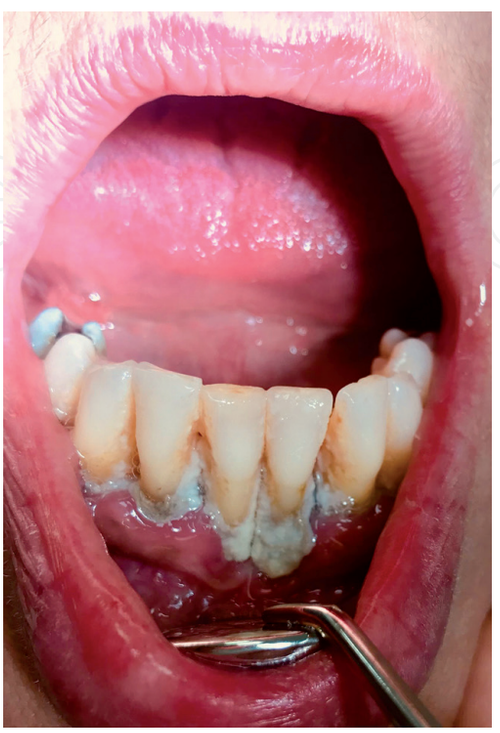

Figure 2.
Deposit of supragingival dental calculus on the vestibular area of teeth in the mandible.

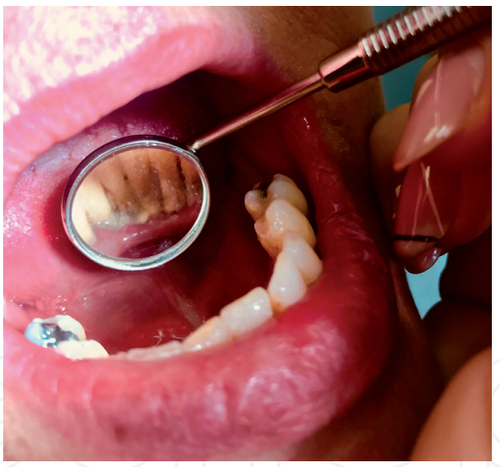

Figure 3.
Deposit of dental calculus on the lingual area of teeth in the mandible.

	Anaerobic microorganisms	**Aerobic microorganisms**
Teeth surface	*Prevotella buccalis*	*Neisseria* spp.
	Actinomyces viscosus	*Protozoa*
	Propionibacterium spp.	*Streptococcus mutans*
	Lactobacillus spp.	*Aggregatibacter Actinomycetemcomitans*
	Actinomyces israelii	*Mycoplasma* spp.
	Actinomyces naeslundii	*Streptococcus sanguis*
	Nocardia spp.	
	Rothia dentocariosa	
	Peptostreptococcus	
	Actinomyces israelii	
	Veillonella spp.	
	Fusobacterium spp.	
	Leptotrichia spp.	
	Prevotella oralis	
	Actinomyces odontolyticus	

Table 1.
Oral microbiota on the surface of teeth.

2.3 Oral microbiota of the tongue

From the tongue, there was isolated particularly *Streptococcus salivarius,* while *Streptococcus mutans* and *Streptococcus sanguis* appeared in the oral cavity only after eruption of teeth [17]. The tongue may become a reservoir of microorganisms participating in periodontal diseases. Bacteria that occur in the saliva may originate from various parts of the oral cavity and the microbial composition of saliva resembles that of the tongue (**Tables 2** and **3**).

2.4 Oral microbiota of the saliva

Free fluoride ions, found in the saliva in concentrations ranging from 0.01 to 0.05 ppm, are an important factor of remineralisation of enamel [18]. Individual proportions of calcium, fluorine and phosphates indicate potential remineralisation effect of the saliva on the dental tissue. Saliva has a positive suppression effect on the development of dental caries. This effect results from the content of unsaturated ions of phosphates, fluorine and calcium while there is a continuous exchange of these ions between the tooth crown and the saliva. At neutral pH, a balance is established between enamel minerals and the saliva. When the action of organic

acids produced by bacteria disturbs this balance, pH in the oral cavity decreases and demineralisation of tooth surface occurs. Some components of the saliva neutralise the acidic environment and reduce the demineralisation rate and thus prevent the dental caries. This buffering capacity of the saliva is ensured by phosphate, bicarbonate and proteinaceous buffers [19].

Glycoprotein mucin acts as a lubricant of the oral cavity surface, produces a protective barrier against the external environment and, at the same time, facilitates chewing, swallowing and speech. It is one of the agglutination factors of the saliva that causes aggregation of bacteria. It can interact with *Streptococcus sanguis*, *Streptococcus mitis*, *Streptococcus gordonii*, *Aggregatibacter actinomycetemcomitans*, *Pseudomonas aeruginosa* and *Escherichia coli*. Saliva also contains other biologically active compounds, such as hormones, glucose, cholesterol, fatty acids and urea [20].

Microorganisms do not tolerate large variations in the level of pH. The pH in the oral cavity is close to neutral and ranges between 6.75 and 7.25. Saliva exhibits remineralisation abilities but the remineralisation process requires some time [21]. Increased frequency of easily metabolizable saccharides at the presence of plaques increases the risk of development of caries [22]. In this respect, saccharose plays a significant role as it easily diffuses into the plaque and is highly soluble [21]. Saccharides use microorganisms as a source of energy and a building material. Organic acids synthesised by microorganisms during metabolic processing of saccharides cause a decrease in the level of pH and a subsequent loss of minerals from the teeth surface [23].

	Anaerobic microorganisms	**Aerobic microorganisms**
Tongue	*Campylobacter (Campylobacter sputorum)*	*Streptococcus mitis*
	Propionibacterium	*Streptococcus salivarius*
	Actinomyces	*Staphylococcus* spp.
	Veillonella	*Enterobacteriaceae*
	Bacteroides (Bacteroides melaninogenicus)	*Streptococcus sanguis*
	Peptococcus	*Corynebacterium* spp.
	Prevotella (Prevotella oralis)	*Candida* and other microscopic fungi
	Peptostreptococcus	*Micrococcus* spp.
		Staphylococcus spp.
		Neisseriaceae

Table 2.
Oral microbiota of the tongue.

	Microorganisms
Saliva	*Streptococcus milleri*
	Streptococcus salivarius
	Actinomyces spp.
	Veillonella spp.
	Streptococcus sanguis
	Streptococcus mitior
	Lactobacillus spp.
	Streptococcus mutans

Table 3.
Oral microbiota of the saliva.

3. Oral cavity diseases

A variety of diseases involve the oral cavity including dentition problems, maxillary and mandibular disorders and diseases, gingivitis, diseases of the tongue,

palate, internal mucosa and lips [24]. In the oral cavity, there are also salivary glands that fulfil very important functions within the digestive system and these paired glands may be afflicted with various inflammatory and noninflammatory diseases that can cause additional complications in the oral cavity [25]. Due to the diversity of anatomical structures and varied microbiota in the oral cavity, this part of the body can be affected by a great number of diseases such as tumour and benign diseases, inflammatory and noninflammatory and inherent or acquired diseases [22]. They are caused by infectious and noninfectious agents. The infectious agents include viruses, bacteria and fungi, and other may be caused by hormonal changes, systemic diseases, hypersensitive responses, immunodeficiency states or tumours [11].

3.1 Focal infection

Focal infection of dentogenic origin is defined as a secondary or total infection caused by spreading of microorganisms to distant organs, while the primary infection is located in the tissues of apical and marginal periodontium. Oral focus is a focus of the chronic inflammatory process of primary infection localised in the tissues of the oral cavity, which is the source of infection. From the point of view of focal infection, the most serious etiological agents are *Streptococcus viridans*, *Streptococcus mitis*, *Streptococcus milleri* and *Streptococcus sanguis* [26]. As a matter of fact, this involves a numerous group of diseases or states that include also periodontitis or periodontitis marginalis. Focal infection is a focus from which the infection spreads to the entire organism and causes damage to tissues and organs [27]. In the course of several years, the opinion about the source of focal infection in the oral cavity gradually changed. In the past, mostly foci in the area of teeth roots, the so-called dead teeth, were considered the sources of focal infection [28]. Due to insufficient possibilities of treatment of root canals, many teeth were extracted [29]. Currently, this very practice is the subject of increasingly serious discussions within professional circles as a potential massive source of infection of an organism. Endodontics is a branch of dentistry dealing with diagnosis and treatment of pathological conditions of dental pulp and periapical tissues [30]. Endodontic treatment means the treatment of the dental pulp, in the majority of cases its complete removal and perfect filling of root canal using correct techniques and treatment procedures.

The role of root filling is to close hermetically the entry to foramen apicale dentis and fill up completely the infection-free tooth canal [31]. Such treatment will prolong functionality and life of inflammation-affected teeth pillars. Imperfect removal of the infected tooth pulp or transfer of infection to the periapical space and incomplete filling of the root canal turns such tooth into a source of focal infection.

There are many foci in the oral cavity that can become potential sources of focal odontogenic infection. Origin of these foci may be attributed to neglected care of the oral cavity, pathological action of some microorganisms or unfavourable anatomic conditions in this cavity.

3.2 Sources of focal infection

3.2.1 Dental pulp necrosis and gangrene

Dental pulp necrosis may develop after injury or as a result of degenerative processes in the dental pulp, and can be affected as a whole or only its part. The principal cause is a pronounced damage to vascular supply. Colliquative necrosis results in decomposition of the dental pulp tissue. At coagulation necrosis, the infected dental pulp produces fluid rich in proteins. Such condition may occur during preparation close to the dental pulp [22]. Dental pulp gangrene is a secondarily

altered necrosis that develops after infection of the necrotic pulp and can be of two types, dry or wet. Dry gangrene develops after partial infection of the necrotic pulp and the remnant pulp dries up. Wet gangrene is more frequent—it develops by the action of multiple microbiota from the carious dentin. Necrotic dental pulp tissue has a strong offensive smell due to accumulated gases such as skatole and indole [31].

3.2.2 Teeth with chronic dental pulp inflammation

Chronic-closed dental pulp inflammations, *pulpitis chronica clausa* in Latin, occur frequently in teeth with caries that penetrated into the dental pulp. The consequence is a chronic abscess with clinically mutedental pulp. During preparation, small amount of pus or dark blood is sometimes discharged from the pulp cavity [22]. Chronic-closed dental pulp inflammations are also frequently clinically mute, and in such cases, the dental pulp shows fibrocystic or at atrophic changes.

The affected pulp tissue is prone to calcification or denticles. The residual pulp shows chronic inflammatory infiltration. Such condition may result in partial or complete obliteration of the root canal [28]. Internal granuloma (*pulpitis chronica granulomatosa interna*) is a chronic productive inflammation with typical finding of considerably hyperaemic granular tissue. A characteristic feature of this process is fibroblasts that form capillaries and cells of chronic inflammatory cellularization [32]. Injury is the most frequent cause of this type of chronic inflammation, also chronic traumatization of the tooth may contribute to damage to the dental pulp [33].

3.2.3 Teeth with periapical findings

Inflammations in the periodontium region affect several types of tissues such as parts of the suspension apparatus of teeth, compacta, spongiosis of alveolar bone and root surface cementum. Such changes are collectively referred to as periodontitis [34]. The causes of periapical inflammation may include infections, chemical irritation and acute or chronic trauma. The most frequent cause of the development of periapical focus is necrotic, passively infected tooth pulp in the root canal. This way altered dental pulp contains compound microbiota with predominance of Gram-positive streptococci, but also enterococci, lactobacilli, *Candida* and *Neisseria* species and anaerobic bacteria such as *Fusobacteria* and *Bacteroides* [35]. Infection causes softening of the dentin wall of the root canal and the metabolic products of microorganisms induce inflammatory conditions in the periodontium region (**Figure 4**). The most frequent site of the development is the apex of the tooth root, but the inflammation process is observed also in the areas of lateral ramifications or sub-pulpal tooth canal. The inflammation is acute or primarily chronic, or chronic with acute exacerbation.

3.2.4 Periodontal abscesses

Abscess is a collection of pus in a newly formed cavity. Periodontitis may be associated with development of periodontal abscesses [34]. They are divided into soft tissue and hard tissue abscesses. They manifest themselves by oedemas and pain, the more advanced forms also by the presence of yellowish pus. Retraction of gingiva may result in evacuation of pus. Bone abscess affects bone spongiosa and is manifested by intense strong pain upon tapping a tooth close to the abscess. Sometimes even shivers may occur and pus is not evacuated after retraction of gingiva [36]. Untreated bone abscess may result in sequestration of the affected bone, but this form is very rare [31].

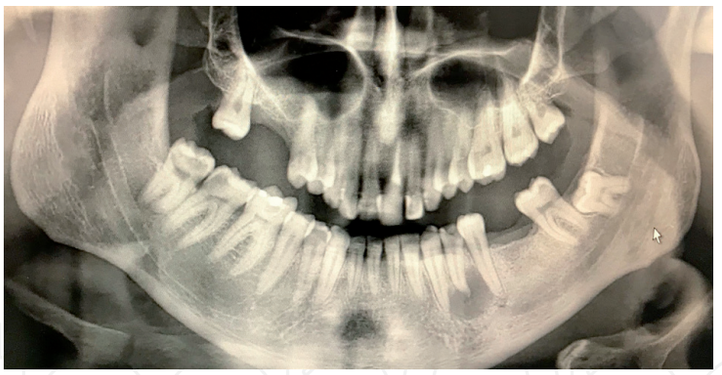

Figure 4.
Periapical finding in tooth No. 34, X-ray - opg 2D image.

3.2.5 Periodontal pockets

Periodontal pockets develop by extension of periodontal fissure, most frequently with approximal localisation. It can be located by one tooth but can affect all teeth in the maxilla and in the mandible. The periodontal pocket mostly contains subgingival dental plaque, subgingival dental calculus, dead microorganisms, leukocytes, proliferating nonspecific granular tissue and inflammatory exudate [37]. Periodontal pockets are classified as true, false, active and nonactive. The false periodontal pockets develop by enlargement of the marginal gingiva without shift of the dento-gingival connection, and the alveolar bone remains intact [11]. The true periodontal pockets are associated with resorption of the alveolar bone. The true periodontal pocket has been described as a space between the gingiva and tooth, coronary delimited by the edge of the marginal gingiva and apically delimited by the base of the periodontal pocket [38]. The difference between the true and false periodontal pockets is diagnosed by X-ray examination [22]. In the active pocket, one may find signs of inflammation, purulent exudations and postprobe haemorrhage. These active periodontal pockets require treatment. The nonactive pockets are free of marked findings. It suffices to carry out regular monitoring of these quiescent forms of periodontal pockets [34].

3.2.6 Gingivitis

Gingivitis is the most frequent microbial inflammation in the human body induced by microbiota of the dental plaque. It can occur as a constant symptom of periodontitis. According to its course, gingivitis may be classified as acute or chronic. Acute gingivitis is painful, the gingiva is red to red-violet and haemorrhage occurs upon stimulus but also spontaneously. Chronic gingivitis manifests itself by a red-pink colour, haemorrhage upon probing and stimulus-induced pain. The shape of the gingiva is altered and large false pockets are frequently observed. The causes are varied and can be divided to local and general [34].

We recognise several types of acute gingivitis. Gingivae affected by gingivitis acuta simplex are slightly reddened while those affected by gingivitis catarrhalis acuta are hyperaemic and swollen. If this process is limited to one or two papillae, we refer to it as papilitis [37]. Gingivitis vesiculosa is manifested by production of vesicles with a clear content and reddened surrounding of vesicles. Gingivae affected by gingivitis pseudomembranosa are red, swollen, associated with production of pseudomembranes—this is fibrinous purulent inflammation. The most frequent form of gingivitis is ulcerous gingivitis that affects younger people [35]. The causes of this disease are many—weakened organism due to infectious disease, vitamin deficit, stress and drugs. The symptoms include swollen gums and the

apexes of papillae truncated by necrosis. It is localised mostly in the zone of frontal teeth and molars [22]. Chronic gingivitis is classified as gingivitis cattarrhalis chronica, gingivitis gravidarum, gingivitis pubertalis, gingivitis scurbutica, gingivitis at epilepsies and leukaemia and elephantiasis fibromatosis gingivae [34].

3.2.7 Retained radices (radices relictae)

This condition occurs in patients with neglected hygiene. If the crown portion of the tooth disintegrates due to untreated caries, the roots of teeth are retained in the gums. Failure to ensure timely treatment of root canal may result in infection of the root pulp and thus in potential dental focal infection [36].

3.3 Diseases of the lips-cheilitis

Inflammation of lips extending to or beyond the border of lips can occur as acute or chronic. The factors most frequently involved in cheilitis are external factors. The currently known forms of cheilitis are actinic, angular, allergic, exfoliative, glandular and granulomatous [39].

Actinic cheilitis is referred to as solar cheilosis or solar keratosis of the lips that develops due to excessive exposure to UV radiation. It is localised in the lower lip in men and in the upper one in women. The risk group are fair-skinned (Caucasian) types of people. The clinical symptoms include dryness and scaliness of lips, their greyish colouration, swelling, ulceration, deepened folds and coarse lesions. Histological examination will confirm hyperkeratosis as a consequence of thickening of the epithelial cells and epithelial dysplasia. The potential ways of treatment include cryosurgery, electro-surgery, laser, and 5-fluorouracyl [40, 41].

Angular cheilitis is also referred to as angular cheilosis, commissural cheilitis or angular stomatitis. It is an inflammation of one or eventually of both angles of the mouth. The causes include bacterial (*Staphylococcus aureus*, haemolytic *Streptococcus*) or yeast infections (*Candida albicans*) mechanical damage to lips by denture prosthesis of fixation apparatus. Also, malnutrition involving deficiency of group B vitamins should be considered. Granulomatos cheilitis presents as swelling of the upper and lower lips and, at the same time, as one of the manifestations of orofacial granulomatosis, which is a separate disease, or as a monosymptomatic form of the Melkersson-Rosethal syndrome. Three symptoms are characteristic of this disease—recurrent orofacial swelling, recurrent facial paralysis and fissured tongue. One can also observe chapped, red-brown lips or buccal nerve paralysis. It is induced by allergic response to cinnamon or various benzoates and can represent also early manifestation of Crohn disease, mycobacterial infection or sarcoidosis. Aetiology of the disease is unknown. It has been assumed that sudden inflammation or random aggregation of inflammatory cells may be involved. Diagnosis is very difficult, important are histological results, which may indicate presence of granulomas and the positive findings may imply the Melkersson-Rosethal syndrome. This finding was obtained also in patients with Crohn disease and affected mouth.

3.4 Diseases of the tongue

The most important diseases of the tongue include atrophy of the tongue fur, rhomboid glossitis, geographic tongue, fissured tongue, herpetic geometric glossitis, black hairy tongue, oral leucoplakia and macroglossia [37].

Rhomboid glossitis also known as central papillary atrophy presents as typical loss of tongue papillae along the midline posterior dorsal tongue, caused by oral candidiasis (**Figure 5**).

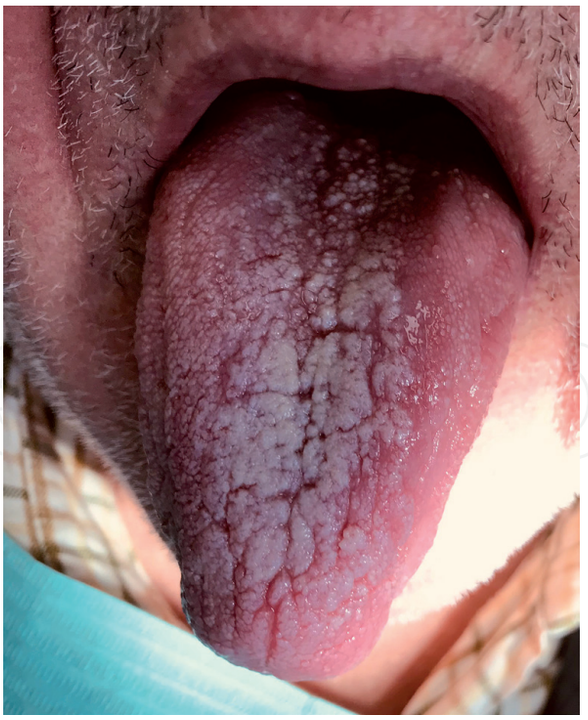

Figure 5.
A white coating on the tongue caused by an overgrowth of Candida albicans.

The tongue lesion is shiny, frequently symmetrical, well delineated, depapillated. The risk factors include smoking, inadequate oral hygiene, use of unsuitable prosthesis and HIV infection. The treatment is based on the use of corticosteroid inhalators and sprays. It occurs worldwide and affects men, women and children. Diagnosis is based on clinical examination and laboratory confirmation of *Candida* spp. The most effective prevention/treatment, especially in smokers, is giving up smoking and the use of antimycotics [39].

The term geographic tongue, lingua geographica, is used to describe inflammation affecting the dorsal surface of the tongue. Its characteristic feature is depapillation of some parts of the tongue resulting in the alternation of depapillated and normal-structure areas producing a map-like (geographic) pattern.

The depapillated areas are smooth and more intensively red coloured, and except this colour differences, the condition mostly causes no other symptoms. However, it may cause burning mouth syndrome after consumption of some foods [34]. The exact aetiology is unknown but association with smoking, stress and genetic association with human leukocyte antigens (HLAs), diabetes or psoriasis has been assumed. Diagnosis is made on the basis of clinical and histological examination. Differential diagnosis must distinguish this condition from oral lichenic planus, erythematous candidiasis and leucoplakia. Effective drug therapy is based on antihistaminics and corticosteroids.

Fissured tongue affects 5–10% of population with higher susceptibility occurring in older individuals. The exact aetiology is unknown but imbalance of the level of salivary electrolytes and haematological abnormalities were observed. This condition affects the dorsal side of the tongue. In the central part, a central fissure (groove) is observed with multiple smaller fissures branching off the central one. Patients with Down, Melkersson-Rosethal and Sjögren syndromes are at risk. Improvement in oral hygiene, particularly the tongue, may result in the recovery from this disease [22].

Black hairy tongue is the term used to refer to the hypertrophy of filiform papillae of the tongue that acquire black colour. This disease affects the dorsal part of the

tongue. There are several causes that induce this disease: keratinization of cells, restoration of the epithelial layer without complete exfoliation of the old layer, change in pH in the oral cavity, use of oxidation agents, smoking, antibiotics, bacterial and yeast infections and radiotherapy. Complication of this disease involves papillae that are markedly elongated and thus can cause tickling sensation, which may result in vomiting. Therapy consists in intensive cleaning of the tongue and administration of antimycotics [42].

3.5 Diseases of the salivary glands

The diseases afflicting salivary glands include xerostomia, siallorhoea, inflammation of salivary glands—sialadenitis, Sjögren syndrome, calculi in salivary glands—sialolithiasis, cysts, sialadenosis and tumours of salivary glands [43].

Xerostomia or dry mouth syndrome is associated with reduced production of saliva, and this condition is also termed hyposalivation. It is caused by carcinomas or unsuitable therapy. An extensive group of diseases are inflammations of the salivary glands—sialadenitis. They are classified as acute bacterial sialadenitis, chronic sialoadenitis, viral sialadenitis, specific sialadenitis and autoimmmune sialadenitis—the Sjögren syndrome [34].

Acute bacterial sialadenitis is most frequently caused by pathogenic bacteria *Streptococcus aureus*, *Streptococcus viridans* and *Streptococcus pneumoniae*. The principal pathways of spreading of this infection are haematogenic and lymphogenic. The risk factors that support the development of infection include decreased production of saliva, cachexia sialolihtiasis and malignancies. Clinical manifestations include purulent and abscess forms.

3.6 Dental caries and periodontitis

Dental caries is the most frequent dental and oral disease. It occurs worldwide [31]. Root caries is caused by *Streptococcus mutans*, *Lactobacillus acidophilus*, *Actinomyces* sp. and *Nocardia* sp. Bacteria first pass through the enamel, then through dentin, and finally, they reach the cementum layer. During clinical examination of dentition, black or dark yellow lesions are observed on teeth [44]. The most important mineral in teeth is hydroxyapatite. Remineralisation of teeth is ensured by prolin and minerals contained in the saliva [45]. Residues of food in the oral cavity, sweet beverages, beverages with high concentration of acids and citrus fruit are sources of bacterial nutrition.

The ability of bacteria *Streptococcus mutans* to form biofilms is important from the clinical point of view, particularly in relation to the development of dental caries. Dental caries has a multispecies aetiology. Mutant streptococci are referred to as a cluster of acidogenic streptococci species inhabiting dental plaques. *Streptococcus mutans* and *Streptococcus sobrinus* are the bacteria most frequently isolated from dental carious lesions. There were published individual case reports involving infectious endocarditis with participation of these bacteria [46]. The development of dental caries starts with dissolution of the mineral portion of tooth manifested by lesions and white sports on teeth, followed by local destruction of the enamel and dentin. If this process is left alone without treatment, inflammation of the dental pulp and periapical tissues follows. Many strategies focused on reduction of the occurrence of dental caries and their specific effect consisting in reduction of counts or acidogenic activity of *Streptococcus mutans* in the dental plaque [47].

In 2011, information about new bacterial species *Scardovia wiggsiae* appeared in professional microbiological and stomatological literature. The authors reported

that in addition to *Streptococcus mutans,* this bacterium participates in the development of dental plaques and acute early age dental caries affecting dentition of children [44]. The relevant investigations were carried out by a team of scientists from Forsyth Institute, Cambridge, headed by A. C. R. Tanner, and involved bacterial population in samples of dental plaques and from the depth of cavities in primary dentition of 2–6-year-old children. The results were compared with the findings in the plaques of children without dental caries or white spots indicating demineralisation of enamel [48]. Because dental caries develops with participation of acidotolerant bacteria, the laboratory cultivation was carried out in anaerobic environment on blood agar of pH 5.0. In this way, the authors selected species that may play an important role in cariogenesis. Partial 16S rRNA sequences obtained from 5608 isolates were characterised on the basis of species. Subsequently, the findings of individual bacterial species from children with and without caries were compared. The species most frequently isolated from children with acute dental caries were *Streptococcus mutans*, *Scardovia wiggsiae*, *Veilonella parvula*, *Streptococcus cristatus* and *Actinomyces gerensceriae*. According to Human Oral Microbiome Database, the authors identified 198 taxons and 45 of them were until then characterised as noncultivable. The results showed that both *Streptococcus mutans* and the new bacteria *Scardovia wiggsiae* were isolated from 80% of the children with dental caries, but these bacteria were absent in 80% of children free from dental caries. The microorganism most frequently present in progressing dental caries was *Streptococcus mutans* and the newly discovered species *Scardovia wiggsiae* co-participated in the development of dental caries but was cultivated also independently from the cases of progressing dental caries. Many saccharolytic bacteria participate in reduction of pH, but their growth is selectively restricted at low pH at which the cariogenic acidotolerant species that include also the newly discovered *Scardovia wiggsiae* are able to multiply.

Periodontitis is a serious infection of gingiva that damages soft tissues and degrades the osseous tissue, can cause looseness of teeth or result in their loss (**Figure 6**). It affects approximately 10% of the world population. It is a subject to internal and external factors and the influence of bacteria, particularly the Gram-positive ones, referred to sometimes as the "red complex", namely *Treponema denticola*, *Porphiromonas gingivalis* and *Tanerella forsythia* [39].

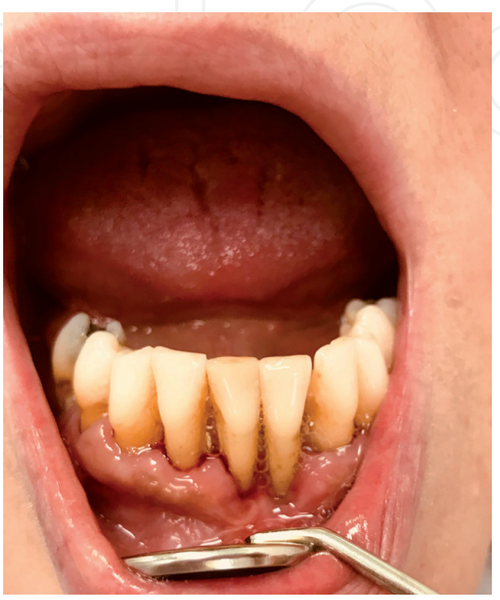

Figure 6.
Periodontitis afflicted lower front teeth in the mandible.

4. Oral probiotics and their influence on oral cavity diseases

4.1 Importance of probiotics to the oral cavity health

The authorship of the concept of probiotics has been attributed to the Russian scientist and Nobel prize winner Elie Metchnikoff, who at the turn of the nineteenth and twentieth centuries theorised that Bulgarian pheasants own their long life to the consumption of fermented milk products. Since then, the scientists confirmed that the use of probiotic strains, particularly those of the genera *Lactobacillus* and *Bifidobacterium*, can support gastrointestinal, genitourinary and oral health by maintaining the microbial balance of these ecosystems [49]. According to the up-to-date definition, probiotics are live microorganisms, which when administered in adequate amounts confer a health benefit on the host [50].

In the past decade, the awareness of probiotics and their contribution to human and animal populations increased and a wide range of probiotic products appeared on the market. Research activities focused on the search for new probiotics help to understand the process of development of probiotic products and their potential role in prevention or treatment of diseases [51]. Composition of microbiota of today's man differs from that in the past. Modern people are exposed to a number of negative influences that affect their microbiological balance. As long as the harmony and balance is maintained, we speak about symbiosis. The imbalance of microbiota is referred to as dysbiosis, which involves changes in proportions and heterogeneity of commensal species resulting in disturbed functioning of protective barriers and subsequent development of diseases [52]. The adverse influences that cause dysbiosis include particularly the use of antibiotics and chemotherapeutics, stress situations resulting from the lifestyle of the modern man, unsuitable eating habits or drinking regimen and changes in composition of food or the environment. Searching for amendment of the developed dysbiosis became the prime stimulus of the study of probiotics.

The increasing bacterial resistance to antibiotics and the demands of the wide public on natural therapy resulted in decreased use of conventional antimicrobials and raised the need for development of new ways of treatment [53]. A separate issue is the probiotics intended for oral cavity. People associate the term probiotic with the health of the intestinal tract and necessity to use them during antibiotic treatment, which became a common practice but oral antibiotics also play an important role in the overall health of an individual. It was demonstrated that probiotics have the potential for modification of the oral microbiota and are effective in the prevention and treatment of oral cavity diseases, such as dental caries and periodontal diseases associated with dysbiosis [54]. Today, the global market already offers some probiotic preparations that prevent formation of dental plaques, support health of gingivae and teeth and help to fight the bad breath [55]. The most frequently investigated bacteria include representatives of the genera *Lactobacillus*, *Streptococcus* and *Bifidobacterium*. Species of these taxons are members of normal microbiota found in the gastrointestinal tract, while some of them prefer to colonise the oral cavity [56]. Potentially, pathogenic microorganisms enter the body through the mouth or nose and thus the oral probiotics constitute and excellent first-line protective barrier of the mouth and throat. Clinical studies in humans that investigated treatment of periodontal diseases by probiotics reported overall contributions such as the decreased bleeding of gums. The studies that involved the use of probiotics as a supplement to clinical periodontal treatment showed a more pronounced improvement of the clinical status of patients in comparison with the clinical treatment alone [57]. One of the preparations used in Slovakia is ProDentis [58], a preparation containing mostly *Lactobacillus reuteri*. One clinical study was

based on the use of pastilles containing *Lactobacillus reuteri* strains as a supplement of therapy of chronic periodontitis. Results of this study revealed a marked decrease of occurrence of *Porphyromonas gingivalis* in the saliva and in subgingival and supragingival plaques [59].

4.2 Properties of oral probiotics and mechanism of their effect

The effectiveness of probiotic microorganisms in the oral cavity depends on their ability to resist to the environmental conditions and protective mechanisms, to adhere to the surfaces coated by saliva, easily colonise the mouth and grow in it and inhibit oral pathogens without harming the host [55]. Ideal properties of oral probiotics are presented as follows [60]:

1. binding to dental surfaces,

2. production of antimicrobial substances against oral pathogens,

3. aberration of environmental conditions in the mouth, and

4. reduction of the inflammatory response.

The mechanism of effect of probiotics in the oral cavity (**Figure 7**) is almost identical with that in the gastrointestinal tract, i.e., modulation of the immune response, metabolic effects and harmonisation of the intestinal or oral microbiota.

Probiotic bacteria excrete various antimicrobial compounds such as organic acids, hydrogen peroxide and bacteriocins [61]. In addition, they compete with pathogens for the adhesive sites on mucous membranes. They can also modify their environment by modulation of its pH or the oxidation–reduction potential, which can interfere with the ability of pathogens to establish themselves on the mucosa. The beneficial effects of probiotics may include stimulation of the nonspecific immunity and modulation of humoral and cellular immune responses [14, 62].

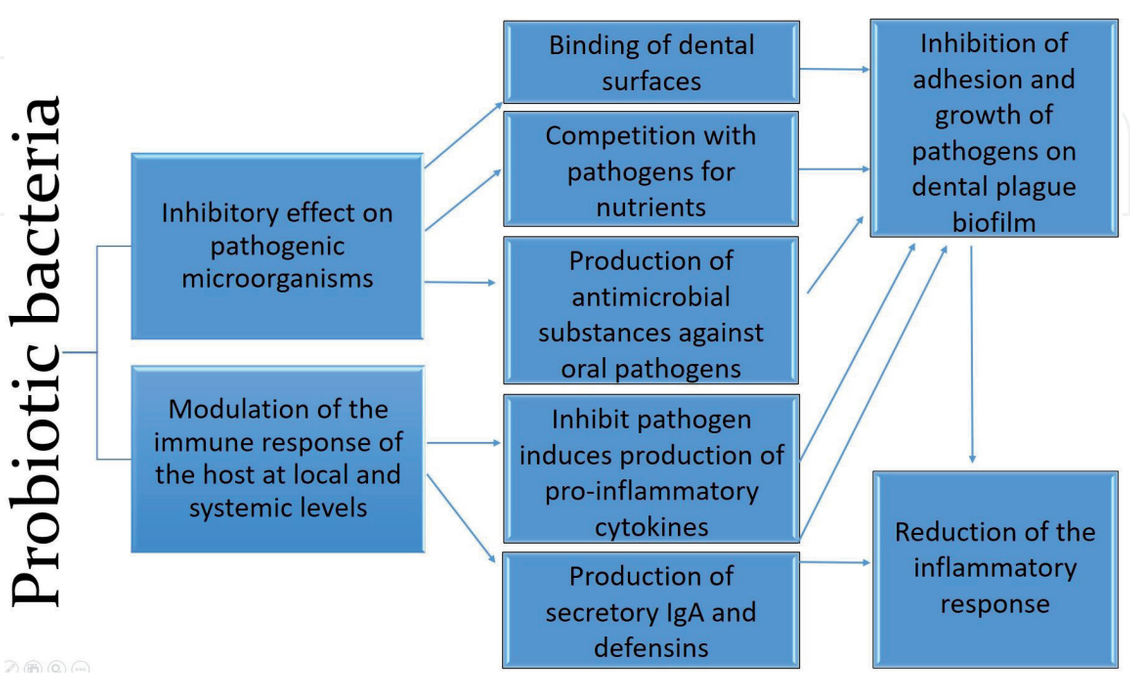

Figure 7.
Mechanism of the effect of probiotics in the oral cavity.

4.3 Potential risks of the use of probiotics

Before introduction of any probiotic product to market, it has to comply with very strict conditions. The product should be a result of thorough research of the relevant strain and each dose should contain sufficient bacteria even after storage of the preparation [63]. Probiotics are considered safe as they contain nonpathogenic microorganisms, and this is one of the reasons for high willingness of patients to use them. Risk to health may occur during a long-term use of probiotic preparation at diseases or states that enable their potential passage to the body at the development of secondary infection. Such states include bloody diarrhoea, immunosuppressive treatment or irradiation. Additional potential risks include transfer of vancomycin resistance by strains of *Enterococcus faecium*, administration of high doses of probiotics to autoimmune patients, infants and newborns with immunity and intestinal permeability disorders and administration to patients with immature or markedly disturbed immune system or patients with AIDS [64].

Probiotics can be routinely used as a food supplement, and their positive health claims were well described [65]. Despite that, some undesirable effects of the use of probiotics can also occur [66]. Usually, this involves only mild reactions that affect small percentage of users. When using probiotic products, it is necessary to consult a doctor about potential indications and undesirable effects [67]. Clinical indications of the use of probiotics are very extensive. One of their unwanted effects are digestion problems that may involve tympany and increased thirst [68]. Biogenic amines are low molecular weight organic compounds produced by degradation of amino acids, which may affect negatively the human organism [69]. The biogenic amines produced from the accepted food by fermentation activity of probiotic bacteria have excitation effect on the nervous system and decrease blood flow through organs, which can result in headaches [70]. Biogenic amines are histamine, tyramine, tryptamine, putrescin, spermidine and phenyl ethylamine [71]. In some groups of people, the use of probiotic products results in increased risk of infections, such as in immunosuppressed individuals or patients after surgeries hospitalised for long time. One should not forget to mention allergic reactions associated with the use of probiotic components. Probiotic products contain various additives such as lactose, eggs, soya or other generally known allergens. The consumers should avoid components that may induce in them hypersensitivity or allergic reactions [72]. Basically, such cases are rare and the probiotic treatment can be referred to as the treatment on a natural basis. At the same time, it is recommended to increase gradually the doses of probiotics until reaching the full dose in order to prevent potential side effects that occur particularly in weakened individuals.

5. Conclusion

There is an increasing concern about the fact that oral diseases put a systemic load on the organism. This stresses the importance of oral health for the overall health of an individual and the population. Predictions have been made in the past that the scientific and technological advances in the field of molecular biology, immunology and genetics, together with ageing of the population, will require future complex health service measures within which the care of the oral health will become important from the point of view of management of overall health and economy, and thus will necessitate novel oral health approaches. Bioactive compounds, as substances capable of affecting the microbiocenosis environment, are considered an alternative when searching for replacement for antibiotics. Results of the studies focused on microbiocenosis of the dental biofilm and interactions

between individual bacterial species indicate a probiotic potential of some oral bacteria and their potential to prevent oral cavity diseases. Qualitative influence on pathogenic bacterial microbiota of the oral cavity, exerted by probiotic bacteria such as *Streptococcus salivarius*, brings not only health but also economic benefits. One should only hope that additional evidence of beneficial effects of probiotics and increased knowledge about biochemical and immunological mechanisms of their action will improve the potential of treatment and prevention of oral diseases and result in more rational and targeted use of bacterial supplements under specific clinical conditions.

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Author details

Andrea Stašková[1*], Radomíra Nemcová[2], Stanislav Lauko[2] and Andrej Jenča[1]

1 Pavol Jozef Šafárik University in Košice, Slovakia

2 University of Veterinary Medicine and Pharmacy in Košice, Slovakia

*Address all correspondence to: andrea.staskova@upjs.sk

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