

Chemical and Biological Factors in Infectious Diseases

The oral microbial flora

IRINA ESANU¹, MIHAELA DEBITA², CARMEN MIHAELA DOROBAT^{3*}, ALEXANDRU ANDREI ILIESCU^{4*},
MADALINA NICOLETA MATEI^{2*}, DRAGOS OCTAVIAN PALADE³, KAMEL EARAR²

¹Grigore T. Popa University of Medicine and Pharmacy of Iasi, Dental Faculty, 16 Universitatii Str., 700115, Iasi, Romania

²Dunarea de Jos University of Galati, 47 Domneasca Str., 800008, Galati, Romania

³Grigore T. Popa University of Medicine and Pharmacy of Iasi, Faculty of Medicine, 16 Universitatii Str., 700115, Iasi, Romania

⁴University of Medicine and Pharmacy of Craiova, Department of Oral Rehabilitation, 2 Petru Rares Str., Craiova, Romania

The wide concept of health does not benefit of a single definition, but of multiple definitions and this plurality is related to the knowledge assimilated and the socio-economic dynamics. This is due to the fact that health is an ongoing process, its notion changing with the passage of time. Thus, at international level, health is nowadays defined considering multiple criteria. In the last decade, the analysis of relevant statistical data presents an unfavourable evolution for the three major components of population dynamics: natality, mortality and external migration, accompanied by the deterioration of the entire demographic construction and tendencies of heading towards an imminent demographic drift. Humans protect themselves against the microbial aggression by using their inborn barriers and mechanisms that are completed and modulated by acquired barriers and mechanisms. For a microorganism to reach the internal environment and generate an infectious process, it must get through and overcome these barriers. In order to overcome these barriers, the infectious agent must first adhere to the surface of epithelial cells and then pass through the epithelium. Local defence mechanisms help limit the infection and present the antigen to the regional lymphatic ganglions, contributing at the initiation of the immune response. On the other hand, the infectious agent present in the lymphatic system causes lymphangitis and satellite adenitis, which stand as a filter in the infections' way. The study included 127 patients with bacterial infections that were studied from 2014 to 2018. Infection can be caused by certain species of germs whose main feature is pathogenicity. Specific infections are caused by a foreign infectious agent that has accidentally reached the oral cavity causing oral lesions (appear in the secondary phase of the general infection). Specific infections are individualized, caused by a single microbe (monomicrobial) while the non-specific ones are associated (polymicrobial).

Keywords: oral microbial flora, bacteria, human host, conflictual reactions, biological unbalance, oral primoinfection.

The oral cavity presents one of the most concentrated and various microbial populations.

The oral cavity hosts a complex microbial ecosystem with different species and development particularities according to the anatomic structure (lips, teeth, tongue, jugal mucosa, palate, saliva, gingival cleft) and the artificial constructions they are located on (bridges, dental prostheses). Numerous bacterial species interact either in a synergetic manner, creating the proper environment or the necessary food for the survival of others, or antagonistic manner - some species are in competition with the others for food and survival [1-3].

Oral microbial flora presents itself as follows: Gram positive bacilli, Gram negative bacilli, cocci or aerobic and anaerobic bacilli. Anaerobic or optional anaerobic streptococci represent almost 80% of the total viable germs [4,5].

Candida and coliforms are indigenous in the oral cavity of adults. Protozoans are present in a smaller number; in high number indicate a poor oral hygiene.

Lactobacilli are found near the cavities. *Candida* is much more frequent in patients who were subjected to a treatment with antibiotics than in those who were not treated. After cortisone treatment plurispesific fungal strains appear.

There are bacteria that attack the specific elements of connective tissues - collagen, chondroitin - sulphuric acid, hyaluronic acid. A single species of diphtheroid, in pure

culture, produces chondroitinase, *Bacillus melanogeneticus*, capable of digesting active collagen [6-8].

The biological unbalance of this flora generates a pathogenic microbial activity favouring orodental infections which lead to focal disease. Multiple cavities, chronic superficial, marginal and profound periodontitis, gangrene are just a few of them.

The constant decline of tuberculosis in developed countries changed in certain areas where the prevalence of AIDS increased. Nevertheless, in Romania, there is still a high prevalence of tuberculosis, regardless of the HIV infections. The initial localization of tuberculosis on the oral mucosa is, classically, considered to be exceptional [9-11].

Oral primoinfection represents only 0.25%. It is the most frequent from the initial extrapulmonary tuberculosis (61%). Almost every time it is caused by bovine bacilli. The contamination has its origin in food, in milk or unsterilized dairy products.

In its typical form, oral primoinfection presents itself as an oral chancre adenitis complex and slight modification of the general condition in children aged between 8 and 12 years old. Submaxillary adenitis is first; it can be mono or pauci-ganglionic. Ganglions are, at first, firm and painless, mobile at superficial and profound level; they rapidly become sensitive, warm, with integumentary infiltration.

Being painless, the chancre can pass unobserved if it is not systematically studied; the ulceration being superficial it is often positioned on the lower arch mucosa at the cervix

* email :carmen.dorobat@yahoo.com; iliescualexandru@gmail.com; madalina.matei@yahoo.com

of a tooth or two; the ulceration is ovoid or cross-like. The general signs are: weakness, asthenia, anorexia, subfebrile state.

Parotid tuberculosis is rare and the diagnosis is very difficult to establish. In 1883 De Paoli presented the first case of parotid tuberculosis. Since then the number of cases increased, well known authors (Dechaume, Firu, V. Popescu, Gafar, Burliba a, etc.) indicating also other cases of parotid tuberculosis.

The disease affects mainly female individuals, aged over 40 years old. The evolution of the disease expands on a very long period of time (2-20 years). In 50% of the cases the disease is unilateral while in 30% of the cases it is bilateral.

The general condition of the sick individuals is generally good; they present unilateral or bilateral tumefaction. The pulmonary radiography is normal, IDR intensely positive to tuberculin, high VSH level [12- 14].

Pathogenically speaking, some authors claimed the tuberculous bacilli reached the lymphatic pathway starting from tuberculosis of tonsils.

The same authors state that, on the same pathway, the infection can reach the teeth. In case of generalized tuberculosis, it can also be taken into consideration the hematogenic pathway. Most authors indicate that in almost 75% of the cases the lesion is isolated - without bacillary antecedents. The rarity of the cases, according to some authors, might be caused by the fact that the salivary parenchyma has an extraordinary defence ability. Bioptic puncture can be extremely useful.

In case of infected gums it can be used the bacteriological examination of the gingival pocket or of the bacterial plaque proliferated in the pockets.

The samples are collected, depending of the case, with one sterile cotton swab placed on a Miller needle or, in case of dental plaque, with a sterile scaler. Afterwards it is inseminated in culture environments and is sent to the laboratory for bacteriological investigations.

Vinzent, Sehmans and Goudert proposed the gingival hemoculture to demonstrate the ethiopathological role of bacteria in chronic marginal periodontitis, whose value was not confirmed by the studies conducted in the Pasteur Institute from Lille [15].

The factors influencing the development of oral microbial flora are: the *oral environment* which creates the favourable conditions for bacterial species to survive and reproduce: humidity, neutral pH, food, and as long as these features of the environment are present, the bacteria will continue to exist; *adherence* to the epithelial cells of the mucosa, dental enamel and dentin form intergeneric coaggregates; *protection areas* are those places that protect the poorly adherent microbial species: occlusion fossette, enamel fissures, polysaccharidic matrix of the pellicle acquired from the surface of the dental hard tissue, gingival sulcus; the *elimination of the microorganisms* from the oral environment occurs naturally through the desquamation of the oral epithelium, the salivary flux, movements of the tongue and soft tissue, through mastication and deglutition and artificially by tooth brushing, use of dental floss and mouthwater; the nutrients necessary for the survival of bacteria come from food, being mainly *carbohydrates* and *saccharides* which through metabolization by part of certain microbial species from the bacterial plaque that adheres to the hard intraoral structures decrease the pH level and initiate the demineralisation process of the enamel; local or systemic *antimicrobial therapy* (antibiotics) affect the balance of the oral flora favouring the proliferation of fungi, involved in the cutaneous-mucous infections [16-18].

The microorganisms from the oral fluid are different from those that survive on the hard tissues forming the bacterial plaque.

These are more vulnerable and easier to remove using the means of oral hygiene unlike the ones forming the microbial plaque that adheres to the teeth and which are more resistant and more difficult to remove.

It is important to know that by respecting the measures of oral hygiene it is intended the removal of the bacterial plaque from the hard structures but the oral environment will never be a sterile one. Maintaining the *balance of the oral microbial ecosystem* is essential because commensal bacteria have a protective role, helping the immune response and preventing the development of other pathogenic species that make the organism ill [19- 22].

Between the microbial flora and the human host (the mouth) can appear conflictual reactions, resulting various infections that manage to overcome the resistance mechanisms of the host.

Sickness is determined by two factors: the bacterial factor (the virulence and number of microorganisms) and the field factor (the organisms' resistance and the local defence system).

Bacterial groups produce organic compounds that protect the pathogenic bacteria (harmful) leading to the inactivation of A immunoglobulins and thus decreasing the local defence ability, causing halitosis.

Non-specific infections are triggered caused by infectious oral agents (bacterial endocarditis). Non-specific infections are mixt infections, caused by bacterial groups acting simultaneously and which associate from a pathogenic point of view; we refer to endodontic (from inside the tooth) and periodontal infections (the tooth's support system), to neighbouring infections (ears, tonsils, sinuses) [23, 24].

Specific infections are caused by a foreign infectious agent that accidentally reached the oral cavity; it generates oral lesions (appear in the secondary phase of the general infection). Specific infections are individualized, determined by a single microbe (monomicrobial), while the non-specific ones are associated infections (polymicrobial).

Experimental part

Material and method

The study includes 127 patients with bacterial infections, studied in the interval 2014-2018. The group of etiological factors cause infectious diseases.

An infectious disease or infection must be seen as the ensemble of phenomena that take place in the organism due to the presence, proliferation and the action of microorganisms. In an infectious process there are important: the microorganism (the pathogenic agent of the infection), the macroorganism (where the germ conducts its biological activity) and the external environment which exerts its influence on the features of both macro- and microorganisms. Infectious diseases are not caused by just any type of germ. Infections can be caused by certain species of germs characterized by pathogenicity. Humans can be carriers of pathogenic germs without getting ill. In the oral cavity of certain people can be discovered pathogenic bacilli of diphtheria or meningococci, but nevertheless, these individuals are not ill of diphtheria or meningitis (healthy germ carriers). The explanation resides in the different causes that are connected with the features of pathogenic germs and with the resistance of that particular organism.

Although the representative species for the microbial flora can be isolated from most of the areas of the oral

cavity, certain surfaces – tongue, dental surface, gums, saliva – tend to favour the preferential colonisation with certain specific microorganisms.

Results and discussions

Based on the clinical signs of the patient, the clinician should be suspicious about the apparition of bacteraemia and choose the right moment for taking the sample for hemoculture. The diagnostic algorithms implemented by different researchers are intended to help the clinician in managing the great amount of clinical data and in transforming this information in predictive scores.

The treatment with antibiotics has only a therapeutic purpose in the basic treatment of post-surgical infection, as helping treatment in surgical infections (abscess, infection of salivary glands), but also in the prophylaxis of superinfection.

The oral cavity hosts a complex microbial ecosystem that includes different species and development particularities depending of the anatomical structure (lips, teeth, tongue, jugal mucosa, palate, saliva, gingival cleft) or artificial constructions on which they locate (bridges, dental prostheses). The numerous bacterial species interact in a synergetic manner, that is they help each other, some create the proper environment.

The normal oral flora contributes at the protection against infection by: producing bactericidal substances; producing Ig A and peroxidase which interact with the thiocyanate ions from food and the hydrogen-peroxidase produced by the commensal flora; producing lysozyme and lactoferrin; the existence of salivary proteins can inhibit, at their turn, the adherence of bacteria on the surface of teeth and the oral mucosa; the quick turnover from the level of the oral epithelium also helps removing the bacteria that adhered at this level.

Gingival inflammation can be associated to bacterial infection. When the pulp is inflamed it results a constant pressure on the dental nerves and the neighbouring tissues. The pressure can generate moderate or extreme pain, depending of the degree of inflammation and the organism's immunity.

The bacterial plaque can be differentiated into two main types, depending of the place where it is formed. Thus, there is a supragingival bacterial plaque (appears on the surface of the teeth and on the oral mucosa, roof of the mouth and the tongue) and the subgingival bacterial plaque, situated in the gingival sulcus and the periodontal pocket. When the plaque is thick enough it can be easily noticed with the naked eye.

The formation mechanism of the dental plaque includes: absorption of proteins and bacteria which form a thin film on the surface of the teeth; the adhesion of bacteria to the already formed film; the irreversible adhesion of bacteria due to the intermolecular interaction between the pellicle and the dental cells; the secondary colonizing bacteria attach to the primary ones; cells divide resulting a biofilm.

The initial phase of this mechanism lasts almost 2 hours, while the surface of the teeth and the mucosa of the oral cavity are invaded by salivary proteins, food remnants and cellular residues. The initial film continues being populated by secondary bacteria and developing and turning into mature bacterial plaque (in almost 30 days).

The causes leading to the offset of the mechanism forming the bacterial plaque are the quantity and the quality of the saliva, diet, age, daily habits of dental hygiene and the eventual secondary disorders of the organism which can increase the predisposition to the formation of dental plaque and tartar.

The bacterial plaque consists of numerous microorganisms as streptococci (*Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus sagitus*, *Streptococcus mitis*, *Lactobacillus*), spirochetes or protozoans. Dental plaque causes cavities when the acids from the oral cavity affect the enamel of teeth. When not removed, it can cause irritations of the gum and gingivitis, periodontal diseases and even tooth loss [25, 26].

Primary dental plaque can be removed through the correct brushing of teeth; it helps eliminating the resulting film and the soft deposits from the surface of teeth and gums. Tooth brushing is recommended after every meal, in the morning and in the evening [27, 28, 29].

The use of dental floss is also important for the effective elimination of the bacterial plaque positioned between the teeth (where the toothbrush has no access).

Bacterial plaque can also be effectively eliminated using oral irrigators, gum stimulators, interdental brushes and special devices for tongue cleaning.

The energy of the laser can have a significant effect on the microbial flora by deforming the walls of cells; a thermic effect by attracting the pigment in the cells of specific microorganisms as *Porphyromonas gingivalis* and a direct effect of thermic heat. Consequently, we must consider the tooth that needs to be extracted is a reservoir of infection and not necessarily the instruments. Hence, when the physician estimates a high microbial load after the extraction, he recommends an antibiotic treatment [30- 32].

For maintaining the optimal state of dental hygiene it is recommended to perform a complete professional hygienization with tartar removal and airflow with bicarbonate, at least once a year.

The use of mouthwash twice a day helps maintaining teeth and gums healthier even in the areas where access is more difficult. Moreover, it prevents and reduces dental plaque, one of the gingival causes, and strengthens the enamel of teeth.

Conclusions

The microorganisms from the oral fluid are different from those that live on the hard tissues forming the bacterial plaque; they are more vulnerable and easier to remove by means of oral hygiene unlike the ones forming the bacterial plaque adherent to the teeth and which are more resistant and more difficult to remove.

Maintaining the balance of the oral microbial ecosystem is essential because commensal bacteria have a protective role, helping the immune response and preventing the development of other pathogenic species that make the organism ill.

References

- 1.SOLOVAN, C., GOTIA, S., GOTIA, L.Patologia mucoasei orale, Ed.Mirton,Timisoara; 2006.
- 2.DUCEAC, LD, STAFIE, L, VALEANU, IP, MITREA, G, BACIU, G, BANU, EA, ROMILA, L, LUCA, AC. Sepsis in paediatrics - a special form of infection associated to medical assistance. INTERNATIONAL JOURNAL OF MEDICAL DENTISTRY, 22, no.3,2018, p. 229-235.
- 3.DUCEAC, L.D., LUCA, A.C., MITREA, G., BANU, E.A., CIUHODARU, M.I., CIOMAGA, I., ICHIM, D.L., BACIU, G., Ceftriaxone Intercalated Nanostructures Used to Improve Medical Treatment. Mat. Plast., 55, no.4, 2018, p. 613-615
- 4.SCHWIERTZ, ANDREAS (2016). Microbiota of the human body : implications in health and disease. Switzerland: Springer. p. 45.
- 5.SCUTARIU, M.M., CIURCANU, O.E., FORNA, D.A. et al. Importance of dental maxillofacial aesthetics in dental therapy. MEDICAL-

- SURGICAL JOURNAL-REVISTA MEDICO-CHIRURGICALA, 120, no.4, 2016, p: 926-931
6. BOTNARIU, G., POPA, A., MITREA, G., MANOLE, M., PACURAR, M., ANGELE, M., CURIS, C., TEODORESCU, E., Correlation of Glycemic and Lipid Control Parameters with Cognitive Dysfunction Scores, in Type 2 Diabetic Persons Results from a cross-sectional study. *Rev Chim (Bucharest)*, **69**, no.12, 2018, p.3486-3489
7. RAFTU, G., MITREA, G., MACOVEI, L.A., NECHITA, A., Chemical Additives from the Composition of Plastic Products and Other Materials in Establishing Diagnosis for Allergy Disease. *Mat. Plast.*, **55**, no.4, 2018, p.609-612
8. SHERWOOD, L., WILLEY, J., WOOLVERTON, C. Prescott's Microbiology (9th ed.). New York: McGraw Hill. 2013, pp. 713-721.
9. RUSU, A.R.G., TARTAU, L.M., STATESCU, C., BOANCA, M., POROCH, V., LUPUSORU, R.V., DIMA, N., BADESCU, C., REZUS, E., REZUS, C., LUPUSORU, C.E. *Rev Chim (Bucharest)*, **69**, no.6, 2018, p. 1493-1497
10. CARAIANE, A., SZALONTAY, A., MACOVEI, L., A., et al. *Rev Chim (Bucharest)*, **69**, no.6, 2018, p. 1581-1584
11. WANG, Z.K., YANG, Y.S., STEFKA, A.T., SUN, G., PENG, L.H. Review article: fungal microbiota and digestive diseases. *Aliment. Pharmacol. Ther.* 2014, 39, no.8, p. 751-766.
12. CALIN, A.M., DEBITA, M., CIURCANU, O.E., SCUTARIU, M.M., SZALONTAY, A.S. *Rev Chim (Bucharest)*, **68**, no.10, 2017, p. 2443-2447
13. URSU, R.G., IVANOV, I., POPESCU, E., COSTAN, V., STAMATIN, O., GHETU, N., PALADE, D., MARTU, C., ANDRESE, E., et al. Human papilloma virus genotyping in fresh head and neck tumors - our first experience. *Rev Med Chir Soc Nat Iasi*, 119, no.3, 2015, p. 676-680.
14. CUI, L., MORRIS, A., GHEDIN, E. The human mycobiome in health and disease, *Genome Med.*, 2013, **5**, no.7, p. 63.
15. BARLEAN, L., TATARCIUC, M., BALCOS, C., et al. *Rev Chim (Bucharest)*, **66**, no. 10, 2015, p. 1696
16. ROGERS A H (editor). (2008). *Molecular Oral Microbiology*. Caister Academic Press.
17. CIURCANU, O.E., MARECI, D., STEFANESCU, O.M., TRINCA, L.C., SCUTARIU, M.M., ILIE, M., HRITCU, LD. *Rev Chim (Bucharest)*, **67**, no.10, 2016, p. 2095-2099.
18. ROMAN, I., CIORTAN, S., BIRSAN, I.G., et al. *Mat. Plast.*, **52**, no.4, 2015, p. 529
19. COBZEANU, MD, PALADE, D, MANEA, C. Epidemiological Features and Management of Complex Neck Trauma from an ENT Surgeon's Perspective. *CHIRURGIA*, 108, no.3, 2013, p. 360-364
20. BARBOI, OB, PRELIPCEAN, CC, COBZEANU, MD, PALADE, D, ALBUSODA, A, FLORIA, M, CHIRILA, I, DRUG, VL, BALAN, G. The tribes and tribulations of laryngopharyngeal reflux: a review of recent studies with implications for interdisciplinary collaborations between otolaryngologists and gastroenterologists. *Rev Med Chir Soc Nat Iasi*, 119, no.4, 2015, p. 967-973
21. PALADE, D.O., COBZEANU, B.M., ZAHARIA, P., DABIJA, M., Combined Approach of the Anterior Skull Base in Sinonasal Tumours. *Rev Chim (Bucharest)*, **69**, no.5, 2018, p. 1191-1193
22. DECUSARA, M., ROMILA, A., PAVEL, L., et al. *Rev Chim (Bucharest)*, **69**, no.5, 2018, p. 1254-1256
23. NOBLE JM, SCARMEAS N, PAPAPANOU PN. Poor oral health as a chronic, potentially modifiable dementia risk factor: review of the literature 2013.
24. VASILCU, T.F., STATESCU, C., SASCAU, R., ROCA, M., COSTEA, C.F., ZOTA, M., BARARU, I., CONSTANTIN, M.L., MITU, F., *Rev Chim (Bucharest)*, **69**, no.8, 2018, p. 2283-2286.
25. CUCIUREANU, D.I., STATESCU, C., SASCAU, R.A., et al. *Rev Chim (Bucharest)*, **70**, no. 2, 2019, p. 685-688.
26. FINE DH, et al. (2008). *Molecular Windows into the Pathogenic Properties of Actinobacillus actinomycetemcomitans*. Molecular Oral Microbiology. Caister Academic Press.
27. LJUNGH A, WADSTROM T (editors) (2009). *Lactobacillus Molecular Biology: From Genomics to Probiotics*. Caister Academic Press.
28. CIURCANU, O.E., STEFANESCU, O., SCUTARIU, M.M., STELEA, C.G. *Rev Chim (Bucharest)*, **67**, no.3, 2016, p.566
29. HINGANU, D, SCUTARIU, M.M., HINGANU, M.V. *ANNALS OF ANATOMY-ANATOMISCHER ANZEIGER*, 2018, 218, p. 271-275
30. WILLEY JM, SHERWOOD L, WOOLVERTON CJ, PRESCOTT LM (2014). *Prescott's Microbiology*. McGraw-Hill Education.
31. RICKARD A H (2008). *Cell-cell Communication in Oral Microbial Communities*. Molecular Oral Microbiology. Caister Academic Press.
32. HAJISHENGALLIS G, RUSSELL MW (2008). *Molecular Approaches to Vaccination against Oral Infections*. Molecular Oral Microbiology. Caister Academic Press

Manuscript received 5.10.2018