

Why Physicians Should Look at the Mouths of Their Patients

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The oral cavity is the initial portion of the digestive tract in continuity with the skin, and consequently it has anatomic, histologic, functional, and pathologic aspects related both to the skin and to the digestive system [1, 2]. Anatomically, the oral cavity includes the lips, gingivae, hard palate, cheek mucosa, tongue, floor of the mouth, and teeth placed in jaw bones; all this is bathed by saliva [1, 2]. The mouth has a very complex and varied pathology which includes infectious, autoimmune and neoplastic diseases that may affect the oral mucosa, the gnathic bones and salivary glands. Although oral pathology is an important chapter in the general pathology, the majority of doctors lack knowledge about oral diseases and their relationship with general health [3]. Therefore, it is very important to improve physicians' information about oral pathology, especially on periodontal disease, bisphosphonate-related osteonecrosis of the jaws (BRONJ), and oral cancer.

Periodontal Disease

From a microbiological point of view, the mouth is a fluvial ecosystem in which more than 500 types of microorganisms interact in a very intricate manner [4, 5]. In the flowing-water systems, life is extremely opulent and diverse on solid surfaces, where microorganisms get firm retention and a favorable nutritional environment. The mouth is the only place in the human body where such solid surfaces are found, that is, the dental surfaces [5]. The teeth are hard and non-desquamative structures that penetrate the gingiva and create a unique denoting microenvironment prone to colonization of innumerable bacteria species generating the subgingival biofilm [5], and the interaction between such bacteria and host defence can cause a common dental infection called periodontal disease [6]. Supragingival biofilm and tongue coating are the other main ecological niches associated with dental caries and halitosis, respectively [4].

Basically, periodontal disease can manifest as gingivitis or periodontitis [6]. Gingivitis represents a stereotyped inflammatory response to biofilm and is confined to soft tissues. In periodontitis, the inflammatory process extends to the supporting tissues, causing bone resorption, pocket formation, suppuration and eventually increased tooth mobility [5, 6]. In 1996, Offenbacher proposed the term periodontal medicine in order to establish this relationship based on human studies and animal models [7]. From this perspective, periodontitis has been suggested as a risk factor, sometimes in a bidirectional fashion, for cardiovascular diseases [8], diabetes mellitus [9], respiratory disease [10], preterm delivery [11], rheumatoid arthritis [12], osteoporosis [13], pancreatic cancer [14], metabolic syndrome [15], renal diseases [16], Alzheimer's disease [17] and other systemic conditions. An accurate analysis of scientific evidence ensures in a more robust manner that periodontitis may be an independent risk factor for cardiovascular events, pulmonary infections and diabetes [18]. Further research is needed to confirm the relationship between periodontitis and other conditions or systemic diseases listed above.

BRONJ

Bisphosphonates (BPs) are a class of drugs widely used for the treatment of osteoporosis, Paget's disease of the bone, multiple myeloma, bone metastases, and other conditions characterized by increased bone resorption [19, 20]. In 2003, Marx warned the medical profession about the association between bisphosphonate therapy and osteonecrosis of the jaws [21]. Since then, growing evidence has suggested that necrosis in the mandible and maxilla can occur as a side effect of treatment with several BPs such as pamidronate, zoledronic acid, alendronate, risedronate, and ibandronate [20].

Clinically, BRONJ is characterized by asymptomatic or painful exposure of necrotic bone in the oral cavity, lasting for more than 8 weeks in a patient receiving BPs who had not received radiation therapy to craniofacial region [22]. Such necrotic areas may undergo secondary infection and progress to abscess formation, osteomyelitis, and pathologic fractures. Usually, there may be a history of dental procedures or local trauma acting as a trigger, but in some cases, no obvious preceding factor can be identified [23]. Since the treatment of BRONJ is problematic and there are no universal guidelines for it, prevention remains the main goal [24].

The question is: why the jaws? Although the exact mech-

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anism of BRONJ is not totally established, the answer may be related to the relatively high turnover of alveolar bone and also the exposure of the maxillofacial skeleton to the external stresses which may be physiologic (e.g., mastication), iatrogenic (e.g., dental procedures) or inflammatory (e.g., periodontal disease, caries) in nature [19]. The mandible and maxilla are covered by a thin layer of mucoperiosteal tissue, and even trauma from wearing dentures can potentially initiate osteonecrosis [25]. In the dentogingival region, the alveolar bone crest is located approximately 2 mm from the subgingival biofilm, and for that reason, bacteria and their products can easily reach to the underlying bone, as occurs in periodontal diseases [25]. Therefore, some anatomic and functional particularities make the jaw bones more vulnerable to trauma and infection and consequently to the osteonecrosis [19, 25].

Oral Cancer

Oral cancer is a major health problem worldwide. According to latest world cancer statistics (Globocan 2012) published in 2015, cancer of the lip and oral cavity accounted for 300,000 cases in 2012, being 2.1% of the world total [26]. More than 90% of all oral cancers are squamous cell carcinoma (SCC). Other less common malignancies include melanomas, carcinomas of the salivary glands, sarcomas, and metastases [27]. Tobacco use, alcoholic consumption, and betel quid chewing are the most important risk factors [28]. Oral SCC can be presented in various clinical forms. Usually, the initial lesion is a white or red patch (leukoplakia and erythroplakia, respectively) that can progress to a necrotic-looking ulcer with irregular, raised indurated borders, and infiltration of surrounding tissues [29, 30]. Treatment options for oral SCC comprise mainly surgery, radio-therapy, and systemic cytotoxic chemotherapy, or a combination of these modalities [29, 30].

It is interesting to note that although oral cancer is a serious and relatively prevalent disease, it has a great potential for early detection at the primary care level [30, 31]. Unlike other lower digestive-tract cancers that require endoscopic techniques for earlier detection, oral SCC can be promptly identified through comprehensive anamnesis and a careful physical examination [30, 31]. Unfortunately, such early diagnosis is not usual, since about 50% of oral cancer patients are diagnosed in the advanced stage, leading to mutilating surgery, difficulties on esthetic-functional rehabilitation, and poor survival rate [31].

In order to improve cure rates of oral cancer, it is imperative that healthcare practitioners, dentists, and physicians identify the patients with risk factors for developing oral SCC in their daily clinical practice [30, 31]. The major risk factors are age older than 45, combined tobacco and alcohol use or abuse, betel nut use, chronic sun exposure on the lower lip, oral human papillomavirus infection, and low intake of fruits and vegetables [32]. In these patients, comprehensive clinical examinations, including neck palpation and oral cavity inspection, should be performed routinely [30-32]. A white or red patch and non-healing ulcers, especially if they are located on the lower lip, floor of the mouth, and tongue should be suspected of being a malignant or premalignant lesion [30, 32]. These

suspicious lesions should undergo biopsy immediately or else referred to a qualified professional to perform it, depending on the experience of the examining physician [30, 32].

Conclusions

Although the mouth has particular characteristics that create a unique milieu in the body, most physicians do not give to the oral cavity its deserved importance in the context of human health and usually keep the mouth and its problems apart from the rest of the body [33]. Indeed, many studies have shown that physicians have a low level of knowledge on oral health in general [3, 34] and on specific issues such as the relationship between periodontitis and systemic health [35, 36], BRONJ [37], and oral cancer [38, 39]. In this scenario, it is urgent that medical schools provide their students with consistent information on this topic and that general practitioners and specialists keep up to date on major oral problems. Finally, we need to improve understanding and cooperation between medicine and dentistry regarding the benefits of science and perception of human health as a whole.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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