ORAL HEALTH IN A CONTEXT OF PUBLIC HEALTH: PREVENTION-RELATED ISSUE

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SUMMARY

This publication analyses current literary knowledge on selected topics in the fields of oral health and pathology, with a particular emphasis on the potential roles of the oral microbiome and preventative approaches to oral afflictions. An important association with floral dysbiosis has been documented in important oral conditions, sometimes as a predisposing factor and at other times as a result thereof. However, much remains to be elucidated regarding the specific mechanisms at play, as well as their meaning in clinical practice. Continued research into the pathophysiology of certain oral diseases is of particular importance considering how widespread they are. A specific emphasis should be placed on understanding the exact mechanisms through which the microbiota facilitates health, and when disturbed, sickness. And perhaps of most importance is the implementation of knowledge already acquired on disease prevention if the burden of oral diseases worldwide is to decline in the future.

Key words: oral health, oral hygiene, oral microbiota, dysbiosis, caries, periodontitis, oral cancer

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INTRODUCTION

Oral afflictions represent a massive portion of health conditions affecting individuals worldwide. According to the WHO, 3.58 billion people were affected by oral pathologies around the globe in the year 2016, making oral illnesses a considerable public health concern. The high prevalence of oral conditions in the population, as well as their significant impact on health and wellbeing have intensified the research into what contributes to their development and the possible therapeutic approaches.

One such approach is to intercept disease occurrence altogether: practicing a variety of preventative measures for preservation and maintenance of oral health, rather than curing an established disease. Hygiene and epidemiology are areas of study heavily focused on prevention through illuminating disease patterns in a population and identifying disease risk factors and aetiologies – aimed at reducing their occurrence or associated negative health outcomes down the line. Information obtained through research and analysis is used to formulate preventative programmes, educate people regarding possible risk factors and how to minimize them as well as to better human health and quality of life.

Oral hygiene is a subdivision of these disciplines, based on an anatomical location. The importance of oral hygiene cannot and must not be underestimated as the oral cavity fulfils many vital functions in human life, including alimentary related functions (tasting, chewing, initiating digestion, swallowing, and vomiting), behavioural communication (speech, smiling and kissing), and respiratory functions (breathing, gasping and cough). Any disease of the oral cavity could hence impact quality of life, significantly decrease one's capacity to function and even jeopardise a person's life if severe enough. However, it should be clarified that primary oral diseases, except for oral cancer, are rarely deadly. At the same time, it could also be maintained that oral health is a prerequisite for one's overall health status (1). When applying the WHO definition of health to the oral cavity – this highlights the significance of not only understanding the underlying pathophysiology of common diseases affecting the mouth, but also the optimal conditions that should be met for health cultivation. This is necessary to implement the best possible ways to positively affect a disease course, hinder its progression and preferably avoid it altogether. It is also worth mentioning that oral health, apart from being a determinant of general health and quality of life, is also strongly correlated with certain systemic conditions, sometime proposed to be a causing factor, a modifying factor or as an outcome thereof.

Notable topics which are commonly dealt with under the branch of oral health are proper hygiene practices and dental caries, the role of oral flora in health and sickness (both localized and systemic), periodontal diseases and oral cancer. This review paper intends to summarize current literature regarding the above specified topics and raise questions which remain unanswered.

DISCUSSION

Microbiome as Potential Risk Factor for Oral Diseases

Risk factors affecting oral health can be divided very broadly into intrinsic and extrinsic ones. Intrinsic factors correspond, as the name suggests, to one's internal milieu (genetic makeup, ethnicity, gender, and the function of various bodily defence mechanisms). Overlying those are the specific functions related

to the oral cavity, for instance salivation and abundance of attachment surfaces. External factors include social, economic (access to medical care, financial stability, living conditions, education), environmental (lifestyle and diet, access to fluoride, sanitation) and factors related to oral health services available to a population such as institutional financing of care, dental manpower and delivery modes. It is expectedly the interplay between the external and internal factors that determines the actual risk for an individual to develop a disease.

The oral microbiome, a term collectively used to refer to the diverse populations of microorganisms harboured within the mouth, is somewhat on the intersection of intrinsic and extrinsic risk factors as it is significantly modulated by the environmental factors within the host, and at the same time it influences the host's internal environment. All humans have a shared basal microbiome, made up of flora which colonizes various body parts under normal conditions. In addition, a proportion of the overall microbiota is composed of individual variations that are unique to every person and stem from their genetic makeup and way of life, known as the "variable microbiome". And even within one person's mouth – the microbiota is incredibly dynamic and keeps evolving as its host ages or undergoes different physiological or pathological processes. Understanding the elements governing the microbiota, and by extension the oral niche, is very promising and can be illustrated by, for example, the new understandings of intestinal flora development: modulation of the microbial colonies may have preventative and therapeutic effect in many systemic diseases (2).

In turn, the flora affects the human organism, establishing a bidirectional relationship. Some of the ways in which this resident population affects the human body include the production of vital compounds such as vitamin K for the host, digesting food products in the lumen of the gut and influencing the release of signalling molecules in the gastrointestinal tract (GIT) (3). When both parties benefit from this relationship, as seen in non-diseased state, it is termed symbiosis. In contrast, a dysbalanced relationship is termed dysbiosis. The next three sections will deal with the contribution of oral dysbiosis to the development of dental caries, chronic periodontal disease and oral cancer, as well as important preventative approaches to those conditions.

Dental Caries

In the year 2016, according to the WHO global burden of disease study, oral diseases have affected around 3.58 billion people worldwide. Caries (or tooth decay) of permanent teeth has been identified as the most frequent condition globally, disproportionately affecting developing countries. In children, dental decay is more prevalent in America and Europe; in adults, caries affects nearly 100% of population in most countries, however, the measure of severity (determined by DMFT – decayed, missing, or filled permanent teeth) is significantly inflated in the developing world. This has much to do with the prevalent dental care techniques in developing countries on the one hand (for instance preferentially extracting affected teeth, even if potentially salvageable due to financial considerations) and the incremental increase in sugar consumption in developed countries on the other (4).

Caries is caused by acid-producing microorganisms that reside in form of a plaque on the teeth surface. The microorganisms utilize sugars from the human diet and ferment them to organic acids which lower pH bellow a critical level, resulting in demineralization of the enamel. Hours after a meal, given there were no carbohydrate-based snacks later, the pH of the oral cavity stabilizes, until the next meal – enabling remineralization of the enamel. This delicate balance between enamel demineralization and remineralization can be disturbed – leading to dental caries. An early caries lesion may first be only a surface problem, but as caries progresses the enamel is further eroded, and the proteolytic bacteria break down the deeper tissues of the tooth including collagen, resulting in a cavity (5); the loss of viable tooth tissue also gives the disease its colloquial name "tooth decay". It is thus understandable that a sugar-rich diet (both in terms of overall quantity and frequency of consumption) contributes to shifting the balance in the enamel towards erosion, leading to the degradation of teeth. However, the potential bacterial culprits and guardians participating in this balancing game are mysterious still. The chemical-metabolic events inciting the evolution from a healthy oral environment to that favouring caries could be more deeply traversed once microbial communities are identified and their characteristics scrutinized. Notable examples of such novel research are discussed below.

Using next generation sequencing, Hurley et al. investigated the biodiversity of samples taken from caries affected children (saliva, caries lesion sample) and caries free children (saliva). They have documented a clear difference in microbiota composition among all groups, with an abundance of Niesseria, Streptococcus and Prevotella species in the caries lesion, consistent with previous publications. However, they highlight the possibility that overrepresentation of some bacteria may not be a useful predictor of caries development. Instead, presence of certain bacteria that are not normally found within the oral cavity, could be more indicative (6). Qudeimat et al. found plenitude of Leptotrichia, Prevotella, and Veillonella in caries affected Middle Eastern children. Interestingly, an association between Corynebacterium and caries was not clear, and this species was cultivated in abundance in the caries free group – suggesting a potential role in oral health, rather than illness, that should be further examined (7). Another publication demonstrated significantly higher levels of Dialister, Selenomonas, Actinomyces, and Mogibacterium in caries cases compared to the caries-free cases in Chinese children (8).

The possible therapeutic approach in modulating of the oral flora is being explored as well. Illustrated by Sivamaruthi et al., supplementation of probiotics has been shown to reduce risk for developing tooth decay in both children and adults. Multiple possible mechanisms are suggested, unique to different probiotic strains tested, from pH alteration and direct toxin mediated killing of cariogenic bacteria to competition for resources and selection of non-cariogenic bacteria (9). It seems reasonably clear that more scientific efforts will be required to understand how exactly oral colonizers (and which) promote/inhibit caries development. However, substantial reduction of caries prevalence in the population can be achieved much prior using preventative approaches, even without fully unlocking the intricacies of the microbiome.

Up to the current time it was known and widely accepted that mechanical removal of the plaques formed by inhabitants of the oral cavity (also "brushing" or "practicing oral hygiene") is effective in reducing plaque, and that addition of fluoride is significant for caries management (10). However, a recent review paper

showed that practicing oral hygiene in itself does not reduce the incidence of oral caries, and merely serves as a delivery mechanism to the active pharmaceutical fluoride, which decreases the incidence of dental caries by sealing defects in the enamel. The sealing of said defects is based on fluorapatite formation on a tooth's surface when utilizing fluoride. Fluorapatite has a higher demineralization threshold than hydroxyapatite, the main native component of enamel, and its formation shifts the balance of demineralization to remineralization, preventing further erosion (11).

Preventing the development of the mature plaque all together can be achieved as well, by frequently disrupting the biofilm which precedes it. A simple method of Gum and tooth rubbing with Index Finger, Tongue cleaning and water Swishing (GIFTS) after consuming anything whatsoever has the potential to modify the microbiome proportions by frequently and effectively preventing plaque formation (12). This method, which is not as abrasive as daily tooth brushing, reduced total bacteria in saliva and substantially reduced streptococcus species compared to other cleaning modalities. Lastly, a meta-analysis by Fraihat et. al from 2019 showed that community delivered oral health programmes (from educating children on proper hygiene practices to interventional preventative procedures at the dentist's) are a useful tool in maintaining dental health, as demonstrated by lowered DMFT rates among children participating in such programmes compared to controls (13).

The findings above showcase the undeniable relevance and importance of hygiene practices in oral care, as well as identifying new techniques for better prevention.

Chronic Periodontal Disease

Periodontal disease has a high prevalence in both developing and developed countries, with an estimated 20–50% of the global population affected, qualifying as an important public health concern. Periodontal disease is defined as a chronic inflammatory process in the periodontal tissue (also periodontitis) – the supporting and surrounding tissue found around the tooth; this includes the gingiva, the periodontal ligaments, and the alveolar bone. As periodontal disease advances, the chronic inflammation results in destruction of the periodontal ligaments, gingival shrinkage, and resorption of the alveolar bone. All these consequences combined, if left untreated, will lead eventually and inevitably to tooth loss. In fact, periodontal disease is the main cause of tooth loss worldwide (14). It has also been shown that number of teeth lost (indicator of disease severity) corresponds to decrease in quality of life (15). The most significant risk factor for periodontitis is smoking of any type (cigarettes, cigars, pipes, cannabis etc.) – all with similar effects. Smoking was also associated with worse outcomes (more frequent tooth loss and less effective treatment, for example, in smokers compared to non-smokers) of established periodontitis (16). Another important risk factor implicated in the development of this condition is poor oral care, which has been shown to have detrimental effects on periodontitis, whereas maintaining good oral hygiene was shown to halt disease progression (17).

An important association has been long recognized between periodontitis and systemic conditions such as type 2 diabetes mellitus and pregnancy related conditions; in this context, periodontitis can be viewed as a double ended sword – a risk factor or an enabler of certain diseases, or interestingly, a manifestation to an underlying systemic condition.

Periodontitis can be a resultant condition of a pre-established systemic disease; periodontitis disproportionally affects type 2 diabetics (T2DM) when compared to the general population. In addition, when compared to the normal population counterparts, they suffer a more severe form of it (18). Interestingly, Xiao et al. have shown that in mice, diabetes leads to overproduction of IL-17 which increases the pathogenicity of their oral environment. The researchers have inoculated germ free recipient groups: one group was inoculated with normal mice flora and another with oral flora from diabetic mice. The first group of recipients have not developed periodontitis, whereas the other group did, proving that diabetes is directly implicated in periodontal disease development via microbiota alteration (19). However, what governs this association in humans remains unclear. An important observation from the opposite view of the periodontitis-diabetes relationship, is that periodontal treatment impacts glycaemic control and inflammatory markers in T2DM (20). And interestingly, a 2021 article identified specific microbial clusters in periodontitis which could be potentially used as a marker for pre-diabetes (21).

As a driving factor for another systemic condition, a positive association between periodontitis and preeclampsia was established. It was shown that periodontitis can be viewed as a predisposing factor for pregnancy-associated hypertension, irrespective of maternal age, parity status and socioeconomic conditions (22). In addition, other authors have found that obstetric complications such as prematurity could be driven by periodontal diseases (23).

The current hypothesis for the chronic periodontitis pathogenesis is the ecological hypothesis: a site of dysbiosis, where there is a significant modification to flora, is predisposed for overgrowth of pathogenic genera, leading to initiation of disease. An integrated hypothesis was suggested, anchoring these diseases' pathophysiology in the dietary effects on the microbiome (24), which relates to hyperglycaemia from high sugar diet. However, the question not answered is to what extent controlling blood sugar levels could be used for curative intents.

What is clear, however, is that oral health as a determinant of overall health should not be underestimated, especially in specific groups such as diabetics and pregnant women.

Oral Cancer

Oral cancer is an umbrella term used to denote malignancies of the oral cavity; these include cancer of the lip, oral mucosa, salivary glands, tongue, etc. According to the WHO, there are 657,000 new cases of cancers of the oral cavity and pharynx each year, and more than 330,000 deaths.

Oral cancers are predominantly a concern in Southeast Asia where a combination of risk factors play an important role in the disease pathogenesis. Prevalent behaviours in that part of the world include betel quid chewing, smoking and alcohol consumption. Smoking and non-smoking tobacco use are by far the most important risk factors for oral cancer (25, 26).

Regarding alcohol consumption, a review from 2016, amidst conflicting evidence, found that alcohol on its own plays an unclear role in oral carcinogenesis. However, the synergistic role of alcohol consumption and smoking in aetiology of oral cancer has been positively established (27). Other important implicated

factors are infectious agents such as EBV, HPV, Candida (in formation of premalignant lesions) and HSV (not yet proven as direct cause but have been implicated as a potential one). In addition, occupational exposure, genetic susceptibility, and age are all contributors to a higher risk of developing oral cancer. Not at all insignificant is one's oral hygiene routines or lack thereof. Interestingly, not practicing a basic routine of tooth brushing has been found to be implicated in developing oral cancer, as well as oesophageal carcinomas. One of the suggested mechanisms is overproliferation of nitrate reducing organisms which contribute to the production of GIT carcinogenic nitrosamines (28). And on the other hand, a systematic review from 2020 showed that another form of hygiene practice – the use of alcohol-based mouthwash – can put one's health at risk; it has been found to compound the risk of oral cancer development in people that smoke and drink alcohol regularly (29). It is worth pointing out that one's immunity status is a significant determinant conferring the ability to keep cancerous developments at bay if properly functional (30).

And so, the association between oral cancers and the residing microbiome is an interesting new direction being explored. Dysbiosis has been linked by multiple studies to the development of oral squamous cell carcinoma (31, 32). Based on that and the publications described in the previous paragraph, one can see the correlation between adequate hygiene practices, dysbiosis and the development of oral cancer – and thus the ever so relevant role that prevention may play in clinical practice.

In addition, oral dysbiosis seems to be implicated in other cancers beyond the oral cavity, such as pancreatic cancer (33). Some researchers went as far to suggest the use of distinct dysbiotic patterns as a biological marker for different cancers, for example colorectal carcinoma (34), whereas others suggest the microbiota be target for modulation, through which cancer progression could be indirectly affected (35).

Nonetheless, current understanding of the oral microbiome and its effects both locally and systemically is insufficient.

CONCLUSION

Extensive research into the microbiome has paved a path into potentially better understanding of some important disease mechanisms (dental caries, chronic periodontitis, and oral squamous cell carcinoma). However, on a more practical level – implementing preventative measures and developing potentially better ones should be intensified if the disease burden of oral diseases worldwide is to decline in the future.

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Conflict of Interests

None declared

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