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REVIEW ARTICLE

The history of dentistry and medicine relationship: could the mouth finally return to the body?

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The relationship between dentistry and medicine has been acknowledged throughout the history of humanity. This relationship was documented in ancient medicine accounts, and has survived until the present day, accompanied by the evolution of molecular technologies. Although we have had very important researchers' contributions in this interdisciplinary area, mainly after the 18th century, the knowledge on oral infections is still ignored by or unknown to the majority of clinical dentists and physicians. These circumstances could be changed through a broader divulgation of this complex relationship, both in the dentistry and in the medicine areas, which in turn would have a significant impact in systemic health worldwide. This movement has already started, as was observed in a World Health Assembly resolution which called for oral health to be integrated into chronic disease prevention programs in 2007. This was a significant indicator of changing perceptions of oral health over the past several decades. This brief review reports the evolution through time of the knowledge on the association between dental infections and systemic diseases, as well as the paths which we could take to consolidate this historical trend.
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The ancient medicine

The interrelation between dentistry and medicine has been documented throughout the history. In the past, where the knowledge of health science was very poor and where people had to survive epidemics of infectious diseases, oral health was far from a priority and likely very precarious, creating terrible images of dirty and decayed teeth with awful smell at the time.

Reports from the ancient Egyptian Medicine suggested that the health of body could be improved after tooth extractions. An association between tooth pain and diseases of women's reproductive system was mentioned in one of the oldest medical papyri of the Middle Dynasty (2100 BC). In a text about the health of King Ashurbanipal (669–626 BC) in Niniveh, the capital of ancient Assyria, it was reported that the pains in his head, arms and feet had been caused by his teeth, which should be removed (O'Reilly and Claffey, 2000). In Greece, Hippocrates (460–377 BC) hypothesized that 'rheumatism' without expectation of cure could be treated by tooth removal.

Evolution of bacteriology: the concept of germ theory

In diverse reports of the history before 1800s, there are related clinical facts and some researches about the relationship between oral infections and systemic diseases. In 1778, John Hunter, Surgeon Extraordinary to the King of England, whose fame also extended to the scientific area, published the very important work of dentistry – 'The Natural History of the Human Teeth.' In the introduction Hunter wrote (Hunter, 1778):

> *'The importance of the teeth is such that they deserve our utmost attention, as well with respect to the preservation of them when in a healthy state, as to the methods of curing them when diseased. They require this attention, not only for the preservation of themselves as instruments useful to the body, but also on account of other parts with which they are connected; for diseases of the teeth are apt to produce diseases in the neighboring parts, frequently of very serious consequences. One might at first imagine that the diseases of the teeth must be very simple and like those which take place everywhere else in the bony parts of our body, but experience shows the contrary. The teeth, being singular in their structure, have diseases peculiar to themselves. These diseases, considered abstractedly,*

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are indeed very simple, but by the relations which the teeth bear to the body in general and to the parts with which they are immediately connected, they become extremely complicated.'

The significance of these fundamental truths, expressed more than 230 years ago by a man of accepted standing in medicine and science, was not appreciated; the opportunity to tighten the interrelation between dental pathologies and the diseases of the organism as a whole was ignored.

Nevertheless, the investigations about the epidemiology of bacterial diseases, such as oral diseases, progressed mainly after the 1800s. In 1801, an article (written before the discovery of germ theory) published by Benjamin Rush, one of the signers of the Declaration of Independence – and one of America's most noted physicians – related his clinical observations about the connection between the extraction of decayed and diseased teeth and the cure of general diseases, particularly nervous diseases. He also believed that the success in the treatment of all chronic diseases would be very much promoted by inquiries into the state of the teeth in sick people, and by advising for their extraction in every case in which they are decayed (Duke, 1918). In 1818, Benjamin Rush recognized for the first time the theory of focal infection, a great feat given the difficulty to imagine the complexity of these processes without the concept of germ theory.

The importance of oral bacteriology was first detailed by the Dutch scientist Antonie von Leeuwenhoek in 1683 (O'Reilly and Claffey, 2000). Louis Pasteur (1822–1895) advanced the investigations about microorganisms, demonstrated the dependence of fermentation on microorganisms, and showed that these organisms could come by air (Funk *et al*, 2009). Subsequently, Robert Koch (1843–1910) revealed after innumerous studies that microorganisms were the cause of an infectious disease, thus originating the Germ Theory (Rosen, 1996). In 1879, Willoughby D. Miller, a recent graduate of the University of Pennsylvania Dental School, heard Koch's theory and traveled to Berlin where he began work within Koch's institute. He was looking into the relationship between oral bacteria and systemic diseases. Miller became really convinced that the mouth was a focus of infection and that this fact could explain most of human illnesses. He observed a role for oral microorganisms or their products in the development of brain abscesses, pulmonary diseases and gastric problems, as well as a number of systemic infectious diseases (Williams, 2002). In the preface to a series of articles entitled 'The human Mouth as a Focus of Infection', he stated (Miller, 1891):

'During the last few years the conviction has grown continually stronger among physicians, as well as dentists, that the human mouth as a gathering-place and incubator of pathogenic germs performs a significant role in the production of varied disorders of the body, and that if many diseases whose origin is developed in mystery could be traced to their source, they would be found to have originated in the oral cavity.'

Miller isolated 58 varieties of microorganisms from the mouth, many of which are pathogenic or may become so under favorable circumstances. At the International Congress of Hygiene, Miller presented his investigations to an audience which included William Hunter (O'Reilly and Claffey, 2000).

Oral bacteria in systemic diseases: the oral sepsis

After Miller's observations on oral focal infection, Hunter, a physician at the London Fever Hospital, started to investigate the existence and the effects of oral septic infection – prevalence, potency, ease of observation and treatment – as an important cause and complication of a whole range of medical diseases (Hunter, 1898–1899). In 1898, Hunter began to stress the importance of dental infection, introducing the term 'oral sepsis' (Hunter, 1900). About this term, he stated:

'My object in seeking for a special name, and after consideration in creating this one, was to emphasize the great fact that it is not the absence of teeth but the presence of sepsis, that is not dental defects but septic effects, that is not defective mastication but the effective sepsis associated with such dental defects or often present in conditions of gingivitis apart from such defects, that are responsible for the ill-health associated with 'bad' mouths.'

The second object was to emphasize the importance of the infection caused by staphylococcal and streptococcal organisms, as distinguished from the purely saprophytic infections in which the mouth abounds; or the temporary presence of specific organism – e.g., typhoid, tubercle, pneumonia,… (Hunter, 1911)

In numerous papers he related the danger of oral sepsis, and how it was frequently associated to gum infections. In 1900, he mentioned for first time the set of systemic diseases (empyema, nephritis, perinephritic abscess, cholecystitis, anemia, and endocarditis) which not infrequently arrived from dental infection through hematogenous distribution of bacteria (Hunter, 1898–1899, 1900, 1911, 1921; Marshall, 1912). In another article published in 1911, he described the complete path through which the oral infections could go through the body (Hunter, 1911):

'The chief feature of this particular oral sepsis is that the whole of it is swallowed or absorbed into the lymphatics and blood.' '…the effects of it, therefore, fall in the first place upon the whole of the alimentary tract from the tonsils downwards. These effects include every degree and variety of tonsillitis and pharyngitis; of gastric trouble from functional dyspepsia up to gastritis and gastric ulcer; and every degree and variety of enteritis and colitis, and troubles in adjacent parts – e.g., appendicitis. The effects fall in the second place upon the glands (adenitis); on the blood (septic anemia, purpura, fever, and septicaemia); on the joints (arthritis); on the kidneys (nephritis); and on the nervous system.'

In the same article, he described with very much knowledge how constant is the physician's omission in this interdisciplinary area (Hunter, 1911). He stated:

> *'There is no part of human body more commonly looked into by the doctor than the mouth.' '…When looking into the mouth of his patients the doctor has often occasion to note incidentally the presence of defective or decayed teeth, as a general accompaniment and apparently as a part result of poor health, poor nutrition, or wasting diseases from which they suffer.' '…And the doctor regards it as such ''It is a matter of teeth and dentistry''.*
>
> *'I desire to impress it is not a matter of teeth and dentistry' '…It is an all-important matter of sepsis and antisepsis that concerns every branch of the medical profession, and concerns very closely the public health of the community. It is not a simple matter of 'neglect of the teeth' by the patient, as is so commonly stated, but one of neglect of a great infection by the profession – a great infective disease'.*
>
> *'I cannot within the time at my disposal bring before you all the facts relating to medical sepsis or to its greatest cause – oral sepsis – on which these conclusions as to their importance are based.'*

It is very interesting to observe these discourses and to compare them with the ones of our days. After a hundred years, this conduct has not changed and there is not enough communication between dentists and physicians.

Sources of infections as causes of systemic diseases: the focal theory

In 1911, the term 'oral sepsis' was complemented and replaced with the term 'focal infection.' The most important phase of medicine in relation to dentistry was focal infection. In 1912, the North American physician Frank Billings made his first report on the relationship between focal infection and arthritis and other conditions (Billings, 1912). He defined which were the sources of focal infection: (1) facial tonsils, the peritonsillar tissues and supratonsillar fossae, (2) abscesses of the gums and alveolar sockets, pyorrhea alveolaris and septic types of gingivitis (actual periodontal disease), (3) sinuses about the head: maxillary, ethmoidal, sphenoidal and frontal, (5) bronchiectatic and pulmonic cavities, (6) chronic ulcers of the gastrointestinal tract, (7) chronic appendicitis, (8) cholescystitis and cholangeitis, (9) the urinary tract, (10) genital tract, and (11) local, septic, submucous and subcutaneous foci anywhere in the body (Billings, 1912). In the years following, Billings and his researchers group reinforced the investigation of alveolar infections and abscesses and their association with systemic diseases through the clinical and laboratory signs (Billings, 1914). After their observations, they reported:

> *'…whether primary or secondary, alveolar focal infection may be the dominant factor in the production of systemic disease, of which malignant endocarditis (Streptococcus viridans), chronic arthritis and myositis are examples.'*

He emphasized to clinicians the importance of examining the patients, exhausting every detail in their personal history. The dentist, the nose and throat specialist, the gynecologist, the genito-urinary expert could all be necessary to locate the foci of infection. He also suggested that the sources of the infection should be removed and bacterial cultures made, and that a long period of investigation should be carried out to control the chronic joint infections and some other systemic diseases of focal origin (Billings, 1912, 1914). Vaccines of dominant bacteria could be made for subsequent use. Billings and other prominent physicians, such as Charles Mayo and Russell Cecil, in advocating the focal infection theory, broke out a boom in tonsillectomies, tooth extractions, and sinus procedures in a period classified as an 'orgy of extractions' (Billings, 1914, 1916; Pallasch and Wahl, 2000).

In the 1919, E. C. Rosenow, a colleague of Billings, published a series of animal experiments and human case reports supporting the concept of focal infection. He defended the importance of dentistry in medicine, as well as the necessity of elimination of focal infection. In a Symposium in which the main theme was mouth infection, he stated (Rosenow, 1914a,b):

> *'…the focus of infection is to be looked on not only as the place of entrance of the bacteria, but also the place where the organisms acquire the peculiar property necessary to infect. In the light of our knowledge the argument that infection the mouth are so common in individuals in apparent health, thus not minimize their importance. These or other foci are so common in patients suffering from arthritis, neuritis, appendicitis, ulcer of the stomach and cholestystitis, goiter,…'*
>
> *'Probably, the most common location of the focus or source of infection is the mouth… While it is proper to remove the teeth that are abscessed in a case of that kind, we should not expect that is necessarily the source of the trouble, but must look still further…'*
>
> *'It will be seen that the question of the focus of infection is a matter not only for the stomatologist or the dentist, but for the general practitioner, the surgeon; every branch of medicine needs to be taken into consideration to run the matter down and find the focus from which the organism gains entrance to the body.'*

At the Rush Medical College and later at the Mayo Clinic, Rosenow also investigated the characteristics of oral bacterial in cultures. He claimed that the microorganisms had affinities for certain organs of the body (elective localization) and that microorganisms could change their characteristics (transmutation) (Rosenow, 1914a,b, 1919).

In the Symposium of Interrelation of Medicine and Dentistry, presented at a meeting of the New York Academy of Dentistry in 1930, an important physician Russell L Cecil described his opinion on this

relationship. In a part of the text, he said (Cecil and Miner, 1930):

'By far the greater part of all the infections that man is heard to can be traced directly or indirectly to the entrance of pathogenic bacteria into the mouth or naso-pharynx.'

'Chronic periapical infection is by far the commonest dental infection responsible for systemic disease.'

'Generalized infections of obscure origin, particularly those in which Streptococci are recovered from the blood stream, are not infrequently referable to periapical infection.'

'I have been impressed (periodontia) more and more as time goes on with the belief that an important part of the etiology of disease of the supporting tissues around the teeth is to be traced to a systemic shortcoming.'

Cecil emphasized the importance of dentistry in the medical clinic and although he was part of a group of physicians who promoted innumerous tonsillectomies and tooth extractions, he advised (Cecil and Miner, 1930):

'The removal of an infected tooth does not necessarily remove the alveolar infection. Not infrequently root fragments and filling material remain after root extraction. If a piece of root or foreign body is left in an infected area, infection may persist for a long time. In such case the extraction accomplishes very little for the patient.'

'Personally, however, I should be opposed to retaining teeth that showed definite signs of periapical infection, even in a healthy patient, for we can never tell how much latent harm such a focus may be storing up for such organs as the arteries, kidneys, or heart muscle.'

On the other hand, he pointed out that there were many physicians who entirely ignored the possibility that dental conditions affected other parts of the body, and advised the extraction of teeth too freely and without sufficient knowledge. Cecil was not only a great physician but a visionary. At that time, he defended the correlation of medicine and dentistry as a public necessity, in the best interests of the health of the population. Recently this preventive vision on dentistry and medicine has had an increasing importance in our health policy (The Lancet, 2009).

The decline of focal infection theory

From 1912 to around 1940, the theory of focal infection was used to explain most human diseases. By about 1930s and 1940s, the theory of focal infection began to be questioned. This theory not only explained the origin of diseases, but also established the treatment through indiscriminate surgeries and attention to hygiene. On the other hand, this era was accompanied by an increase in surgery specialization and this fact created distrust in focal theory in the academic medical area. In 1926, Kopeloff described his affliction (Kopeloff, 1926):

'If the craze for violent removal goes on, it will come to pass that we will have a gutless, glandless, toothless, and I am not sure that we may not have, thanks to false psychology and surgery, a witless race.'

In addition, with further progress in the microbiology area, other studies, such as the Holman's study, could not reproduce the experimental work of Rosenow (Holman, 1928; Cecil and Miner, 1930). The research which could support the theory was completely discounted. In a study realized in 1938, Cecil and Angevine (1938) observed prospectively in 200 consecutive cases of rheumatoid arthritis that the effects of tonsillectomies and tooth extractions did not provide benefits for the curing of arthritis. They found that for 70% of cases there was no evidence of focal infections. After these results they concluded (Cecil and Miner, 1930):

'The time has arrived for a complete revaluation of the focal infection theory. Undoubtedly there are cases of infectious arthritis which result from focal infection. However, as far as typical rheumatoid arthritis is concerned, it would appear from this study that chronic focal infection plays a comparatively unimportant role.'

In 1940, Reimann and Havens made a systematical review of the literature about focal infection. In their major critique they reported that the theory had not been proved, that the infectious agents were unknown, and that some people whose tonsils were present were no worse than those whose tonsils were out. Moreover, they argued that individuals whose teeth and tonsils were removed often continue to suffer from the original disease because of which they were removed (Reimann and Havens, 1940). During this expansion of bacteriology knowledge, the focal infection did not appear as the principal cause of all diseases, as it was previously believed.

This period pointed the second split between dentistry and medicine. The first rupture occurred in 1840 when the discipline of dentistry was removed from the medicine course. Then the world's first Dental School was created in Baltimore. This fact was very important for the development of oral knowledge and science. On the other hand, physicians almost forgot the existence of the mouth and its potential to act in the development and progression of systemic diseases.

The great evolution of scientific and technology knowledge in dentistry

While innumerous studies questioned and denied the focal theory in medicine, the concept of dental foci of infection was not forgotten in dentistry, especially with reference to the periapical area and periodontal pockets (Easlick, 1951). Burket and Burn, 1937 showed that massage of gums as well as extraction could lead to bacteremia (Burket and Burn, 1937). In the same year,

Fish reported that bacteremia occurred in one out of four gingivectomies performed for the treatment of periodontal disease (Fish, 1937). In 1944, Appleton, who believed that more than one mechanism could be involved in the production of oral focal infection, named the most important path of dental infection: (1) an actual metastasis of organisms from a focus by way of blood or lymph channels, (2) a diffusion into the lymph or blood and hence into remote parts of the body of products of bacterial metabolism, (3) a sensitization, in an allergic sense, of various tissues by products of bacterial autolysis at the focus, which had diffused into the blood or lymph (Appleton, 1944). In the same line with this reasoning, Miller stated:

> '*The routes by which infection from periodontal pockets may spread are:'*
>
> (1) Through the blood and lymph
>
> (2) By the direct extensions within the tissue
>
> (3) By direct contiguity of the gastrointestinal and pulmonary tracts, through the swallowing and aspiration of infective material.

And he also added that there was abundant lymph which supplied the gingiva and soft tissues, and that infection could readily reach the neighboring lymph nodes. In a previous study published in 1943, Miller and Burman affirmed (Miller and Burman, 1943):

> *'…when it is realized that a much greater and more vascular area is involved in periodontal breakdown than in periapical infection, and that gingival pockets provide an excellent place for bacterial growth, it is apparent that there is a definite possibility of periodontal foci infection.'*

Hatton (1926) considered periodontal pockets as important as periapical infections in their role as sources of blood bacteria (Miller, 1950). In the 1940's, this concept was greatly explored. Miller (1950) summarized this concept which classified periodontal disease as the most significant oral focal infection in systemic disease:

> *'…evidence has been accumulating in the past few years to show that periodontal pockets are much more dangerous factors in producing focal infection disease because:'*

1. A much greater zone is involved than that in a periapical abscess, considering the total surface area of the walls of all the pockets. It can safely be stated that at least 20 times the absorption surface is involved in an average case of periodontal disease than in a well developed chronic periapical abscess.
2. Absorption from the gingival sulcus is more rapid since the blood and lymph supply to the gingivae is much greater than to the periapical area bone, especially when the latter is surrounded by even a slight degree of condensation or encapsulation.
3. Resistance to bacterial growth is lower in the gingival sulcus than anywhere else in the oral cavity because of food accumulation and stagnation.

Another historic example of dental foci was related in the investigation of oral infection and systemic diseases by transient bacteremias following tooth extractions and dental prophylaxes and the incidence of bacterial endocarditis (Okell and Elliott, 1935; Fish and MacLean, 1936; Feldman and Trace, 1938; Rhoads, 1948). Studies published by Fish and MacLean (1936), Feldman and Trace (1938), Geiger (1942), and Rhoads *et al* (1950) demonstrated that bacteremia after extractions was more prevalent in the presence of periodontal disease.

The antibiotic prophylaxis before and after dental extractions or periodontal treatment was suggested by many workers since 1940. This conduct was suggested to reduce the incidence of transient bacteremias and sub acute bacterial endocarditis. The medicament initially utilized was the sulfonamides after the manipulations of infected teeth (Hageman, 1940; Paquin, 1941; Rhoads *et al*, 1950). Penicillin started to be used in dentistry as mouth rinse and remedy, and was very important in the management of periodontal disease (Hageman, 1940; Paquin, 1941; Geiger, 1942; Pressman and Bender, 1944; Rhoads *et al*, 1950). Rhoads advocated the removal of foci under the protection of antibiotic therapy (Rhoads, 1948).

The modern concept of oral foci infection: can the mouth finally return to the body?

In 1952, the concept of focal infection was rapidly reported in a medical article and the authors alerted physicians and dentists to the false idea which suggests that the removal of foci of infection can treat or prevent diseases (JAMA, 1952). From 1952 to 1989, few articles were published exploring the concept which associated oral infection with systemic diseases.

Mattila *et al* (1989) published an important study where poor dental health was highly associated with acute myocardial infarction, independently of other risk factors for cardiovascular disease (CVD), such as total cholesterol, triglycerides, hypertension, diabetes, age, and smoking (Mattila *et al*, 1989). In the subsequent years, the oral foci theory, accompanied by the evolution of molecular technology and statistical analysis, started to be explored again in innumerous studies of association between oral disease, principally periodontal disease, and certain systemic diseases. In addition, in the medicine area, modern technology has also revived the focal infection demonstrating an association of specific infectious agents as cause of ulcer, neurologic illnesses, some types of arthritis, and CVD (Lorber, 1996).

In the dentistry area specifically, the techniques of molecular biology, including genomic sequencing, have largely collaborated with the profound knowledge in oral microbiology and its behavior in oral health and oral diseases, with genetics of bacterial and host, with environmental and risk factors, and with mechanisms of

local immunoinflammatory response. For example, current estimates suggest that 700 species can colonize the subgingival biofilms (Haffajee and Socransky, 2006). Micro array techniques permit the rapid detection of as many as 600 bacterial species in individual biofilm samples. The substitution of the term bacterial plaque for the more conceptual 'biofilm' represented a significant advance in the knowledge on oral microbial behavior. These techniques also collaborated with the identification of specific mechanisms of oral bacterial action and oral immunoinflammatory response in transient bacteremias in the blood, as well as the mechanisms of installation of these microorganisms in the parts of body (Haffajee and Socransky, 2006).

The consequence of these significant improvements in laboratory and clinical researches has been seen in the literature where a large number of models of cause-effect relationship between oral infections and systemic diseases. In 1996, the World Workshop in Periodontics introduced the term 'Periodontal Medicine.' This new discipline was created to validate biological plausibility of periodontal disease effects in systemic diseases, mainly observed in the periodontal disease and CVD relationship (Offenbacher, 1996). Innumerous studies investigated the behavior of periodontal pathogens in the atherosclerosis process, as well as the association between periodontitis and high levels of inflammatory markers (including the proteins of acute phase response in the liver), high values of intima media thickness, alteration of cholesterol levels, and glicemic uncontrolled in diabetic individuals (Cutler *et al*, 1991; Herzberg and Meyer, 1996, 1998; Beck and Offenbacher, 1998, 2005; Deshpande *et al*, 1998; Beck *et al*, 1999, 2001; Armitage, 2000; De Nardin, 2001; D'Aiuto *et al*, 2004; Brodala *et al*, 2005; Desvarieux *et al*, 2005; Garcia, 2009; Vidal *et al*, 2009).

Nowadays, these studies have concentrated in the next step of this investigation. In this new phase, the works have evaluated the effects of the removal of periodontal disease in diabetes, respiratory infections, adverse pregnancy outcomes, rheumatoid arthritis hyperlipidemia, inflammatory markers, endothelial dysfunction, and in intima media thickness. Although the impact of periodontal therapy should be further investigated (Kinane and Bouchard, 2008), the preliminary results have demonstrated that the treatment of periodontal disease results in improvement and regression of systemic diseases (Taylor *et al*, 1998; Taylor, 2001; López *et al*, 2002; Pussinen *et al*, 2004; López *et al*, 2005; Ortiz *et al*, 2009; Seinost *et al*, 2005; Al-Katma *et al*, 2007; Tarannum and Faizuddin, 2007; Tonetti *et al*, 2007; Scannapieco *et al*, 2003; Piconi *et al*, 2009; Vidal *et al*, 2009). Not only this, there is a new movement which investigates the genetic similarities in the development of some chronic diseases in susceptible individuals, including periodontal diseases, CVD, and metabolic disturbances. Furthermore, genetic factors could finally close the gap in the thorough understanding of this complex relationship (Noack *et al*, 2000; Kornman and Duff, 2001; Nibali *et al*, 2007; D'Aiuto *et al*, 2008; Khader *et al*, 2008; Kornman, 2008; Rogus *et al*, 2008).

In another example of modern oral focal theory, cariogenic bacteria and periodontal pathogens are found to be risk factors for respiratory infections. Indeed, poor oral health, oral pathogens of biofilm, and oropharyngeal bacteria have been associated with the occurrence of pneumonia in hospitalized patients (Azarpazhooh and Leake, 2006; Paju and Scannapieco, 2007). Scannapieco (1999) described the mechanisms of the oral pathogens in the pathogenesis of respiratory diseases. Oral interventions have improved oral hygiene by mechanical and/or topical chemical disinfection or antibiotics and reduced the incidence of hospital-acquired pneumonia by an average of 40% (Scannapieco *et al*, 2003).

Periodontal diseases have also been associated with preterm birth, low birth weight, fetal growth restriction, and preeclampsia (Jeffcoat *et al*, 2001; Boggess *et al*, 2003, 2005; Polyzos *et al*, 2009). This association has also been assessed in the next step of this investigation where randomized trials have been published assessing the benefits of periodontal therapy towards the reduction of adverse pregnancy outcomes (López *et al*, 2002, 2005; Tarannum and Faizuddin, 2007). However, the beneficial effects of this treatment remain unclear. In a clinical controlled trial, Michalowicz *et al* (2006) observed that although pregnant women had improved periodontal parameters after non-surgical periodontal treatment, this was not enough to reduce preterm birth, low birth weight, or fetal growth restriction.

The majority of studies on the association and intervention by elimination of oral focal infection, such as periodontal disease, have reported a positive relationship between oral diseases and systemic disease. However, some of these were unable to confirm such an association. The mechanisms underlying this association are not clearly understood. Future randomized clinical trials and well-designed prospective cohort studies with uniform definitions of periodontal disease would be needed to complement the understanding of a possible relationship between oral diseases and systemic diseases.

On the other hand, although the investigations of mechanisms of dental infections as a model of focal infection have advanced very fast in the past two decades, we do not observe the effects of these discoveries in government programs of oral health in the great majority of countries. It is important to integrate oral disease prevention into programs to prevent chronic diseases and into public-health systems. This neglected attitude observed in the oral health area results in the subestimated prevalence of oral diseases and their possible consequences in systemic health worldwide (The Lancet, 2009).

Nevertheless, the statistic data demonstrate that dental caries are the most common chronic diseases in worldwide. Ninety percent of people have had dental problems or toothache caused by caries (The Lancet, 2009). Despite the multiple benefits of the multiple forms of fluoride in common use, dental caries is still by far the most common disease in children in the United States. Nearly 60% of children aged between 5 and 17 have either decayed teeth or filled primary and

permanent teeth (Mandel, 2002). The prevalence of periodontal disease is also high in the U.S. population. It is estimated that 95% of adolescents and 75% of adults have gingivitis, and that 35% of adults aged over 30 have periodontitis (Albandar, 2002). It is possible that these indicators may not represent the complete reality. Indeed, the lack of oral health programs coupled with the small number of prevalence studies (mainly in developing countries) and the vast varieties of existing methods of diagnosis of dental diseases results in incomplete and confused data of prevalence.

Other difficulties to access 'complete' data about oral diseases statistics are the inaccessibility to dental treatment for all of the population in the world, and the high costs of oral treatment and oral hygiene. In addition, even more difficult to assess is what oral health (rather than oral disease) means to individuals, communities, and societies (Mandel, 2002).

On the other hand, some advances can be observed in the world in the importance of oral health. One indicator of changing perceptions of oral health over the past several decades has been a steady decline in tooth loss and edentulism, and a concomitant increase in tooth retention. Tooth loss is no longer considered an inevitable consequence of aging, and the retention of teeth for a lifetime has become increasingly possible for successive generations (Mandel, 2002). In 2007, a World Health Assembly resolution called for oral health to be integrated into chronic disease prevention programs. Health workers, including physicians, nurses, pediatrics, and pharmacists can all deliver prevention messages about the use of fluoride and the risk factors for oral disease (The Lancet, 2009).

In this review, we were able to evaluate the historic evolution of the concept of oral foci infection and its relation with systemic diseases. In the beginning of the 20th century, when great advance and enthusiasm occurred in this theme, we observed in the majority of studies the existence of science based on poor technologies and high levels of intuition and passion. Nevertheless, this idea was not abandoned and nowadays we are able to understand the complexity of various mechanisms of oral infections possibly involved in systemic disease processes, covered by innumerous studies in the past. Throughout history we have had very important researcher's contributions in this interdisciplinary area which enlightened us in following this track with the same passion, which nowadays is supported by advanced technologies. In 1914, Dr. Frank Billings left us the following very significant excerpt (Billings, 1914):

> *'Modern bacteriology and clinical research are adding day by day incontestable proof that bacterial invasion and infection of tissue is the fundamental cause of many of the systemic diseases, which have been classed as toxic, metabolic or nutritional.'*

In 1930, Dr. Russell Cecil suggested an important path to follow, which we still have not been able to accomplish (Cecil and Miner, 1930):

> *'Dentistry is a branch of medicine, and though nowa-days the two professions seem to have strayed apart, I believe that, as time goes on, this divergence will be corrected and the dentistry will assume its logical place in the medical clinic.'*
>
> *'I call this position of dentistry strategic, because the mouth, as the point of entrance into the human body, occupies by reason of this fact a strategic position. This applies particularly to that perhaps most important department of medicine, namely, infectious diseases.'*

The last chapter in this story may not yet be finished. Indeed, there is still a big gap separating dentistry and medicine. The knowledge about oral infections and their effects should be further investigated and then largely divulged in medicine, so that the mouth can finally regress to the body with due significant importance. The concept of periodontal medicine may ultimately guide clinicians in making evidence-based decisions to improve not only patient oral health but also systemic health. With the union of dentistry and medicine, it will be easier to assess this connection more accurately and to possibly integrate oral preventive programs into programs to prevent chronic diseases and into public health systems.

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Carolina LZ Vieira executed a literature review in PubMed Central and in American and British Libraries. The authors analyzed this article and approved the final version.

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