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Focal Infection

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Ideas tend to be many, good ideas few. Ideas also tend to become entrenched, and the protagonists adopt glowing stances on opposite hills, like David and Saul of old, although, as with them, the real glowing is usually somewhat one-sided.

The real problem is the good idea, or, in scientific terms, the sound hypothesis. These take many years to establish, and computers don’t seem to help. Fashions come and go. Many seek fame and fortune by betting on the prevailing fashion. Often they achieve. Arguably this can prove regrettable, since few scientific hypotheses stand the test of time.

What can be even more frustrating is the perennial re-invention of the wheel. Scientists seem to be at least as prone to this malady as any other group. The result is a waste of time, effort, and resources which would have been more profitably directed in the pursuit of human welfare. This is particularly relevant in matters of health and disease. Most news bulletins carry items—usually lurid, misinformed, exaggerated, and scare-mongering, not to say somewhat misleading—about diseases and their treatment or prevention.

Therefore, before we contact the wider media, let me preface this review by saying that this is about a re-discovery, not a discovery. I wonder why it has taken so long to be accepted—and then not unanimously, I would guess—that oral health is so important in relation to systemic health that the dentist has a responsibility for general health. That comment came from a great parent with no scientific training.

About a century ago, William Hunter first synthesized the notion that oral micro-organisms and their products were involved in a range of systemic diseases not always of obvious infectious origin, such as arthritis (Hunter, 1900, 1921). Arguably, as in so many other spheres of dentistry, perhaps the first actually to draw attention to the relationship between oral and systemic infections was W.D. Miller (1890), especially with his study of the human mouth as a focus of infection (1891). The orgy of extraction that ensued, without clear positive results, resulted in the notion of "focal infection" or "focal sepsis" falling into disrepute. By relegating this notion to the professional back burner, we compromise our role as oral physicians—physicians whose area of specialization is the mouth.

The problem about the original discovery was the tenuous nature of the link between putative oral foci of infection and related disease. And that is the warning to us: that for the hypothesis not to fall into disrepute for a second time, there must be no unsubstantiated attributions, no theories without evidence. Many original publications were anecdotal. Direct cause-and-effect evidence was lacking. Apart from the association between oral bacteria and endocarditis in patients with congenital heart disease or after rheumatic fever, the subject lay dormant for decades. Yet now there is a resurgence of interest, and it may be salutary to observe the extent of current evidence for and the farsightedness of our predecessors in recognizing the relationship between oral foci of infection and a wide range of diseases. Some are clearly infectious, some inflammatory without direct evidence of microbial infection, and some one would never have thought of as attributable in any clear way to micro-organisms. [What about toxic shock syndrome in a patient with Down’s syndrome (Navazesh et al., 1994)?]

Direct infection

Focal infection of oral origin may derive from closed or open sites. Open foci include caries lesions, periodontal pockets, and extraction sockets; closed foci, infection around root apices, unerupted but infected teeth, and infected pulps (Newman, 1968). Focal infection leading to infective endocarditis can even occur via a dens in dente (Whyman and MacFadyen, 1994). From the oral foci, micro-organisms—bacterial, viral, or other—or their products may gain entry to the deeper tissues directly, by spreading along fascial planes, through bony cavities, or even along blood or lymph vessels or nerves, or via salivary gland mucous surfaces. Can one die of such simple chronic infection? One may cite the coroner’s court, but there is also extensive literature evidence.

The susceptible patient

In this context, it is also important to recognize the relevance of lowered resistance. Patients who are more susceptible seem more subject (Thoden van Velzen et al., 1984; Goldberg, 1987), even the older age groups, without apparent underlying systemic cause (Navazesh and Mulligan, 1995). Fevers of unknown origin but with a dental infection link have been recorded without other systemic disease (Nashchitz and Yeshurun, 1985; Shindoh et al., 1987) and in patients with leukemia (Chapman et al., 1976), cancer (Peterson and Sonis, 1982), joint replacement (Little, 1983;
Lindqvist and Slätis, 1985), diabetes mellitus (Harrison et al., 1983), rheumatoid arthritis (Iida and Yamaguchi, 1985), and liver transplants (Svirsy and Saravia, 1989). Immune suppression resulting from treatment of malignant neoplasias may be a cause of focal infection. Vertebroosteomyelitis and pneumonia due to systemic candidiasis followed treatment of an oral carcinoma (Hashimoto and Tanicka, 1991). Arguably the best-known focal infection, infective endocarditis, has been a sequel in a patient with Hodgkin's lymphoma (Meehan et al., 1994). Further, oral infection has been shown to be a principal cause of febrile episodes in lymphoma patients receiving cytostatic drugs (Laine et al., 1992).

Infection of dental or periodontal origin is a major problem in cancer patients, likely to be enhanced by chemoradiation therapy. Immunosuppression as in HIV-related conditions plainly has a similar effect, although many of the resulting infections tend not to be attributable to the usual oral commensals. Optimal oral hygiene may be considered a prerequisite in patients due to receive chemoradiation therapy (Wright, 1990; Blaha and Reeve, 1994; Mealey et al., 1994; Semba et al., 1994). Secondary or opportunistic infection—candidiasis, for example—may be controlled by conventional oral hygiene with antimicrobials (Ferretti et al., 1988, 1990; Ellegaard et al., 1989; Bergmann et al., 1992; Rutkauskas and David, 1993). Nor should one overlook the link between chronic inflammatory periodontal disease and osteoradionecrosis of the jaws (Galler et al., 1992; Carl, 1993), or the consequences of extraction in this regard (Mealey et al., 1994). Bone marrow suppression is also likely to predispose to increased systemic risk from oral infections (Peterson et al., 1987; Peterson, 1990; Glick and Garfunkel, 1992; Barrett and Schifter, 1994).

Localization of infection

It is fascinating to observe, so many years since the suggestion of a link between chronic focal infection and chronic arthritis (Miller, 1890, 1891; Hunter, 1900, 1921; Billings, 1912, 1913), the advances in supporting evidence over the years (Davidson et al., 1949; Ebringer et al., 1989; Dixon, 1990). And yet earlier workers had considered that different organisms selectively colonized specific loci—the theory of elective localization (Rosenow, 1919, 1921, 1923). By this hypothesis, bacteria would localize from the source focus to the distant, systemic focus, and Rosenow demonstrated a targeting process in a series of experiments, reviewed by Hughes (1994). This should not surprise us. Micro-organisms cause infections of tissues, organs, or systems, clearly depending on an ability to survive and grow better in those loci—a clear extension of the principles of microbial ecology in general.

It may be noted that Hughes (1994) reviewed the topic from the rheumatologist's standpoint. He cites perhaps the earliest relevant reference, none other than Hippocrates, whom he quotes as reporting a patient whose arthritis was cured by extraction of an infected tooth (see also Mayo, 1922). Further, while we may think it a modern discovery that bacterial products rather than the whole cells are the source of focal infection, the same point was made many years ago (Swift et al., 1928), with further proof through the years (Schwab and Cromartie, 1957; Ebringer et al., 1989).

Lens and Beertsen (1988) showed that injection of an antigen into the gingiva produced (mouse) knee joint inflammation. Focal infection has been cited in arthritis of the knee (Morer, 1975) and infected joint prostheses (Rubin et al., 1976; Schurman et al., 1976; Jacobsen and Murray, 1980; Lindqvist et al., 1989). There has even been a suggestion that dental infectious foci may be involved in other obscure inflammatory disorders, such as erythema nodosum (Kirch and Duhren, 1992).

The mechanisms of spread are direct, through the local tissues and along fascial planes, along mucous surfaces, including ducts such as the salivary, and by inhalation and ingestion along respiratory and gastrointestinal mucosal surfaces, respectively, via the bloodstream, the lymphatics, and even, possibly, along nerves (Newman, 1968). Debelian et al. (1994) identify three pathways: metastatic infection from the oral cavity due to transient bacteremia, metastatic injury due to oral microbial toxins, and metastatic inflammation due to immunologic injury caused by oral micro-organisms.

The development of labeled stabilized liposomes may be expected to extend our ability to localize infection foci (Goins et al., 1993; Boerman et al., 1995), as may the use of labeled chemotactic peptides (Babich et al., 1993; Hovi et al., 1993; Fischman et al., 1995). As well as being used to identify sites of focal infection, liposomes and analogous carriers may also serve to target antimicrobial treatment to such sites (O'Connell et al., 1992).

The target tissues

Head and neck

Direct infection has clearly been shown to spread from defined oral foci to various locations in the head and neck, and from thence to the mediastinum. Many such conditions are fatal but fortunately are comparatively rare. Most are common, such as maxillary sinusitis (Dayal et al., 1976; Smith et al., 1979) and infections of the deep and superficial tissues of the face (Mitchell and Nelson, 1993). Implants may become infected due to recurrent dental pathology (Williams, 1994), as with prosthetic joints (Lindqvist and Slätis, 1985), and even cardiac pacemakers (van Winkelhoff et al., 1993).

Infection may involve the ethmoid (Helidonis et al., 1979) or spread to surrounding soft tissues, as in masticatory muscle space cellulitis (Bird and Smith, 1973), and the floor of the mouth (Ludwig's angina—Whitley, 1986), or cause cavernous sinus thrombosis (Goteiner et al., 1982; Ogundiya et al., 1989).

Fascial planes

A major path of spread is through the fascial planes nearest to the teeth and may lead to parapharyngeal cellulitis (English and Kaiser, 1979), retropharyngeal space infection
Intracranial sequelae

Intracranial infections constitute another serious sequel of oral focal infection. Brain abscesses are recorded (Churton and Greer, 1976; Gallagher et al., 1981; Goteiner et al., 1982; Aldous et al., 1987; Marks et al., 1988; Andrews and Franham, 1990) and may be more localized, e.g., to frontal (Ingham et al., 1978), parietal (Andersen and Horton, 1990), or frontoparietal lobes (Saal et al., 1988), with occasionally fatal consequences, often being resistant to antibiotics (Gallagher et al., 1981; Schuman and Turner, 1994). The role of focal infection in relation to brain abscess in particular draws attention to the need for care in the assessment of evidence, referred to at the outset. As Schuman and Turner (1994) observe, dental infection or treatment was frequently incriminated in the articles they reviewed "solely because an infection or treatment occurred within several months of brain abscess, when non-dental bacteria were cultured from the brain abscess and without culturing both the dental infection and the brain abscess to ascertain flora match." It is a caution one might invariably apply to all focal infection. In relation to brain abscess, however, it would be misleading to conclude that all the reports were vague, since for this as for a range of focal infections oral organisms have been directly associated with the condition (Navazesh and Mulligan, 1995).

Meningitis has also occurred as a focal infection (Hedström et al., 1980; Zachariades et al., 1986; Fernandez and Phipps, 1988), as has acute hemiplegia following a dental abscess (Hamlyn, 1978). Larkin and Scott (1994) reported a case of metastatic paraspinal abscess and paraplegia secondary to dental extraction. Nerves themselves may be affected, including such problems as actinomycosis of the gasserian ganglion (Perna et al., 1981) and trigeminal nerve anesthesia (Barrett and Buckley, 1986).

Respiratory system

Concerning focal infection involvement of the respiratory tract, it has been observed that solitary lung abscesses are rare in the absence of teeth (Newman, 1968) and have been noted secondary to dental infection (Latronica and Shakes, 1973; Terezhalmy and Bottomley, 1978; Rams and Slots, 1992). A particular problem in the susceptible elderly group is aspiration pneumonitis of oral microbial origin (Loesche et al., 1995).

Cardiovascular system

Infective endocarditis remains the most clear instance of focal infection (Engle斯顿, 1975; Strauss, 1975; SpaULDing and Friedman, 1975; Kraut and Hicks, 1976; Kaplan, 1977; Oakley, 1979; Whittington, 1979; Thornton and Alves, 1981; Bayliss et al., 1983; Siegman-Igra et al., 1984; Lieberman, 1992). As mentioned previously, some malignancies may lead to nonbacterial thrombotic endocarditis, which in turn may predispose to infectious endocarditis (Meehan et al., 1994). It may also be observed that the causative oral organisms of infective endocarditis include anaerobes as well as aerobes (Asikainen and Alaluusua, 1993). It is also clear that bacteremia is more frequent after extraction due to inflammatory dental diseases (Okabe et al., 1995). Of the 132 cases of bacteremia the latter examined, nearly 80% yielded anaerobes, mostly eubacteria, peptostreptococci, and propionibacteria. It is pertinent to note that significant bacteremia may follow routine dental procedures apart from extractions, including toothbrushing, intraligamental injection, rubber dam or matrix placement, and polishing of teeth (Roberts et al., 1996). Baseline bacteremia was also evident in a minority of subjects in this study.

With regard to other cardiovascular problems, septicemia secondary to oral infection has been a sequel of internal jugular thrombophlebitis (Mitre and Rothran, 1974), and an oral isolate, E. corrodens, has been associated with septicemia and pleural effusion (Stiegl, 1979). A fatality has been reported as a result of acute dento-alveolar abscess and the subsequent development of septicemia with disseminated intravascular coagulation (Carter et al., 1992;
Currie and Ho, 1993).

One of the most intriguing developments in focal infection research is the recent association of dental infections and myocardial infarction, apart from the more direct link between dento-alveolar abscess and acute bacterial myocarditis (Palank et al., 1979). A series of case control studies has been reported (Mattila et al., 1989; Mattila, 1993) indicating an association between dental infections and acute myocardial infarction and chronic coronary artery disease. An epidemiological survey indicated a possible association between missing teeth and coronary heart disease (CHD), and a 14-year follow-up study associated periodontitis with an increased risk of CHD (DeStefano et al., 1993). As a possible mechanism, it was suggested that bacterial aggregation of platelets could relate to the pathogenesis of atherosclerosis and arterial thrombosis. A caution: Although the association between dental infection and severe coronary atheromatosis in males remained significant after adjustment for the effects of age, blood lipids, body mass index, hypertension, smoking, and social class, no such association was observed in the (small) number of females studied (Mattila, 1990; Mattila et al., 1993). Mattila (1990) based his research concerning a possible oral link on observations of connections between bacterial and viral infections and atherosclerosis or myocardial infarction. In a recent study, Beck et al. (1996) demonstrated that inflammatory periodontal disease was a significant risk factor for the development, morbidity, and mortality of cardiovascular disease, the odds of fatal CHD and stroke being 1.6- to 2.1-fold higher in such cases after adjustment for the usual risk factors. Syräjänen et al. (1989) had previously noted an association between chronic inflammatory periodontal diseases (CIPD) level and stroke.

Gastrointestinal tract

In view of the possible association between H. pylori and gastritis and gastric and duodenal ulcers, and its occasional detection in the mouth (Mapstone et al., 1993; Nguyen et al., 1993), one may consider this another possible instance for focal infection research. Liver infections have also on occasion been cited as attributable to dental infections (Crippin and Wong, 1992). Micro-organisms from periodontal lesions have also been implicated in the pathogenesis of inflammatory bowel disease (Van Dyke et al., 1986).

Fertilization, pregnancy, and birth weight

At the outset, it was mentioned that many interesting areas now involve the possibility of focal infection. There are now reports of a high level of potential dental foci of infection in relation to bacteriospermia, with "the bacterial spectrum of the intraoral samples being almost identical with the spermograms", with improvement in spermatological parameters following appropriate dental treatment (Bieniek and Riedel, 1993). It has also been observed (in animals) that infection with Gram-negative periodontitis-associated organisms may adversely affect pregnancy outcome (Collins et al., 1994), and that severity of maternal inflammatory periodontal disease is associated with a risk for low birth weight in humans (Gibbs et al., 1992; Offenbacher et al., 1996), this development deriving from the concept of an association between subclinical infections and premature birth.

Conclusions

New knowledge this may not be, but we certainly now have the means of evaluating these rejected and now re-awakened theories of focal infection. These may lead to a time when we will be true oral physicians, less pre-occupied with the commonest of human diseases, and with more concern and time for their systemic implications. We certainly need to realize that there are links between oral and systemic health and oral and systemic disease. For some, the evidence is strong, for others tenuous, and for many indirect but intriguing. Only our research, in collaboration with other medical colleagues in their specialties, will enlighten. Let us prepare to broaden our minds.

References


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