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## **Guest editorial science transfer: oral health and general health - the links between periodontitis, atherosclerosis, and diabetes**

Jepsen, Søren ; Stadlinger, Bernd ; Terheyden, Hendrik ; Sanz, Mariano

**Abstract:** The transfer of knowledge from research and academic communities to clinical practice presents an enormous challenge. This is particularly true for when attempting to convey the clinical relevance and implications of laboratory-based research. A landmark consensus workshop was staged in Europe (La Granja, Spain, November 2012) jointly by the European Federation of Periodontology (EFP) and the American Academy of Periodontology (AAP). This article is protected by copyright. All rights reserved.

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**Guest Editorial Science transfer: Oral Health and General Health - the Links between  
Periodontitis, Atherosclerosis, and Diabetes**

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**Short running title:** Science transfer: oral and general health

**Keywords:** Periodontitis, Atherosclerosis, Diabetes, Bacteremia

**Conflict of interest and Source of Funding:**

The authors do not declare any conflict of interest with regard to the promotion of the scientific content of the joint EFP/AAP workshop on “Periodontal and Systemic Diseases” by this project. Funds for the production of the educational film and its dissemination were provided by educational grants from Quintessence and Sunstar.

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The transfer of knowledge from research and academic communities to clinical practice presents an enormous challenge. This is particularly true for when attempting to convey the clinical relevance and implications of laboratory-based research.

A landmark consensus workshop was staged in Europe (La Granja, Spain, November 2012) jointly by the European Federation of Periodontology (EFP) and the American Academy of Periodontology (AAP). The subject was “Periodontal and Systemic Diseases“ and the proceedings were published in a supplementary issue of the *Journal of Clinical Periodontology* which is freely available online (at <http://onlinelibrary.wiley.com/doi/10.1111/jcpe.2013.40.issue-s14/issuetoc>).

Apart from systematically reviewing the scientific literature on epidemiological associations and clinical intervention studies, special attention was paid to the biological mechanisms underpinning the proven epidemiological associations between oral and systemic diseases. Whilst it was recognised that many of the cellular and molecular details remain to be fully characterised, and that our current knowledge is based principally on findings from in vitro

and experimental animal research, a clear picture has emerged in which systemic inflammation appears to provide the missing link.

A landmark computer animated 3D scientific film has been created to visualize some of the key aspects of the molecular and cellular links between periodontal infection/inflammation and systemic diseases/conditions such as atherosclerosis and type 2 diabetes, based upon the evidence analysed at the consensus conference (Tonetti & van Dyke et al. 2013, D'Aiuto et al. 2013, Reyes et al. 2013, Schenkein & Loos 2013, Chapple & Genco et al. 2013, Taylor et al. 2013, Engebretson & Kocher 2013). The film had its world premiere at the recent EuroPerio 8 conference in London and will now be made available on the EFP website ([www.efp.org](http://www.efp.org)). Both, an expert as well as a public version of the film have been prepared, and it is hoped that it will serve multiple purposes, such as the education of health professionals, patients and the general public on the systemic consequences of periodontal disease. It will also serve as the backbone of the upcoming EFP awareness campaign "*periodontal health for a better life*".

The film opens with an animated portrayal of periodontitis and its pathological processes within the periodontal pocket, where there is close interaction between the bacteria residing within the subgingival biofilm on the root surface and the ulcerated pocket epithelium. A storyboard was developed that described the following sequence of events:

- 1) Dissemination of periodontal bacteria into the circulation, thereby eliciting systemic inflammation that leads to;
- 2) Promotion of atherosclerosis;
- 3) Impaired glycemic control, with negative effects on the periodontium and
- 4) The potential benefits of periodontal treatment.

Periodontal bacteria from the biofilm at the interface with the ulcerated periodontal pocket epithelium enter the circulation during speech, eating and tooth brushing and disseminate throughout the body via the blood circulation (Tomás et al. 2012) (Figure 1).

There is evidence that periodontal bacteria can invade the endothelial lining cells of blood vessels (in vitro), can induce atherosclerosis in animal models of disease, and also that the host's inflammatory-immune response favours atheroma formation, maturation and exacerbation (Reyes et al. 2013, Schenkein & Loos 2013, Kerschull et al. 2010). Therefore these events were animated to illustrate the different stages of atherosclerosis.

Bacteria within the bloodstream also activate an acute-phase response by the liver and activate immune cells, such as neutrophils, to release oxygen radicals, thereby generating 'oxidative stress' within the circulation, further driving systemic inflammation. As illustrated in the subsequent scene of the film this may in turn lead to reduced  $\beta$ -cell function, apoptosis and insulin resistance (Figure 2). These conspire to promote impaired glycaemic control and type 2 diabetes. The mechanisms by which diabetes negatively impacts upon the periodontium are illustrated (Taylor et al. 2013, Preshaw et al. 2012, Duarte et al. 2014) with a specific focus on the formation of advanced glycation end-products (AGEs), emphasising the bi-directionality of the relationship between periodontitis and diabetes.

Finally, the potential benefits of periodontal treatment on systemic health are graphically illustrated. A reduction of the oral infectious burden can result in a reduction of the overall inflammatory load, with positive effects demonstrated on surrogate measures of atherosclerosis (D'Aiuto et al. 2013, Teeuw et al. 2014) and on glycaemic control, as evidenced by several meta-analyses (Engebretsson & Kocher 2013, Li et al. 2015).

In summary, this project has focussed on making the invisible very visible, in order to facilitate a better understanding of biological processes through the power of graphic imagery. The overall goal is to motivate specialists, dental practitioners, as well as dental students using computer animated science films, in order to engage these groups in current biologically relevant topics for their day-to-day practical activities. Understanding of pathophysiological processes should be greatly facilitated by the movie and this project should be viewed as a contribution to “Science-Transfer“, as already takes place in other biomedical disciplines and scientific journals (i.e. <http://multimedia.mcb.harvard.edu>,

<http://www.nature.com/nature/videoarchive/>,

<http://www.nature.com/ni/multimedia/index.html>,

<http://video.sciencemag.org>).

With the explosion of scientific knowledge over the last two decades and an ever-increasing number of original scientific publications it has become more and more important to translate current highly relevant research topics in an easy to digest manner for oral health professionals. This approach also facilitates the dialogue with our medical colleagues as well as communication with our patients and the public.

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**Figure Legends:**

Figure 1: Periodontal bacteria from the biofilm repeatedly enter the blood vessels of the gingiva through the ulcerated pocket epithelium. Similarly, locally produced inflammatory mediators will shed into the bloodstream.

Figure 2: Membrane-bound insulin receptors register the presence of insulin in the blood.



