

# Orale Präventivmedizin

Eine interdisziplinäre Herausforderung

 Online-Version in der eRef

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Heinz H. Renggli  
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 Thieme

Cover of the book "Orale Prävention – Eine interdisziplinäre Herausforderung" (Oral Preventive Medicine – An Interdisciplinary Challenge) published by Georg Thieme Verlag in January 2022; ISBN 978-3-13-205181-2. (Image: Georg Thieme Verlag).

\* This interview has been previously published in German by SWISS MED 44 (2022) Nr. 1, 11 – 23. The translation into the English language was done by Dr. G. E. Steimer, member of a team of co-authors providing the 2024 upcoming edition, an expanded version of the book Oral Preventive Medicine<sup>5</sup>, soon to be released. (see page 14)

# On the correlation between oral and systemic health – “Genesis of Health begins in the mouth” – A textbook for oral preventive medicine

## Suggestions for increasing cooperation between dental and medical disciplines – Recommendations for health policy and health-related economic issues for decision-makers

Interview with: Dr. med. dent. René B. A. Sanderink, Würzburg (Germany) Prof. em. Dr. med. dent. Heinz H. Renggli, KH Malden (Netherlands) [1] Prof. Dr. med. dent. Ulrich P. Saxer, Forch ZH (Switzerland)\*

**Interview: Dr Felix Wüst, SWISS MED Editorial Board (14/03/2022) - the translation has been approved by both authors**

*In January 2022 publisher Georg Thieme, Stuttgart (Germany), released a book entitled “Oral preventive medicine – An Interdisciplinary Challenge”, dealing comprehensively with the topic on complexity of the correlation between oral and systemic health [2]. The authors R.B.A. Sanderink, H.H. Renggli and U.P. Saxer have created a textbook addressing the target group of dentists and physicians alike. Thieme publisher proclaims boldly that the book promises most profound content “most of which has never been printed before.” In this interview, published below, the authors discuss their work in full detail.*

*Dr Sanderink, I learned from Professor Saxer that you were the 'lead' of the book “Oral preventive medicine – An Interdisciplinary Challenge”. Can you give us some details about the creation of this work?*

R. B. A. Sanderink: Mr Wüst, let me first extend my warmest thanks for your willingness to publish a special issue of your SWISS MED journal on our book “Oral preventive medicine – An Interdisciplinary Challenge”. The ingenious thing about this magazine is that it will be available not only to dentists, but also to general practitioners in the German-speaking regions of Switzerland who regularly receive your SWISS DENT magazine. But now

to your question! For years, my colleagues - not only my co-authors, but many academic colleagues too - have observed that almost everywhere in Europe there has been an ongoing regression in networking between medical and dental university curriculums, which is related in part to the Bologna Process. This realization, symbolically speaking, demands action on our side and has brought us to the conclusion that the oral cavity must gain appropriate attention as to its integrational significance within the human body, so to speak. This applies not only to university educational curriculums, but also to everyday clinical practice, where there is a strong need and demand for structured cooperation between dentists and medical doctors - with the exception

of oral and maxillofacial surgeons – in order to adequately serve patient needs, especially those needs overlooked due to never being addressed.

It was our goal to demonstrate the need to combat this lack of awareness in the context of a book dealing dually with most recent fundamental basic knowledge and combining optimal clinical practice for integrational treatment concepts. Figure 1 shows the content of our work in graphic form. At the very first glance it is immediately obvious that oral and general health inseparably interact influentially with each other and that microbial, metabolic, immunological and environmental factors are involved.

*The central concern of your book is the correlation between oral health and general health. How long have those participating in professional circles been aware of this fact?*

U. P. Saxer: The correlation between oral biofilm infections such as caries and periodontal disease and diseases affecting remote organs have been well known in medicine for more than seventy years [3]. There is a statistically significant correlation between tooth loss and life expectancy. In addition, increased mortality rates have been reported in patients with severe periodontitis.

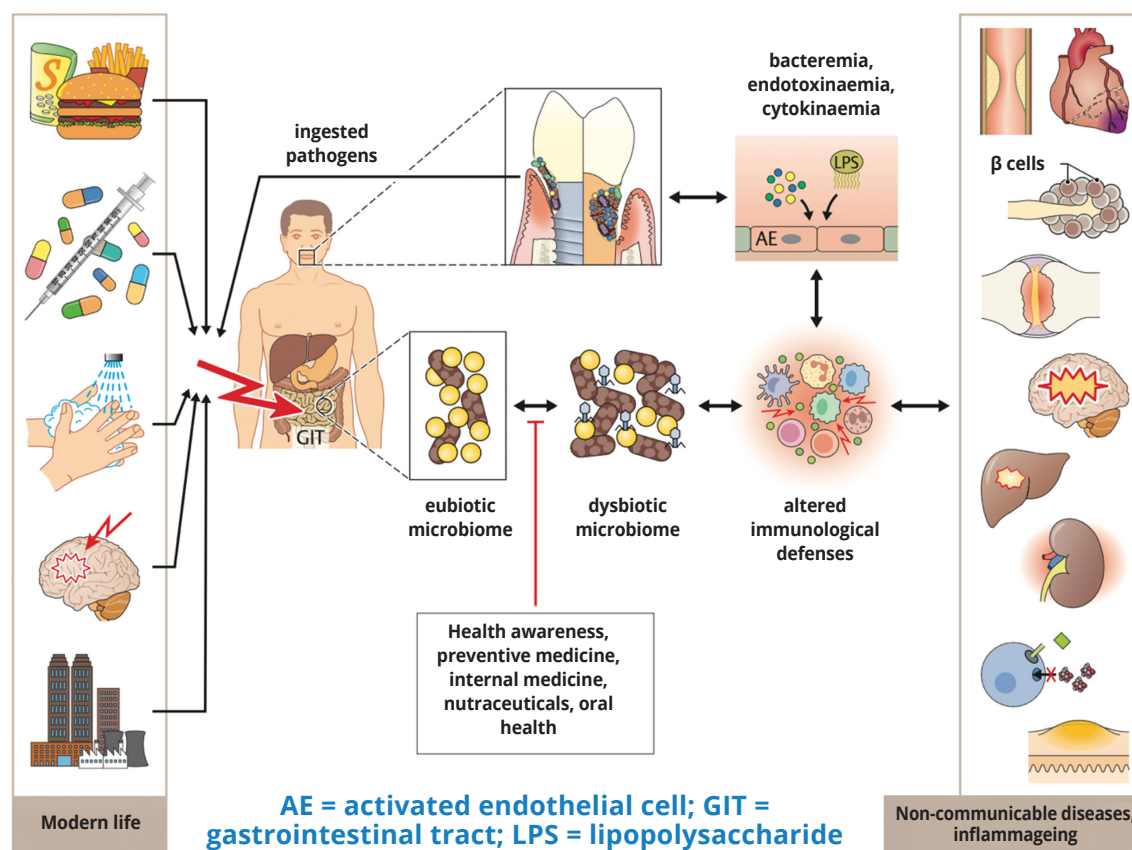
Accordingly, almost one third of periodontal research currently deals with the interplay between periodontal diseases and systemic pathologies. Results indicate that severe periodontitis, which affects about ten to twelve per cent of the world's population, is a risk factor for non-communicable diseases (NCDs) (Fig. 1). Conversely, it cannot be ruled out that periodontitis is often an oral component of certain lifestyle diseases such as obesity or appears as a concomitant disease or metabolic condition.

*Who is the target audience for your book? Which groups do you want to address?*

R. B. A. Sanderink: In accord with a systematic review and systemic view of etiology, treatment and prophylaxis, this book, also deemed for purposes of reference, is suitable for general practitioners, specialists and dentists, psychiatrists, nutritionists, environmental experts as well as decision-makers involving health policy and health-related economics. Close cooperation between all these people is essential for a sustainable promotion of public health.

U.P. Saxer: The target groups just mentioned should be made aware that there are clear links between the occurrence of oral

## Modern lifestyle, consequences relating to the microbiome and the spread of non-communicable diseases

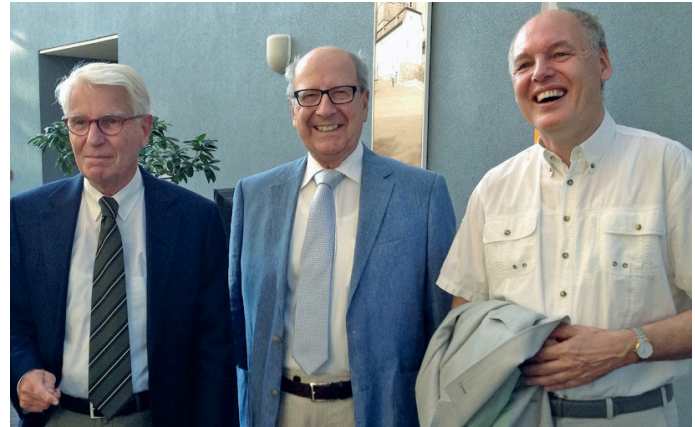


(Fig. 1): Graphic summary of the book's contents. This book describes the relationship between modern life, the emergence of NCDs (non-communicable diseases), the inflammaging process, as well as the role of the microbiome including immune system interaction during these processes. Curative and preventive interventions require interdisciplinary cooperation between oral and general medicine. (Source: Sanderink R. B. A., Renggli H. H., Saxer U. P., Oral Preventive Medicine – An Interdisciplinary Challenge. Georg Thieme Verlag Stuttgart 2022, p. 12; with kind permission of the publisher).

diseases such as periodontitis and other NCDs such as obesity and diabetes (Fig. 2), arteriosclerosis, rheumatoid arthritis, Parkinson's disease, depression, as well as during pregnancy and in patients with implants of all kinds. We explain these individual interconnections in our book based on circumstantial medical history factors concerning immunological, metabolic and neuroendocrine processes.

Can you describe this rather general statement in more detail?

R. B. A. Sanderink: Please – let me explain: For many thousands of years, the microbiome and the immune system have peacefully evolved in conjunction in the digestive tract. This is no coincidence, as the vast majority of microorganisms reside therein (work-life balance) and congruently the intestinal wall seats by far the largest number of immune cells in our bodies. Consequently, an impressive repertoire of immune cells have evolved, rendering a physiological and a tolerogenic phenotype simultaneously to the immune system: This expression of duality in function must both capably and effectively eliminate infectious and sterile noxae and tolerate the presence of endogenous macromolecules and harmless environmental antigens, such as pollen, without reactive attack.

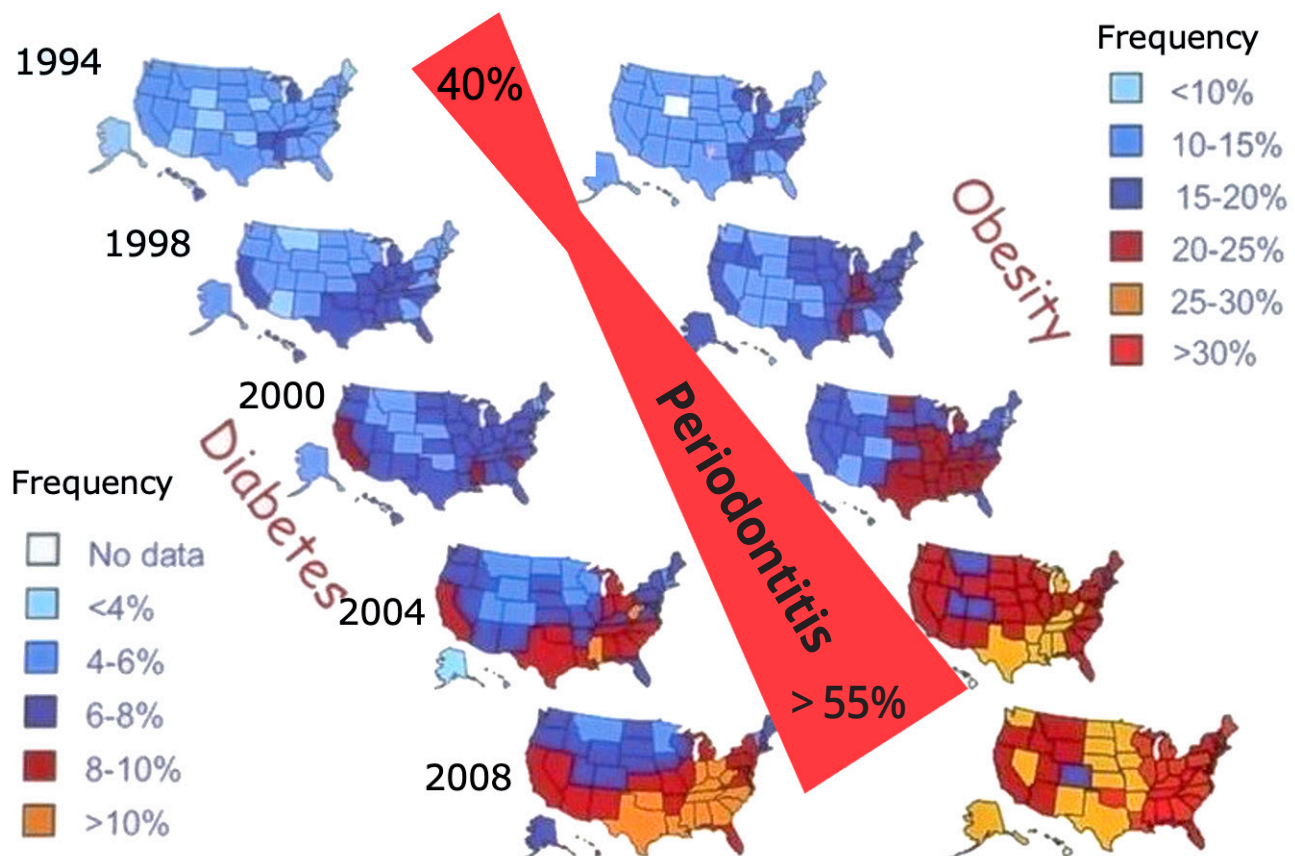


Group picture of the three authors of the book "Oral preventive medicine - An Interdisciplinary Challenge". From left to right: Prof. em. Dr. med. dent. Heinz H. Renggli (Nijmegen, NL), Prof. Dr. med. dent. Ulrich P. Saxer (Forch ZH/Zurich, Switzerland) and Dr. med. dent. René B. A. Sanderink, Würzburg (Germany) The picture was taken on 31 August 2015 in Erfurt, Germany, celebrating Dr Sanderink's 60th birthday. That occasion hallmarked the decision for Dr. Sanderink, together with Professor Renggli, to write the aforementioned book and including inquiry for contributions from Professor Saxer.

(Photo: Dr. St. Niemela-Sanderink)

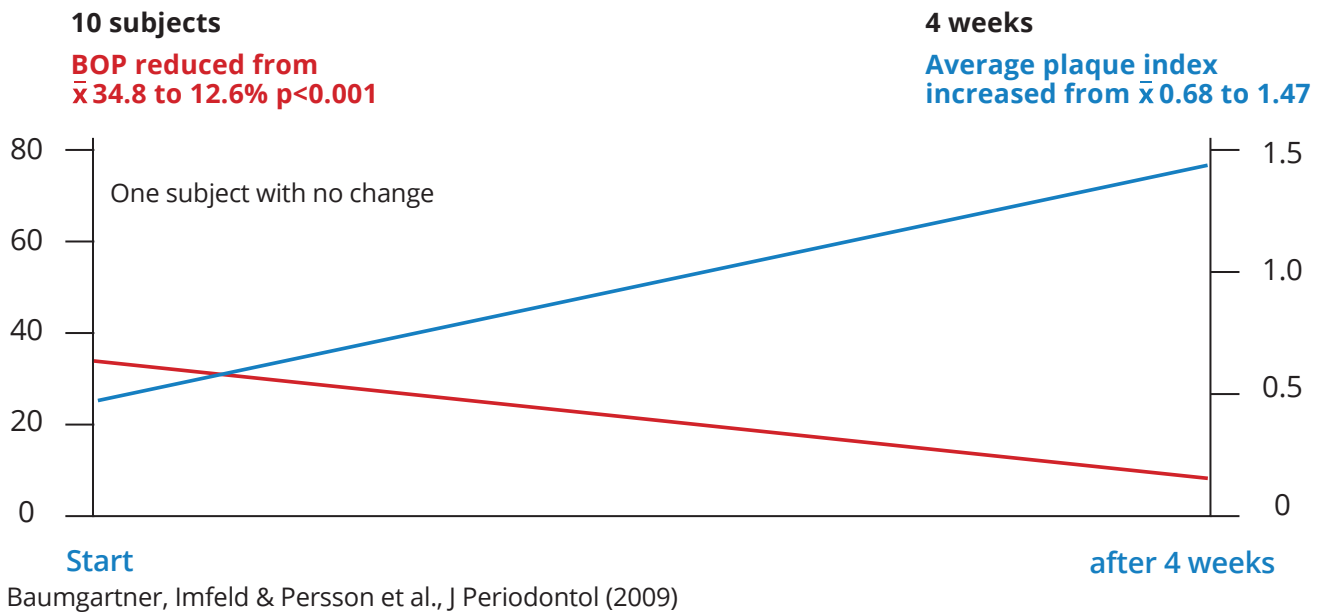
## Obesity and diabetes in the USA: two parallel epidemics coinciding with an increase in periodontitis

### Obesity and Diabetes - Parallel Epidemics



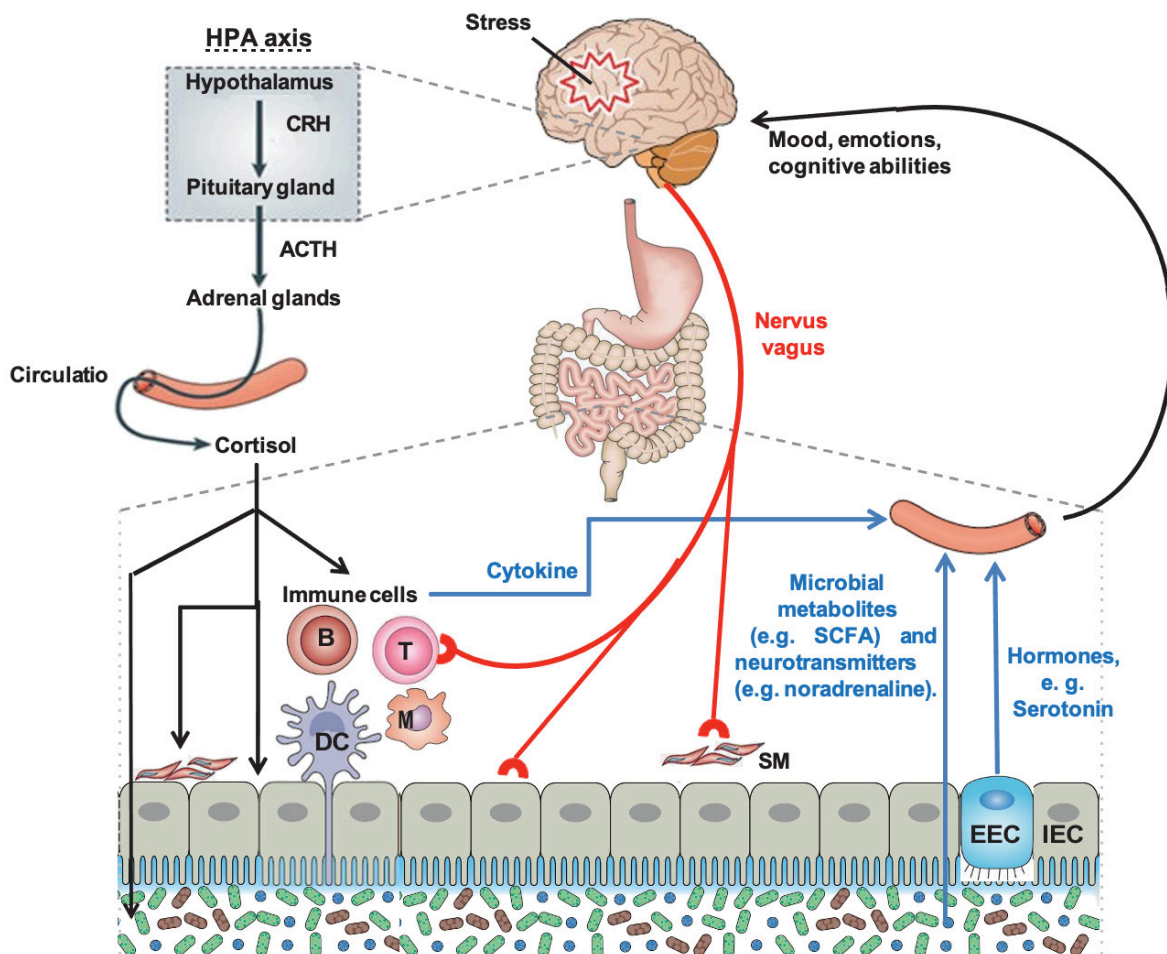
(Fig. 2): Epidemiological development of obesity, diabetes and periodontitis in the USA from 1994 to 2008. (Periodontitis data from: Eke et al, J dent Res 2016; 95: 515-522; image archive U. P. Saxer).

## Live as in the Stone Age – Swiss television, 2007 Inflammation index (BoP) & plaque index without oral care



(Fig. 3): The science-led program on Swiss television in 2007 followed ten people who lived like humans did in the Stone Age and despite abstinence from hygiene, after four weeks had unexpectedly healthier gums and less aggressive bacteria, despite increased dental plaque. The explanations of these relationships are shown in the book by Sanderink/Renggli/Saxer.

(U. P. Saxer picture archive)



(Fig. 4): Bidirectional communication between the gut and the brain (gut-brain axis= GBA). This simplified representation demonstrates neuronal connections (mainly via N. vagus X) and humoral communication pathways (hormones, immunological messengers, neurotransmitters). ACTH = adrenocorticotropic hormone; B = B lymphocyte; CRH = corticotropin-releasing hormone; DC = dendritic cell; EEC = enteroendocrine cell; SM = smooth muscle; HPA axis = hypothalamic-pituitary-adrenal axis; IEC =intestinal epithelial cell; M = macrophage; SCFA = short chain fatty acids; T = T lymphocyte.

(Image: R. B. A. Sanderink)

*Has anything changed which could explain the current increase in NCDs?*

R. B. A. Sanderink: Since the beginning of the industrial revolution, homeostasis in the mouth and gut has become increasingly elusive due to an increase in velocity of evolutionary developmental stages, i.e. the immune system cannot keep up with the speedy evolution of the microbiome. Modern living conditions concur loss in state of equilibrium, diversity of species and gene expression of the microbiome at fast pace. Lifestyle factors such as the ubiquitous presence of xenobiotics and diets highly concentrated and enriched with sugar and energy, provoking reactive biological processes such as age-related cell senescence, age-related cell damage and age-related changes in gene activity which contribute to destabilization along with neuroendocrine mechanisms. Consequently, dysbiotic microbiomes are increasingly present in modern day digestive tracts. These show characterization of a microflora which deviates both in quality and quantity from the norm expressing reduction in bacterial diversity and increase in pathobiontic germs – including fungi. This disrupted microbial homeostasis imposes a non-physiological response situation to the immune system which leads simultaneously to loss of tolerance and impairment for elimination of pathogenic noxae. In 2007, a scientifically guided program on Swiss television featured ten people who lived in conditions as humans of the Stone Age and, despite abstinence from oral hygiene, after four weeks achieved unexpectedly healthier gums and greater reduction of aggressive bacteria, despite increased dental plaque (Fig. 3). Explanations and correlations are presented in our book.

*What are the clinical implications?*

R. B. A. Sanderink: Autoimmune diseases, allergies and other inflammatory phenomena such as arteriosclerosis, obesity, insulin resistance – as precursors of type 2 diabetes mellitus – and neurodegenerative diseases, as well as decay and periodontitis, are among the NCDs that can be regarded as clinical consequences of dysbiotic microbiomes, a result of the so-called “fundamental etiological evil of the modern age” (Fig. 1). Correspondingly, the book shows that by restoring eubiotic conditions, health can be sustainably improved, also influencing the psyche.

*The fact that the psyche, the microbiome and health influence each other requires further explanation!*

R. B. A. Sanderink: Yes, of course, but then I must return to the digestive tract! The digestive tract communicates with the brain via the gut-brain axis (GBA) and does so bi-directionally. A wide range of signals are involved, which are transmitted via neurons, endocrine system or metabolites. It is now generally accepted that a homeostatic, eubiotic intestinal microbiome is of utmost importance not only for digestion but also for intact GBA. Intestinal dysbiosis with high numbers of what are known as “mind-altering bacteria” changes the GBA into a dysfunctional state, which can trigger behavioral changes, cognitive impairment and altered pain perception. Conversely, a psychologically stressed brain impairs the microbial homeostasis in the intestine via the GBA (Fig. 4). In turn, the resulting dysbiosis influences the occurrence of NCDs as previously explained.

*What is it that drives the development of these dysbioses exactly?*

R. B. A. Sanderink: In a newborn, acquisition of the microbiome occurs by vertical transmission – mainly through direct contact with the mother and influenced by genetic and environmental factors.

**Dr. med. dent. René Bernardus Andreas Sanderink**

*University education*

- August 1974 to May 1978: Dental Studies at the University of Nijmegen
- October 1978 to October 1980: Dental Studies at the University of Zurich, graduating as a dentist

*Professional experience*

- October 1980 to December 1983: Assistant at the Department of Cariology, Periodontology and Preventive Dentistry at the Dental Institute of the University of Zurich (Prof. H. R. Mühlemann)
- Promotion to the title of “Dr. med. dent.” September 1981: with the dissertation “Parodontale Taschenmessungen”.
- Dentist in independent practice since 1984

*Academic teaching positions*

- 1982-1983 “Cariology” at the University of Zurich (Prof. H. R. Mühlemann)
- 1989 to 2003 “Oral Preventive Dentistry” at the University of Tübingen (Prof. C. Löst)
- Since 2003 “Oral Immunology” at the University of Würzburg (Prof. U. Schlagenhauf, Prof. Y. Jockel- Schneider)

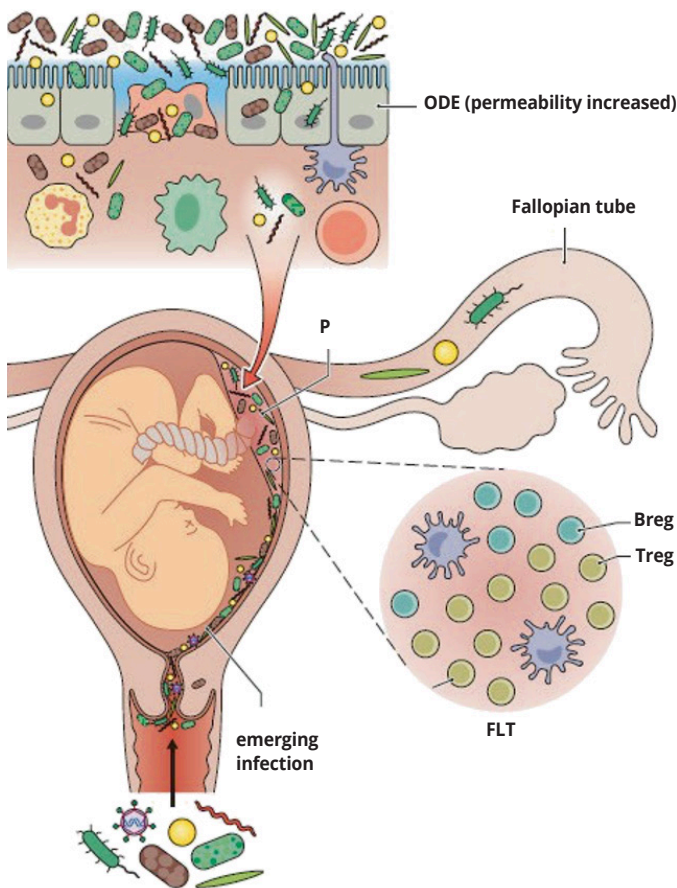
**Prof. em. Dr. med. dent. Heinz H. Renggli**

1963–1968	Assistant to Prof. H. R. Mühlemann/ Conservative Dentistry, Dental Institute, University of Zurich
1969–1972	Senior assistant to Prof. H. R. Mühlemann/ Periodontology
1973	Head of Conservative Dentistry, University of Basel
1974	Training in Microbiology/Immunology, Guy's Hospital, London
1974	Post-doctoral qualification with Prof. H. R. Mühlemann/University of Zurich
1974–1975	Lectureship in Periodontology, University of Zurich
1976–2001	Full Professor, University of Nijmegen (NL), Head of the Department of Periodontology
2001	Emeritus status

**Prof. Dr. med. dent. Ulrich P. Saxer**

1960–1995	Military: Commander of an infantry company
1961–1967	Studies in dentistry, University of Zurich 1967 State examination in dentistry, University of Zurich
1967–1984	Assistant and senior assistant to Prof. H. R. Mühlemann, University of Zurich
1969	Dissertation, University of Zurich
1972	Specialist and Certificate in Periodontology, University of Zurich
1972–1973	Assistant Professor in Occlusion (Prof. M. Ash, University of Michigan, USA)
1973–1993	Development and establishment of the School of Dental Hygiene, Zurich, Director
1981–	Lecturer in Preventive Dentistry and Periodontology at the University of Zurich
1986	Habilitation at the University of Zurich in Preventive Dentistry & Periodontology
1994	Sabbatical (Prof. S.L. Yankell, University of Pennsylvania)
1994–2013	Founding of the Prophylaxis Centre Zurich (Private Dental Hygiene School); Clinical Manager; co-founder of the North Zurich Dental Centre
2000–2004	President of the Swiss Society of Periodontology (SSP)

## Periodontopathogenic bacteria (including harmful metabolites) are also detectable in the amniotic fluid.



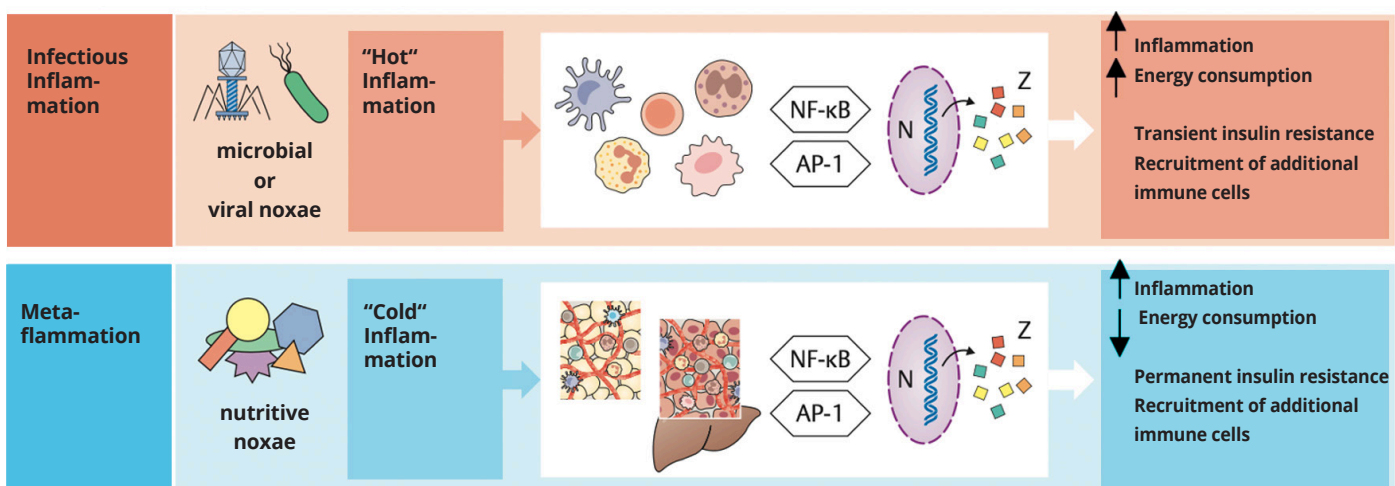
- Ascending over the vagina and cervix
- Hematogenous spread via the placenta
- Retrograde seeding from the peritoneal cavity through the fallopian tubes

FLT = fetal lymphoid tissue  
 ODE = orodigestive epithelium  
 P = Placental tissue  
 Treg/Breg = T-/B-regulatory cells

(Fig. 5): If periodontitis is present, periopathogenic bacteria and metabolites nest in the peritoneal cavity during pregnancy, which can have an unfavorable effect on the course of the pregnancy. (Source: Sanderink/Renggli/Saxer, 2022; fig. 19.2, Georg Thieme Verlag Stuttgart, with kind permission)

## Infectious and sterile forms of inflammation

“Hot” inflammation with cardinal signs:  
 Rubor, Dolor, Calor, Tumor & Functio laesa



Metaflammation: sterile inflammation due to nutritive noxae - “cold” inflammation without cardinal signs but with involvement of identical transcription factors and mediators as with “hot” inflammation - runs chronically and irreversibly damages physiological functions such as insulin sensitivity

**AP-1 = Activating Protein-1; N = Nucleus; NF-KB = Nuclear factor kappa-B; Z = Cytokine**

(Fig. 6): Differences between acute inflammation with fever and sterile, cold inflammation which is invisible but chronic. The arising insulin resistances are only reversible in the case of “hot” inflammation (Warnberg et al. Br J Nutr 2007; 98, Suppl. 1; p. 116–p. 120). Environment and lifestyle such as smoking, alcohol, incessant food intake, stress and inactivity are triggers of metaflammations. (Source: Sanderink/Renggli/Saxer, 2022; fig. 9.2, Georg Thieme Verlag Stuttgart, with kind permission)



If the maternal or paternal epigenomes are severely damaged, the microbiome of a newborn also develops a phenotype prone to dysbiosis. Among environmental factors, pregnancy stress, method of birth and time of birth – premature births are unfavorable – play a role. Postnatal diet also has a significant influence. In this context, breastfeeding with prebiotic breast milk is beneficial. The environment in which the microbiome develops is also relevant: For example, growing up on a farm with a greater microbial diversity is much more beneficial for the development of a dysbiosis-resistant microbiome compared to childhood in a big city. As young as infancy and over the timespan of a complete lifetime, frequent intake of anti-infectives and unhealthy diets have a dysbiosis-promoting effect. Both in the oral cavity and in the gastrointestinal tract, dysbiosis is often substrate-driven. A familiar example in the oral cavity is the overgrowth of acid-tolerant bacteria in cases of frequent consumption of fermentable carbohydrates, which causes cariogenicity of supragingival plaque. In the case of active periodontitis, periopathogenic bacteria and metabolites nest in the peritoneal cavity during pregnancy, which can have an unfavorable effect on the course of pregnancy (Fig. 5). However, an excessive oral substrate supply in the form of serum proteins and iron in gingival sulcus fluid of the inflamed gums can also drive oral biofilms into a dysbiotic state, due to periodontopathogenic bacteria which utilize these substrates preferentially and proliferate exponentially as a result.

*Back to the topic of "Nutrition and Health". What nutritional influences are at play here?*

U. P. Saxer: Unhealthy diets are characterized by nutrients that "dysbiotic" the orodigestive microbiome, activate the innate immune system, unbalance redox homeostasis in the body and damage epigenomes in cell nuclei. As a result, the constitutive inflammatory overload of the body – what is known as the silent inflammation – increases, which accelerates the ageing process of the body. This process is summarized under the term "inflammaging".

*How is this reflected clinically?*

U. P. Saxer: The most common consequence of an unhealthy diet with excess calories is the process called metaflammation. This is a sterile, persistent inflammation which disseminates into the body and is triggered by pathological storage of immunogenic nutrients. Metaflammation is an inescapable consequence of obesity (Fig. 6). The nutrient/calorie surplus axis → Obesity → Metaflammation → Insulin resistance with other inflammatory comorbidities is crucial to health expectancy. Again, what is essential in the development of obesity is the state of the intestinal microbiome, since the organism's ability to extract and store energy from food depends crucially on the composition of the bacterial organism. This was demonstrated as early as 2006 showing how the intestinal microbiome dominates the development of obesity. Besides bacteria, adipogenic viruses also contribute to this process. Anti-inflammatory nutrition includes an ample intake of omega-3 fatty acids, fiber, antioxidants, nitrate-rich vegetables and nutraceuticals; the latter in the form of probiotics and prebiotics (Fig. 7). Teaching this in dental practice is a perfect example for interdisciplinary preventive medical care. The vast majority of the population visits the dentist annually. The dentist observes and follows the development of each patient. He or she can also detect incipient obesity and refer the patient to the General practitioner so that inflammatory comorbidities of the metaflammation process – especially NCDs such as insulin resistance or arteriosclerosis – can be treated early on.



Cover of the book published by Georg Thieme Publisher in January 2022 "Oral preventive medicine – An Interdisciplinary Challenge" (ISBN 978-3-13-205181-2). The volume comprises 512 pages with 371 illustrations. (Image: Georg Thieme Verlag)

*For decades, the prevention of carious processes and periodontal diseases has focused on fighting bacterial plaque by destroying as many bacteria as possible. What are the main focuses of the diseases today?*

R. B. A. Sanderink: Something promising for combating NCDs, including caries and periodontal disease, is therapeutic microbiology. The goal is eubacterial restoration to achieve eubiotic microbiomes thus a healthy immune system with physiological, tolerogenic response activity. The focus is on the administration of probiotic bacteria, which are available in various forms. Ideally, they should not only manifest as transient colonizers, but should establish proper residency. In clinical dental practice, this means that the recolonization of professionally cleaned tooth and mucous membrane surfaces requires probiotic-support at exactly an immediate time frame, when resistance to direct colonization is at its weakest. Accordingly, the mouth and throat require disinfection in order to clear out competing microorganisms prior to probiotic treatment. Previous informed consent is recommended in order to increase patient compliance and trust through information: The patients concerned are informed of this beforehand and told that, as well as why the bacteria have to be "replaced" also, how to favor a successful outcome implementing probiotic tooth-pastes as a good option for perpetuating eubiosis in the orodigestive tract. Unfortunately, the industry is still more interested in developing products which kill as many bacteria as possible and thus, like all anti-infectives, have a dysbiosis-promoting effect. Following dysbiotic biofilms, nicotine consumption is the second greatest risk factor for periodontal disease and tooth loss. (Fig. 8). Anti-nicotine advisory and

## Inflammation-protective food components

### Antioxidants

Carotenoids, lycopene, vitamin C, E; sulphides, zinc, selenium, tomatoes, peppers, spinach, kiwi fruit, citrus fruits, berries, garlic, chives, fish, nuts

Reducing the formation of harmful oxygen radicals

### Nitrate-rich vegetables, juices rich in nitrates

Promoting vascular homeostasis, lowering blood pressure, improving oxygenation & digestion

### Omega-3 fatty acids:

Linseed, soya, hemp, walnut oil; fatty fish (salmon, mackerel, herring)

Highly anti-inflammatory through suppression of pro-inflammatory transcription factors and inflammasome activation

### Nutraceuticals:

Probiotic bacteria prebiotics. Reducing the formation of harmful oxygen radicals

Bacterial species which, in a multi-modal way, consolidate homeostasis in the digestive tract, or food components for targeting promotion of probiotic microbes

### Dietary fiber:

Indigestible carbohydrates

In the colon: proliferation of bacterial species producing short-chain fatty acids highly anti-inflammatory through suppression of pro-inflammatory transcription factors and inflammasome activation

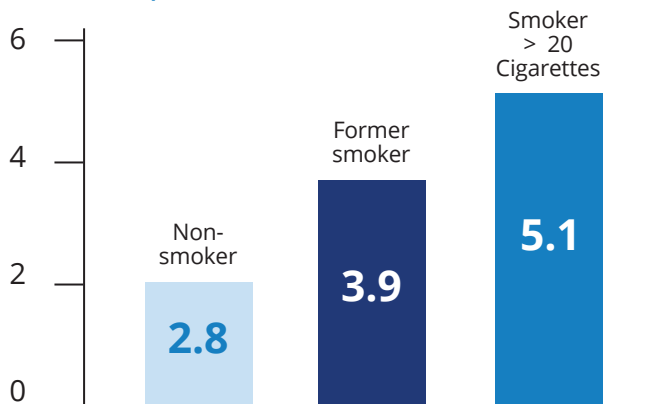
(Fig. 7): Nutraceuticals such as antioxidants and unsaturated fatty acids in food have many positive health effects. They reduce reactive oxygen species (ROS), lower blood pressure, promote oxygenation and, as with some probiotics (Lb. Reuteri), are important for mucus production in the gut. (U. P. Saxer picture archive)

## Influence of smoking (S) on teeth and vascular health

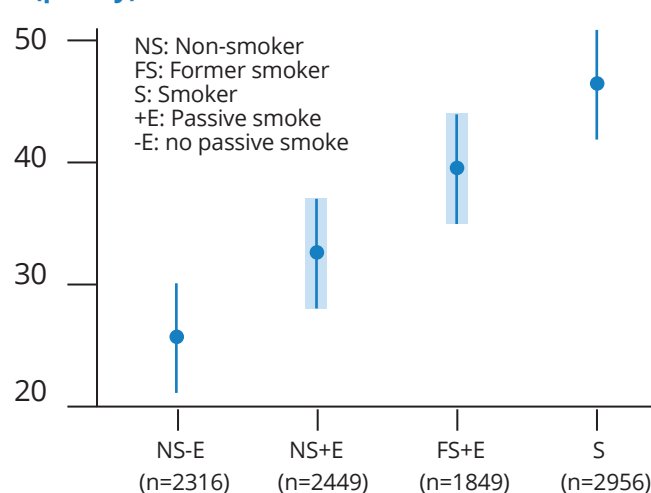
N = 705 subjects in 3 groups  
NS (non smoker), FS (former smoker)  
and min. 10 years of smoking

Intima-media thickness:  
Increase after S-exposure

### Tooth loss, N



### ( $\mu\text{m}/3\text{y}$ )



(Fig. 8): Influence of smoking on tooth loss in a non-smoking group, former smokers and > 20 cigarette smokers (left, Albander et al. 2000) and change in intimamedia in  $\mu\text{m}/3\text{y}$  in non-smokers (NS), non-smokers with passive smoke exposure (NS+E), former smokers (FS) and continuous smokers (right, Howard, et al. 1998).

follow-up consultations could be a means to help patients quit smoking. These measures belong "in the line of duty" for practices of periodontology. The same applies for nutritional advice, record-taking and counselling.

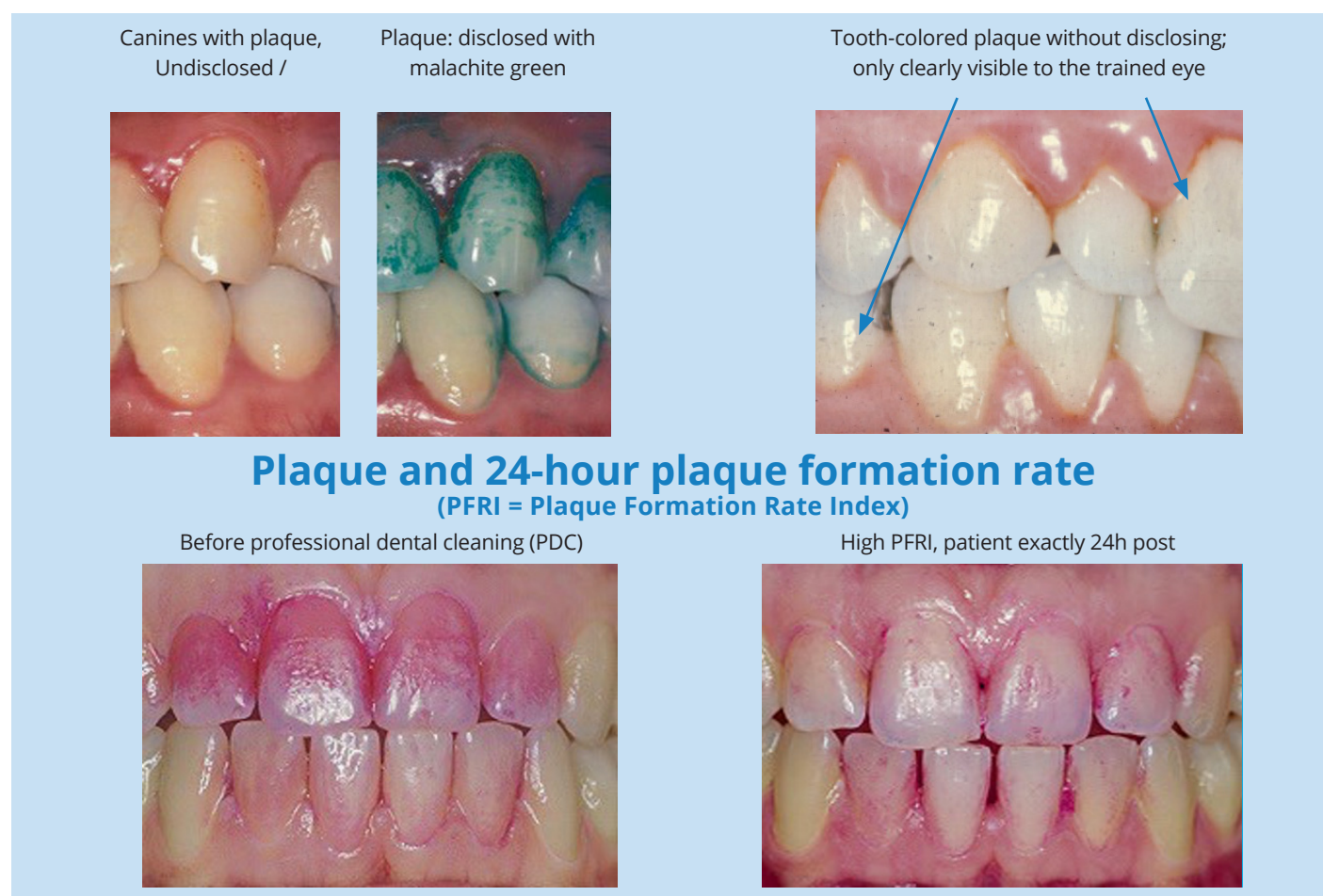
*The term plaque has become widespread during the last twenty years and more recently, there is increasing discussion about biofilm, oral microbiome and oral disease. Are the correlations and terms in this regard sufficiently clear in dentistry?*

U. P. Saxer: It's a problem! The term biofilm is often used today instead of plaque, but this can lead to confusion and distortion. In chapters 14 and 21 of our text-book, these terms are not only clearly explained, but their physiological and pathological significance is also discussed. For example, the standardized 24-hour plaque formation rate in professionally cleaned teeth – the Plaque Formation Rate Index, or PFRI in short – is an essential indicator of the status of oral homeostasis (Fig. 9). Unfortunately, the index is seldom used in dentistry today. The lower the saliva flow, the longer and more often the oral fluid contains significant amounts of carbohydrates, and the more inflamed the gingiva, the higher the PFRI value. Increased PFRI levels due to saliva deficiency can also reveal systemic diseases, such as prediabetes or even full on-set diabetes. Here, once again, latent risks would have to be clarified on an interdisciplinary basis through cooperation between dentists and general practitioners. It is also evident that the oral microbiome influences the intestinal microbiome, and in a multimodal way: there are the dysbiotic effects triggered by ingested oral pathogens, which Dr Sanderink will certainly talk about later. On the other hand, these

bacteria enter the blood through permeable pocket epithelia, which are pathognomonic for periodontal diseases (Fig. 10). They then reach distant organs where they trigger immune reactions. If the intestinal mucosa [4] – in the form of inflammatory bowel disease – is affected then the microbiome present "dysbiotizes", driven by substances or, under the influence of the inflammatory serum exudate, which enables pathogenic bacteria to proliferate. It has also been demonstrated with the oral cavity that eubiotic microbiomes are an important prerequisite for general health. For example, a eubiotic oral microbiome hardly causes any caries and gingivitis whatsoever, even under Stone Age conditions – i.e. a lifestyle without any oral care (Fig. 3).

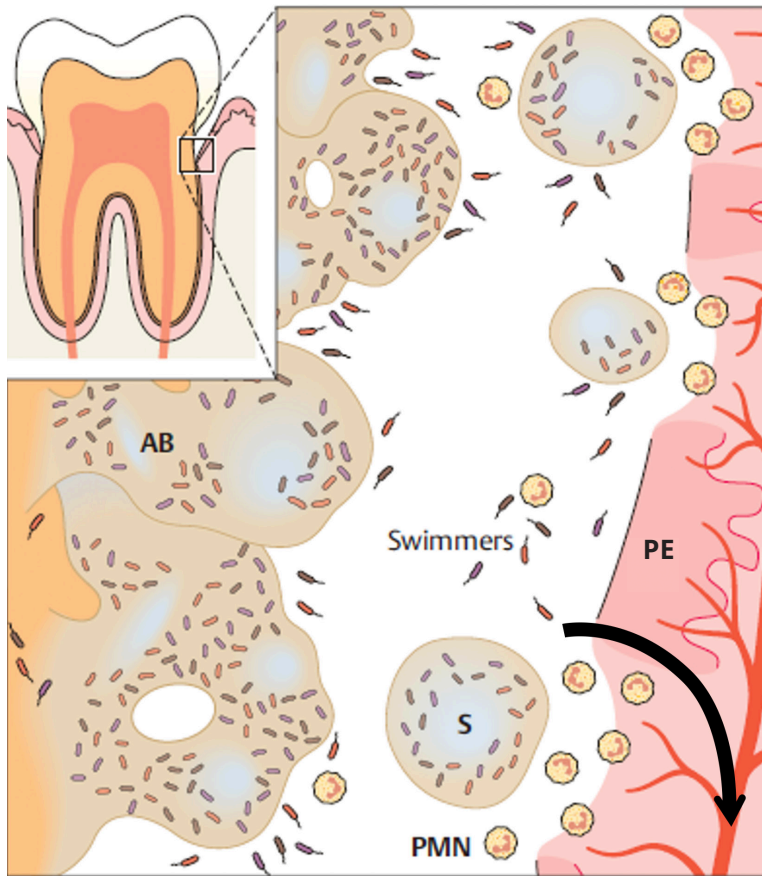
*But isn't it the case that swallowed bacteria are destroyed in the stomach or cannot pass through it at all?*

R. B. A. Sanderink: Patients with severe oral biofilm infections swallow a multitude of oral pathogenic bacteria, especially during main meals. This means that 1 ml of saliva from a patient with severe periodontal disease may contain more than  $10^6$  colony-forming units of the inflammophilic pathobiont *Porphyromonas gingivalis*. These bacteria survive the temporarily elevated pH values in the stomach – straight after a meal these are up to pH 5–6 – and also resist the antimicrobial bile acids in the duodenum. They subsequently emerge in the intestinal tract as "dysbiotic". In the long run, this condition damages the microbiome. The intestinal mucous membranes pathologically increase in permeability and there is an overflow of microorganisms into the lymphatic and blood vessel circulatory systems.



(Fig. 9): The plaque was disclosed with different plaque revealators to provide a better visible demo-effect for the patient. In the top right picture, plaque on the teeth is visible to the trained eye without disclosing, but it luminates the color of the tooth, a bit like snow bunnies! The lower images show, a case before and exactly 24 hours after professional teeth cleaning without any oral hygiene, demonstrating new plaque formation (PFRI = Plaque Formation Rate Index).

(Images U. P. Saxer and R. B. A. Sanderink)

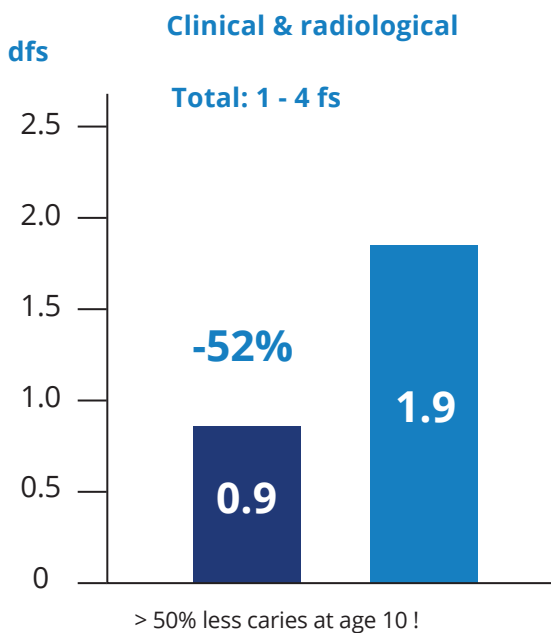


## Hyperpermeable pocket epithelia foster bacteremia

- AB** = adherent biofilm
- PMN** = polymorphonuclear neutrophilic granulocyte
- S** = biofilm satellite
- PE** = pocket epithelium

(Fig. 10): Subgingival biofilms in a periodontal pocket. The high permeability of the pocket epithelia gives rise to constant bacteremia. (Sanderink/Renggli/Saxer, 2022; fig. 14.18, Georg Thieme Verlag Stuttgart, with kind permission)

## Caries and gingivitis in 9-year-old children



Test group (n = 60)

1. 1. Mothers: 5 drops of oil daily, with probiotic *Limosilactobacillus reuteri* ( $\approx 10^8$  CFU) from mother's milk, during the final month of pregnancy.
2. 2. Offspring: dito, during their 1st year (365 days), in the presence of an immature microbiome.

Control group (n = 53): Oil without probiotic, more intensive fluoride

### Gingivitis index after 9 years

Test group	4.35 ± 6.87	- 43 %
group placebo	7.58 ± 9.58 (p<0.05)	

**All of the children over two years of age demonstrated, through unsupervised developmental randomization in double blind trials, statistically highly significant results**

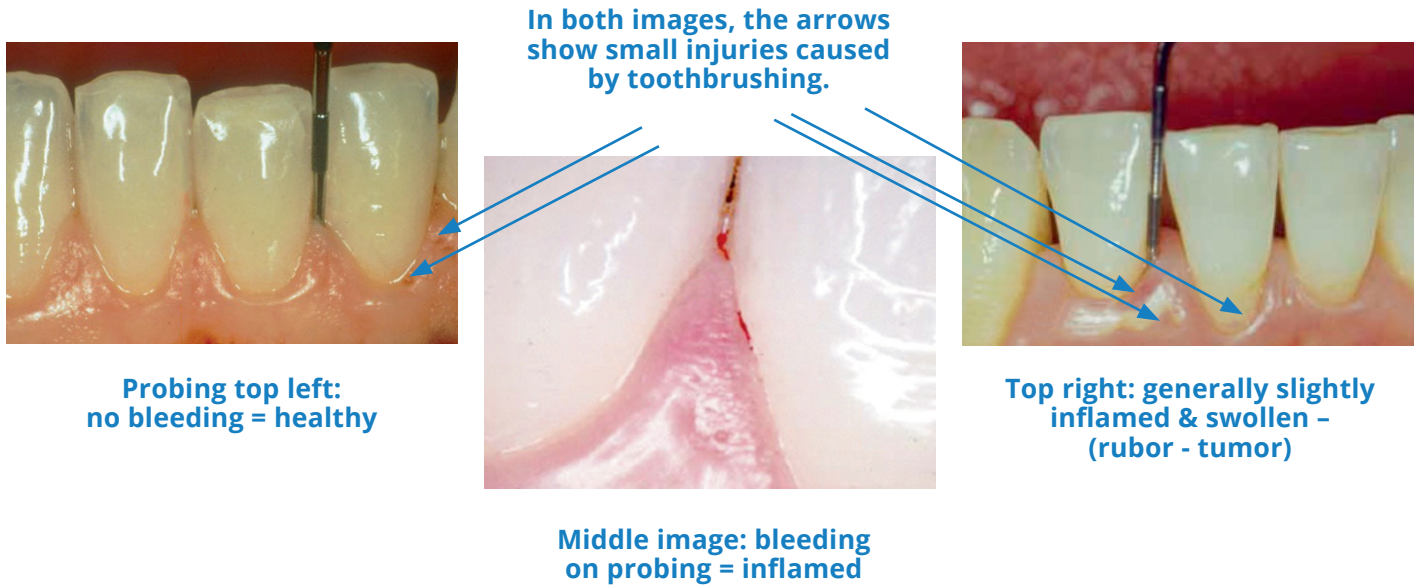
**d = decayed by grades 1-4, f= filled/s= surface**

(Fig.11): During this trial, the mothers took five drops of oil containing the probiotic *Limosilactobacillus reuteri* daily for four weeks before birth (for habituation). Post partum, the infants/toddlers further received five drops of oil containing the probiotic *Limosilactobacillus reuteri* or a placebo oil administered daily by the mothers during their first year. Shortly after nine years of age, all children were examined, in accordance with blind methodology, on caries prevalence and other parameters (gingivitis). (Stensson et al. 2014).

(Image archive U.P. Saxer)

## Healthy and diseased, inflamed gums

When probing between the gingiva and tooth, there is no bleeding in healthy individuals.



(Fig. 12a): Healthy and inflamed gums can be recognized during the initial stage, even by a specialist, only upon close inspection. Therefore, a probe is used to touch the gums with slight pressure (30 pound). The presence of bleeding constitutes the first sign of inflammation.

(U. P. Saxer picture archive)

## Healthy and diseased, inflamed gums



**Note:**  
papillae & interdental spaces - inflammation is more intense in the areas where the toothbrush cannot access for proper cleaning.

(Fig. 12b): Representations of various gum conditions. A: healthy, B: inflamed, C: severely inflamed, possibly with previous irreversible destruction of periodontal supporting tissues (periodontitis).

(U. P. Saxer picture archive)

The pathological increase in permeability in fact worsens in cases where infected periodontium causes constant, daily bacteremia – for example during toothbrushing or during meals – which perpetuate a mainly gram-negative, dormant blood microbiome. This also encompasses systemically relevant pathogens such as *Porphyromonas gingivalis* and establishes immunogenic endotoxemia with possible organ-specific sequelae including NCD.

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*How do you view the relationship between oral and general diseases?*

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U. P. Saxer: The course of periodontal and peri-implant inflammation can be negatively affected by systemic diseases. This is dominantly influenced by the microbiome. The correlation between oral and systemic diseases is not only based on the systemic dissemination of virulent germs from oral biofilms, it is also connected to a disturbed cytokine homeostasis, continuously advancing telomere attrition of nuclear DNA as well as age-related gene regulatory changes, immune senescence, replication errors in mitochondrial DNA and the accumulation of immunogenic metabolites, including radicals, amyloid and saccharified proteins or lipids.

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*What about the relationship between oral diseases during the course of pregnancy and the prospective risk of disease in the offspring?*

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U. P. Saxer: The main goal regarding structured cooperation between gynecologists and dentists is aiming to avoid undesirable pregnancy outcomes. However, it is of paramount importance to promote the development of a dysbiosis-resistant microbiome for future generations. This is why the dental professional should monitor the individual healing response and the degree of recovery of periodontal tissues and caries activity over time in order to qualify and give perspective within the general patient pool. Emphasis on providing special attention to women who wish to have children or who are planning to become pregnant is an imperative contribution to well-being. If possible, dental and periodontal rehabilitation should be carried out before pregnancy. Gynecologists should inform patients as to the risk of unfavorable pregnancy outcomes due to inflamed periodontium and, if necessary, immediately refer them to a dentist for a thorough examination and consultation. It is quite remarkable that, if pregnant women take probiotics perinatally, this remains immunologically detectable in their offspring even for decades later. This may be in the form of a healthier intestinal microbiome, an associated beneficial development of physiologic responsivity paired with a simultaneously tolerogenic immune system and nervous system. Clinically, this is reflected in a lower susceptibility to caries and gingivitis (Fig. 11), obesity, metabolic diseases, chronic inflammation – including allergies and autoimmune diseases – and even psychological disorders. Obesity and metabolic diseases in turn promote periodontitis. The upshot is that perinatal probiotics predispose to the development of a dysbiosis-resistant microbiome, thus suppressing later susceptibility to NCD and the progression of the offspring's inflammaging process.

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*Key question: what would have to change with physicians and dentists in the future and what would actually be the main goal of oral preventive medicine?*

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U. P. Saxer: The future clinician, in order to master applied oral preventive medicine, will have to undergo further training in the fields of medical case taking, i.e. internal medicine, microbiology and immunology, in order to become familiar with, at minimum, the

essential principles concerning “state of the microbiome and research”. One example of this topic is the discovery that pathognomonic ulcerative pocket epithelia of marginal periodontitis analogously represent the oral equivalent of hyperpermeable intestinal epithelia – often referred to as leaky gut syndrome – with common etiology, namely dysbiotic microbiomes. In the nearby future, physicians should routinely integrate oral inspection thereby being capable of recognizing the healthy versus the diseased gingiva while providing guidance for appropriate health supportive measures. (Fig. 12a, Fig. 12b).

R. B. A. Sanderink: The therapeutic microbiology already mentioned must become the cornerstone of oral preventive medicine. As far as caries is concerned, we all know that fluoride has without doubt been the most successful anticariogenic agent for more than sixty years. However, the following, admittedly somewhat provocative, question may be asked: “Haven't fluorides also euthanized cariologists?” In view of the fact that caries is by no means a disease of fluoride deficiency, but rather a disease with many factors including those primarily of microbial origin. Recent remineralization strategies with fluoride-free preparations being increasingly propagated pose merely symptomatic therapeutic approaches. For example, a more causal concept would be an oral enrichment with favorable microorganisms, so-called keystone stabilizers, such as *Streptococcus dentisani*. Given the fact that dietary recommendations, such as abstinence from fermentable or cariogenic carbohydrates, regularly fail – often due to an unfavorable social environment – suitable proportions of stabilizing microbes (probiotics) would contain the acidogenicity of biofilms (and thus, dysbiosis due to the overgrowth of acid-tolerating microbes) even in presence of regular sugar consumption. In regard to the field of periodontology, anti-infectious therapy – with “scaling and root planing” – always previously considered as the gold standard, now requires adjunctive therapeutic measures, additional strategies entailing quitting smoking, nutritional counseling and probiotics must be increasingly implemented. Unfortunately, the latter have the disadvantage that they require continuity, meaning high level compliance on the part of the patient. The bottom line is that the primary goal of oral preventive medicine must be to decrease velocity of the inflammaging process. This would substantially improve the quality of life of all people ageing and reduce the economic burden in societal health systems thus, on the population. An essential requirement for oral preventive medicine is interdisciplinary cooperation between dentistry and general medicine. This is why these recommendations for action must be urgently implemented to accomplish adequate education for physicians and dentists. By the way, our book is absolutely instrumental for referential and teaching purposes. It deems international dissemination in estimation and appreciation for the globally operating international scientific publisher Springer Nature which has recently commissioned an extensive team of authors to produce a compiled working edition in the English language. [5].

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*Final question: if the oral microbiome is so important, shouldn't we have noticed differences in the progression of the diseases during the Coronavirus pandemic?*

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U. P. Saxer: Correct! On the one hand, patients with periodontitis have also been infected more frequently, experiencing, in general, a more severe and protracted course of disease. Obviously, SARS CoV-2 viruses were able to establish themselves in the inflamed periodontium more easily, which most likely increased chances of predominantly safe viral transport into the lungs (dissemination). These correlations have already been proven in initial studies. Along with the fact that

aspiration of oral pathogens, a manifestation with major involvement, promote development of respiratory tract infections.

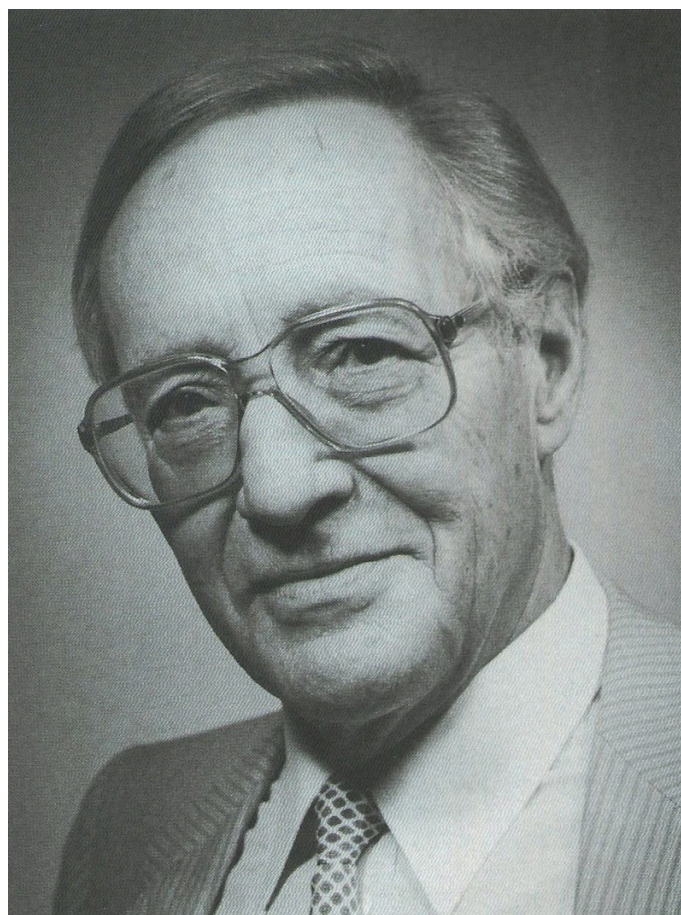
R. B. A. Sanderink: Mr Wüst, please allow me to express a final word and our gratitude. This interview with SWISS MED, has been an honor, providing your readers with details about our book "Oral Preventive Medicine – An Interdisciplinary Challenge". Finally, we would like to mention that it is not without reason that we have dedicated our work to our highly esteemed teacher, Professor Hans R. Mühlemann. Without him, all of his knowledge, experience and engagement for the causes of humanity which, he as our mentor, endowed upon us on our journey through life, our book never would have existed. Without any doubt, Mühlemann is regarded and remembered nationally and internationally in the fields of medicine and dentistry as one of the most outstanding clinicians, teachers and researchers of the 20th century.

PS. Even as a student during his earliest days (!) Hans R. Mühlemann recognized that there was a desperate need for therapeutic measures to reduce incidence of caries and periodontitis which could only succeed by means of preventive measures. Combined with his determination in research, his innovative thinking, and his ability to inspire young academics – also by giving them the greatest possible freedom and support in planning and implementing team-work for new ideas in research – this all was the innovative seed allowing the Zurich University clinic to become famous and world renowned during his tenure. "Mühli", as his friends called him, was both a medical doctor and dentist. He further inspired us to think and treat in an integrative way. And so the circle around the title of our book actually closes with the thought that problems related to non-communicable diseases must be tackled by the medical profession on the whole - not only therapeutically as in previous practice, but above all preventively and in an interdisciplinary way!

*Dr Sanderink, Professor Saxer, many thanks for this interview. Now we can only hope that your book will find enthusiastic recipients in the target groups and that the appropriate lessons and consequences will be learned and implemented.*

## Notes

- [1] Professor H. H. Renggli was unable to attend this interview on 14 March 2022 due to illness. He died on Monday, 11 April 2022.
- [2] Sanderink R. B. A., Renggli H. H., Saxer U. P., Oral Preventive Medicine – An Interdisciplinary Challenge. Georg Thieme Verlag Stuttgart, 2022, 1st ed., 512 p., 371 fig., hardcover, ISBN 978-3-13-205181-2; 230 CHF, 199.99 EUR (D), 205.60 EUR (A).
- [3] Lübeck, A., Der heutige Stand der Parodontose-Behandlung. Deutsche Zahnärztliche Zeitschrift (German Dental Journal) 1: (1946), Issue 2
- [4] Vavricka, SR; Manser, CN; Hediger S; Sanderink R; Attin T et al., Periodontitis and Gingivitis in Inflammatory Bowel Disease: A Case-Control Study. Inflamm Bowel Dis 2013; 19:2768-2777
- [5] Sanderink R. B. A., Renggli H. H., Saxer U. P., Schlagenhaut U., Fischbach W., Steimer G., Oral and Systemic Health – Hidden interdependencies modulated by microbial, metabolic and environmental factors. Springer Nature Switzerland AG, Cham (CH) (to be published 2024).



Professor Dr. med., Dr. med. dent., Dr. h. c. mult. Hans R. Mühlemann (\*1917–†1997), long-term Head of the former Dental Institute of the University of Zurich (1953–1983). The authors of the book "Oral Preventive Medicine – An Interdisciplinary Challenge", Dr. R.B.A. Sanderink, Prof. Dr. H.H. Renggli and Prof. Dr. U.P. Saxer, were all three students and assistants of Professor Mühlemann and experienced the epochal impact of his work on the global development of dentistry. (Image: Cariology Today, International Congress in Honour of Professor Dr. H. R. Mühlemann, Zürich, September 1983. Editor: Guggenheim, B., Zurich. ISBN: 978-3-8055-3761-2. With kind permission of S. Karger Ltd, Medical and Scientific Publishers, Basel. [www.karger.com](http://www.karger.com)).

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## SUMMARY AND CONCLUSIONS, TODAY:

How we, as dentists and physicians, should take action!

Conclusions in summary according to present comprehension of the microbiome

1. Most important for women of child-bearing age or who are already pregnant: Establishing dysbiosis-resistant microbiomes for mother and child, pre- and post- (Hitch 2022, p.1095, Heiss 2019, p.1,8)
2. In women of child-bearing age, oral health examinations, preventive measures, recall intervals: prevention of untoward courses of pregnancy
3. Recall appointments are mandatory for classic oral prophylaxis – securing health by confirmation of health-status information (I Top)
4. Actively minimize the xenobiotic load on the body
5. Pathologic and non-pathologic plaque formation must be distinguished on evaluation of the PFRI Index
6. Thorough case taking of medical history including analysis, past and present, especially issues concerning internal medicine, conditions of morbidity, establishing possible interference with oral health
7. Periodontitis requires a polypragmatic treatment approach.
8. Therapeutic measures for establishment of oral eubioses using FMDE (“Full-Mouth-Disinfection and Eubiosis”)

**SANDERINK R. B. A., RENGGLI H. H., SAXER U. P.,  
SCHLAGENHAUF U., FISCHBACH W., STEIMER G. E.**

### **Oral and Systemic Health**

Hidden interdependencies modulated by microbial, metabolomic and environmental factors in preparation, Springer Nature, Switzerland, Cham, to be published in 2024