

1

**Chronic inflammation disrupts immune tolerance:**

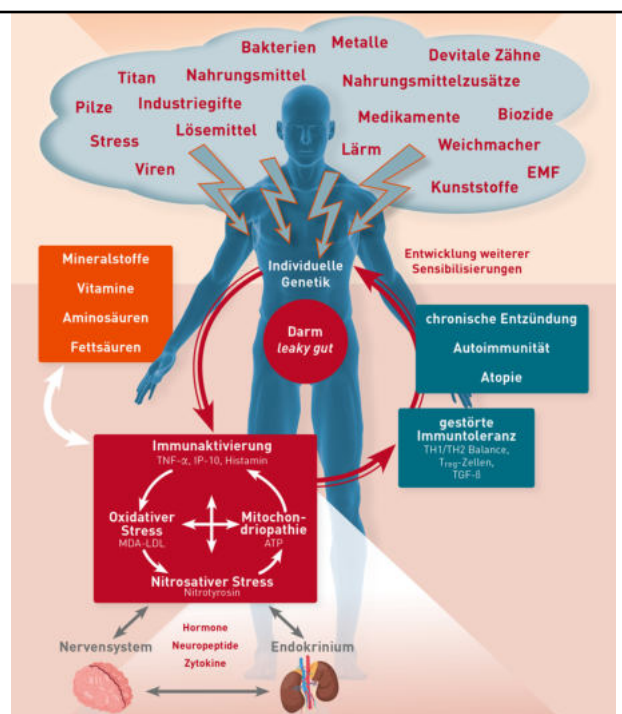
The figure shows that chronic inflammation disrupts the ability of our cellular immune system to maintain immune tolerance.

This explains why, as a result of chronic systemic inflammation, triggers that were previously tolerated and did not induce immune activation can become relevant as stimulus.

**Abb. 1** modified according to Martin L Pall: Explaining „Unexplained Illnesses”: Disease Paradigm for Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, Fibromyalgia, Posttraumatic Stress Disorder, Gulf War Syndrome and Others, ISBN 078902389X

<https://www.imd-berlin.de/fachinformationen/>

Diagnostic Information/Inflammation Diagnostics for Multisystem Diseases



2

### Causes of leaky gut syndrome:

A disturbed intestinal barrier has been described for intestinal diseases, but also for other systemic inflammatory diseases such as rheumatoid arthritis, migraine, autism, ADHD, depression, multiple sclerosis or chronic fatigue syndrome (CFS).

Apart from inflammatory bowel disease, the pathogenesis of intestinal permeability disorder is often unclear. Bacterial overgrowth of the intestine is often associated, but is probably more of a consequence than a cause.

Numerous circumstances can favor a leaky gut, e.g. infections, intestinal exposure to toxic metals, medications (NSAID, antibiotics, etc.), spicy foods, and alcohol consumption.

Stress can also promote leaky gut, probably via psychovegetative alteration of the microbiome or sympaticoadrenergic stimulation of mast cells. Food intolerances can be both the cause and consequence of a leaky gut.

leaky gut - IMD Institut<https://www.imd-berlin.de/spezielle-kompetenzen/leaky-gut-für-medizinische-Diagnostik-Labor-imd-berlin.de>

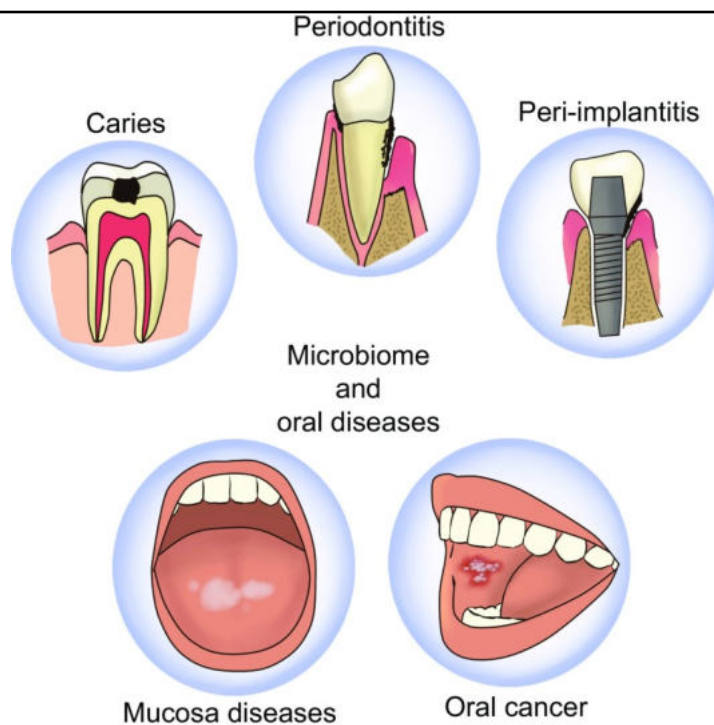


3

### Oral microbiomes and oral diseases:

Different types and different numbers of bacteria have been found in people with different oral diseases.

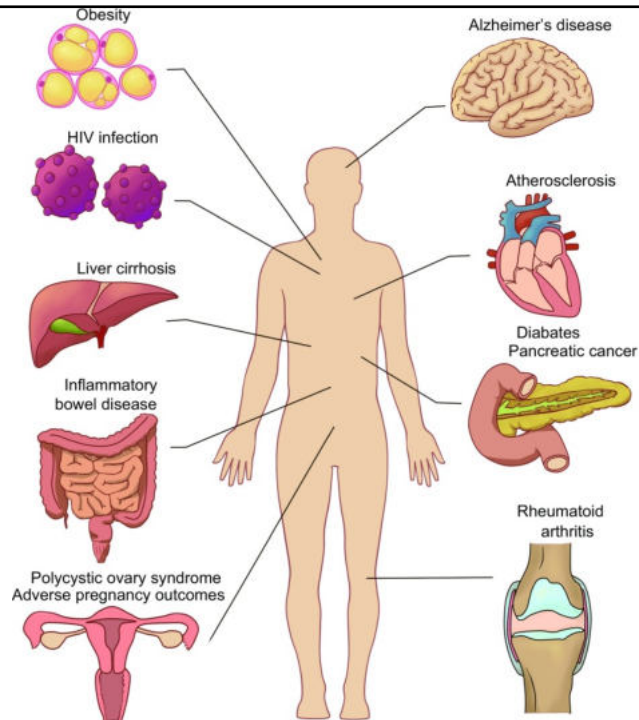
Gao L.: 2018 Protein Cell: Oral microbiomes: more and more importance in oral cavity and whole body



4

**Oral microbiomes and systematic whole-body diseases.**  
Oral microbial dysbiosis contributes to the development of variable systemic diseases.

Gao L 2018



5

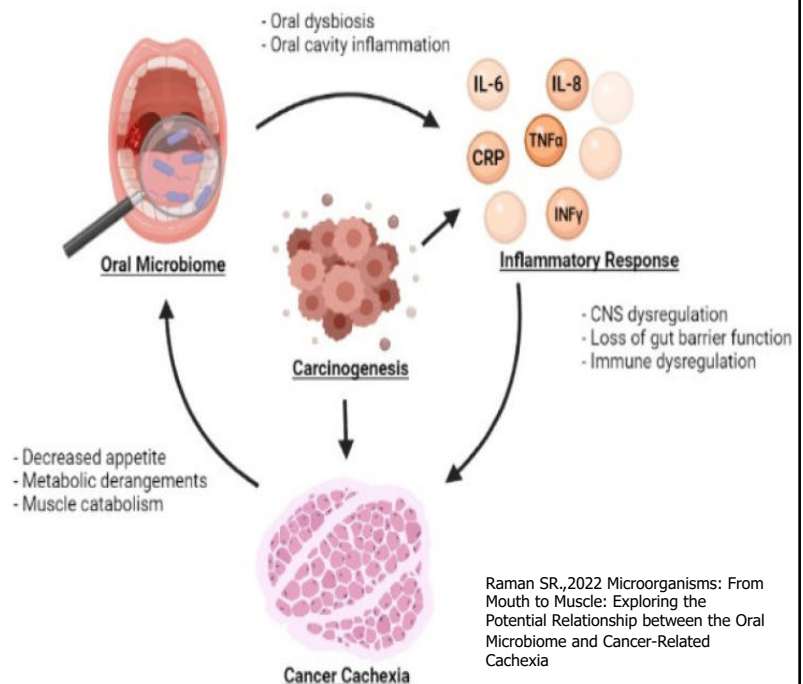
**The oral cavity is the second largest microbial habitat in the whole body.**

**Due to the divergence of oxygen, metabolic substrates, and rate-limiting enzymes, oral bacteria are classified into sugar-metabolizing and nitrogen-metabolizing bacteria according to their metabolic properties.**

**Metabolites include organic acids, carbon dioxide, amino acids, proteins, and ammonia.**

**Oral bacterial metabolites are very important for the growth and reproduction of oral bacteria and also play an important role in systemic diseases such as periodontitis, oral cancer, intestinal diseases, diabetes and atherosclerosis.**

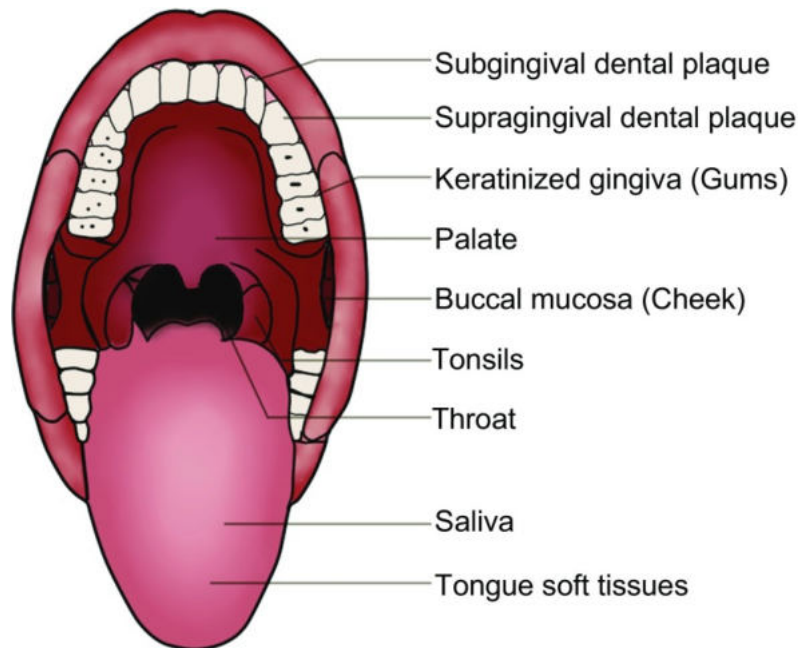
Li YC, Zhang SW, Pan YP 2022, Zhong hua kou qiang yi xue za zhi: Effects of oral bacteria metabolites on systemic diseases



6

**Nine habitats were differentiated in the Human microbiome project (HMP) population.**

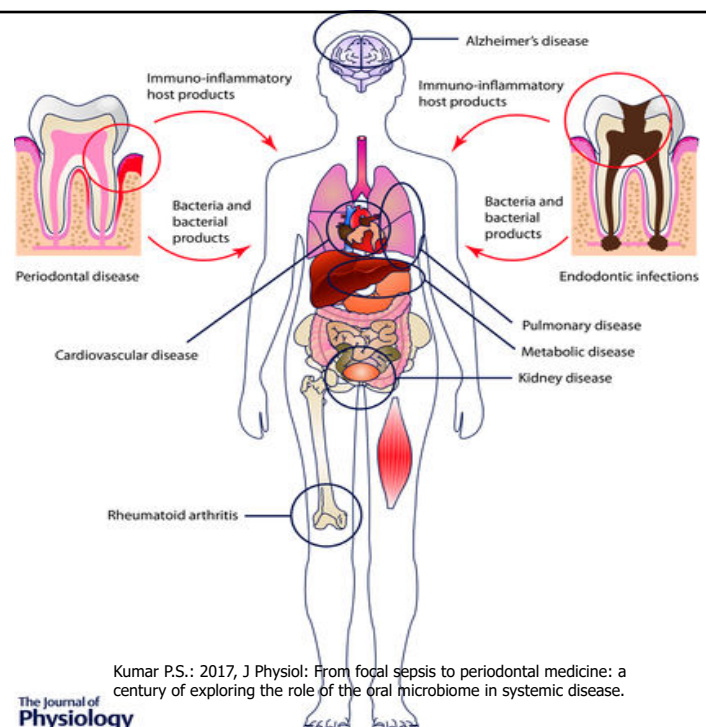
Gao L.: 2018 Protein Cell:  
Oral microbiomes: more and more importance in oral cavity and whole body



7

**Oral microbes affect the process of systemic diseases through the inflammatory response caused by oral infection or the ectopic colonization of oral microorganisms in other organs or tissues of the human body, such as tumor, intestine, heart, blood, brain, joint, placenta.**

Peng X.: 2022 Int.J.Oral.Sci: Oral microbiota in human systematic diseases



Kumar P.S.: 2017, J Physiol: From focal sepsis to periodontal medicine: a century of exploring the role of the oral microbiome in systemic disease.

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**Transient physiological bacteremia, triggered by periodontitis and dental interventions, allows oral pathogens to expand systemically.**

**Patients with periodontitis possess a less diverse gut microbiota, and higher levels of oral taxa in the gut lead to more severe intestinal inflammation.**

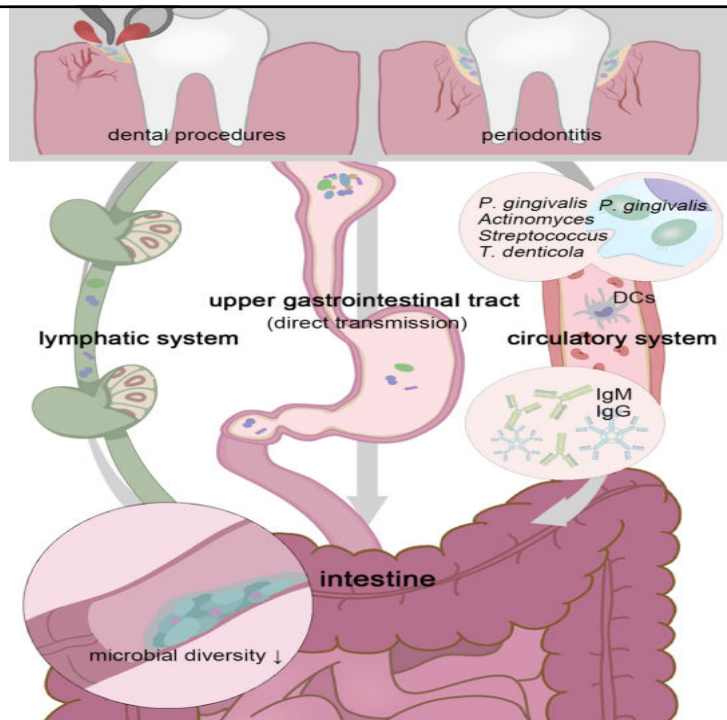
**In order to tolerate the inactivation of gastric acid and bile acid, high acid resistance is expected from these unexpected "visitors".**

**In addition, *Porphyromonas gingivalis* and *Fusobacterium nucleatum* can be parasitic on dendritic cells or macrophages, destroying extraoral tissues.**

**Oral microbes, including *P. gingivalis*, *Actinomyces*, *Streptococcus* and *Treponema denticola* have been confirmed as colonizing sources of non-oral organs.**

**Chronic oral infection establishes *F. nucleatum* colonization, which significantly induces systemic humoral IgG and IgM antibody responses.**

Lu Y. et al.: 2023, Front Cell Infect Microbiol: Regulatory effects of oral microbe on intestinal microbiota and the illness



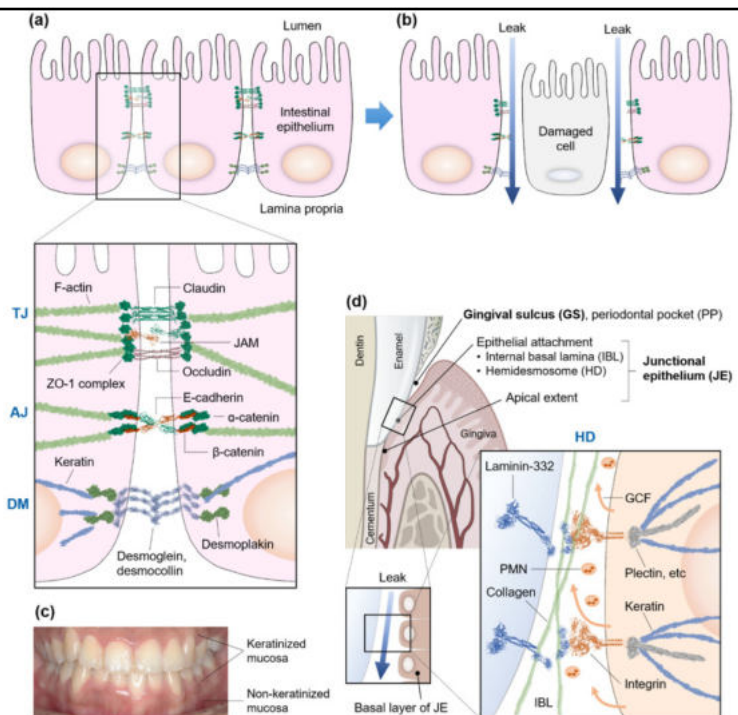
9

## Leaky Gum - Leaky Gut

**Many bacterial toxins, ... also exert biological activations to partially degrade intercellular junction proteins, including tight junction ZO-1 and E-cadherin, as well as extracellular matrix.**

Silbergleit M. et al.: 2020 Prog Mol Biol Transl Sci: Oral and intestinal bacterial exotoxins: Potential linked to carcinogenesis

Park D.Y. et al. 2022, Cells: Leaky gum: the revisited origin of systemic diseases.



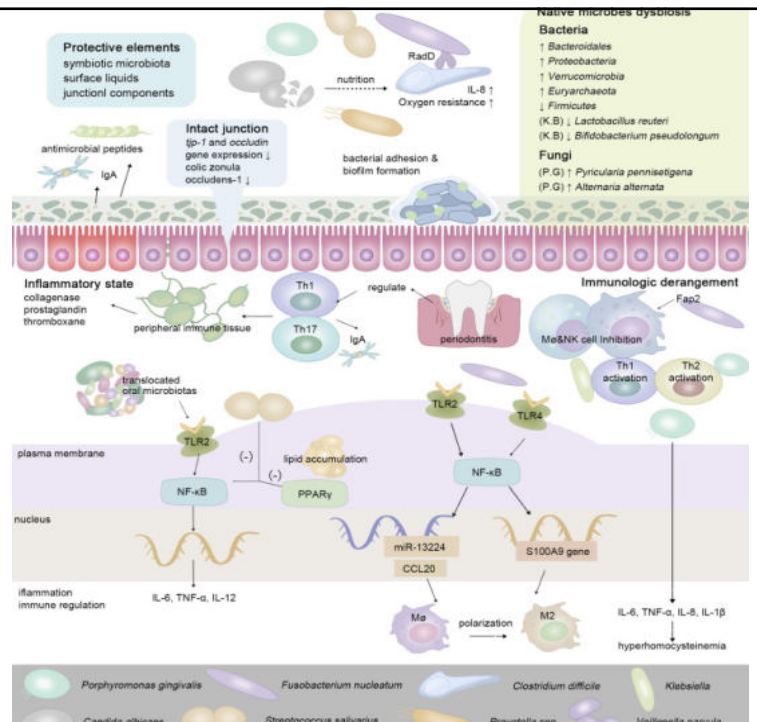
10

Oral microbes and their products induce immune responses via the bloodstream, which regulates the overall inflammatory state of the host, stimulates the TLR-NF- $\kappa$ B pathway, and regulates the TH17/Treg ratio.

Among other things, endotoxin detection triggers the activation of the "antigen-specific acquired immune system".

Lu Y. et al.: 2023, Front Cell Infect Microbiol: Regulatory effects of oral microbe on intestinal microbiota and the illness

**Note.** Due to the permanent effect of chronic inflammation or chronic infection, the vicious circle occurs due to overstimulation and blockages of the regulations.



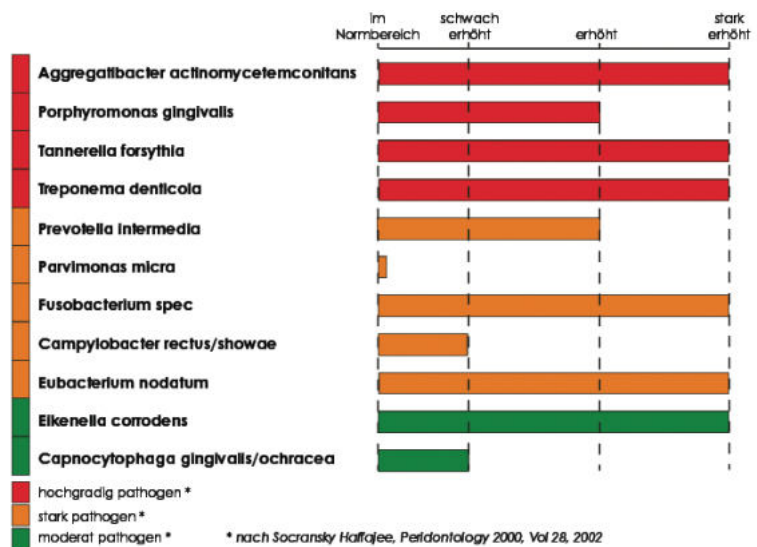
11

**Bacteria of the red and orange complex are significantly involved in oral inflammation:**

The marker germs mentioned above represent an immunological focus and are to be considered as potential inflammatory stimuli in therapy-resistant, refractory, but also acute, rapidly progressing periodontitis as well as in peri-implant infections.

Example of aggressive periodontitis:

[Labordiagnostik bei Parodontopathien - IMD Institut für medizinische Diagnostik, Labor \(imd-berlin.de\)](http://Labordiagnostik.bei.Parodontopathien-IMD.Institut.für.medizinische.Diagnostik.Labor(imd-berlin.de))



#### Beurteilung:

Der deutlich über dem Normwert nachgewiesene A.actinomycetemcomitans gilt als Leitkeim für juvenile, aggressive und refraktäre Parodontitiden. Die insgesamt vorliegende deutlich positive Markerkeimbefundkonstellation hat daher eine prognostische Bedeutung für weiteren Attachmentverlust und kann ursächlich sein für eine

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**Periodontitis:**

**Biofilms built on ( a ) a tooth surface and (b ) extracted implants.**

**The hard surface of a tooth root, implant and crown prosthesis adjacent to an implant shaft provides a solid surface on which biofilms can accumulate for a lifetime if not well cared for.**

**( c ) The edentulous oral cavity:**

**The edentulous oral mucosa is free of gingival sulcus and junctional epithelium and is therefore less susceptible to infections.**

Park D.Y. et al. 2022, Cells: Leaky gum: the revisited origin of systemic diseases.

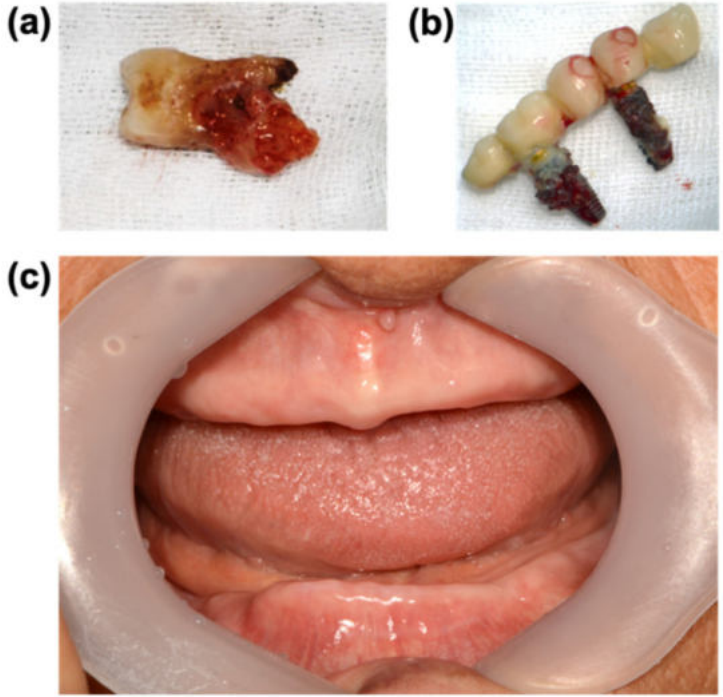


Image (a) shows a close-up of a tooth root with a thick, reddish-brown biofilm accumulation. Image (b) shows an extracted implant with a similar biofilm. Image (c) shows the interior of an edentulous (toothless) mouth, highlighting the oral mucosa.

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**Ozone acts as a bioregulator through oxidative stress and as a local disinfectant. Viebahn R. 2023**

**Ozone and periodontitis:**

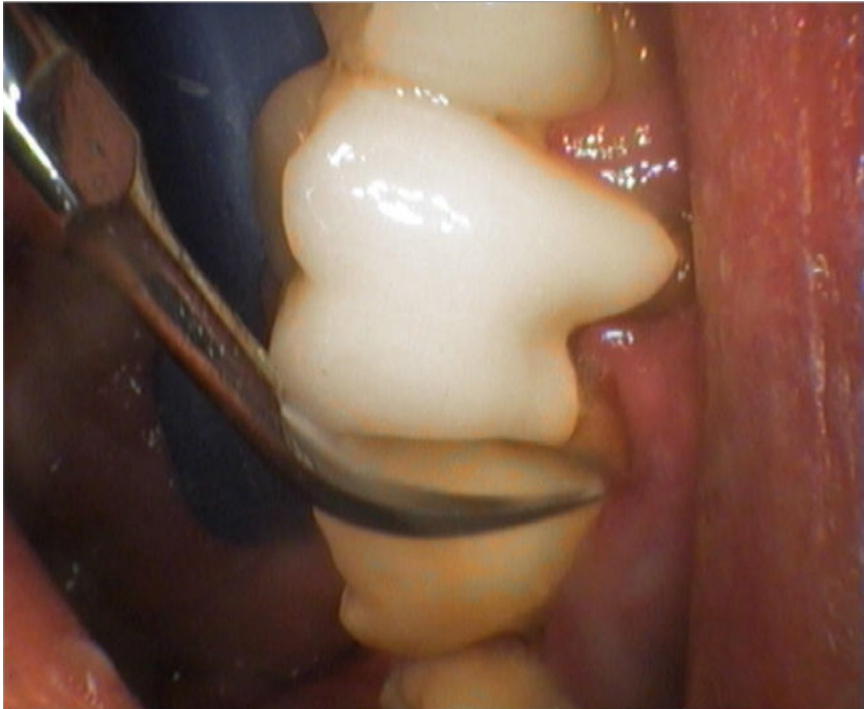
**Most studies on ozone therapy for periodontitis have yielded positive results.**

Ramirez-Penao A.M.: 2022 J.Clin.Med: Ozone in Patients with Periodontitis: A Clinical and Microbiological Study

**Ozonated water can be used as a rinsing liquid in the ultrasound machine or the piezo surgery device.**

**„This will reduce the pathogenic load of the patient locally and systemically.“**

Naik S., et al.: 2016, OpenDent J. :Ozone-A Biological Therapy in Dentistry-Reality or Myth? Vol.10:196-206



The image shows a close-up of a dental procedure where a piezo surgery device is being used on a tooth. The device is a small, handheld tool with a fine tip, and it is being applied to the tooth surface. The tooth is white and has a natural shape. The surrounding tissue is pink and appears to be the gingiva.

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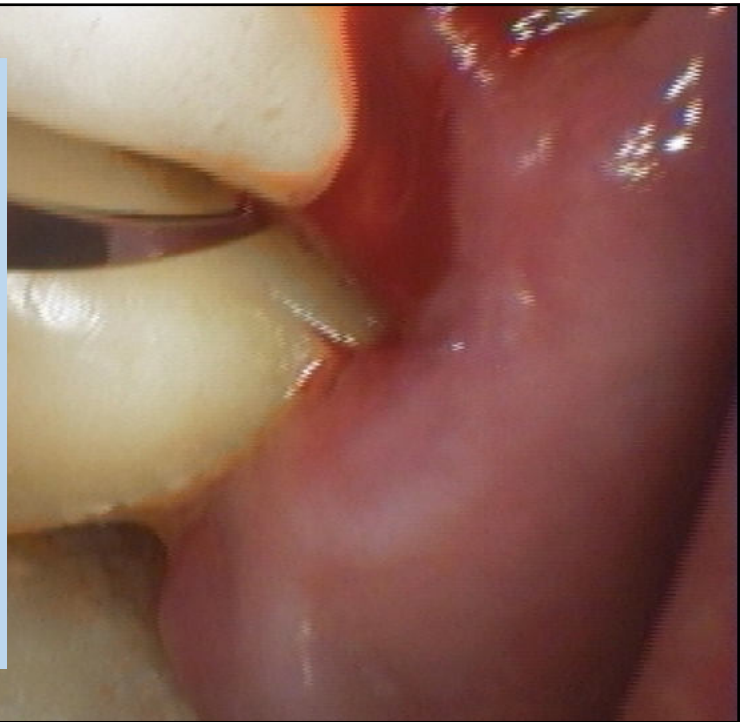
### Ozon in therapy of periodontitis:

„Ozonated water (4mcg/ml) strongly inhibited the formation of dental plaque and reduced the number of subgingival pathogens both gram positive and gram negative organism.“

„Gram negative bacteria, such as *P. Endodontalis* and *Porphyromonas Gingivalis* were substantially more sensitive to ozonated water than gram positive oral *Streptococci* and *C. albicans* ....“

„The application of ozone therapy in chronic gingival and periodontal diseases showed subjective and objective improvement...“

Naik S. et al. 2016



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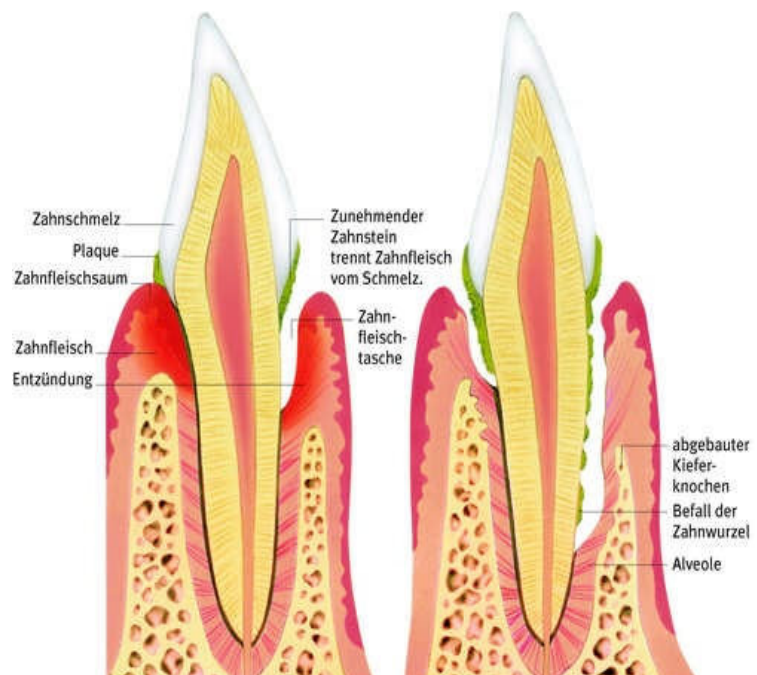
**Periodontitis is a chronic inflammatory disease triggered by dysbiotic microbiota. Conventional mechanical debridement often requires complementary measures to control the disease process**

**Ozone flushing, together with non-surgical periodontal therapy, provides an additional benefit in reducing clinical parameters and inflammatory mediators in saliva.**

Ranjith A.: 2022 Int J Dent Hyg: Adjunctive benefit of ozonized water irrigation with mechanical debridement in the management of Stage III periodontitis: A randomized controlled clinical and biochemical study

**Subgingival irrigation with ozonated water can improve clinical and microbiological parameters in patients with chronic periodontitis when used as an adjunct to scaling and root planing.**

Isaac A.V.: 2015 J Clin Diagn Res: Management of Chronic Periodontitis Using Subgingival Irrigation of Ozonized Water: A Clinical and Microbiological Study



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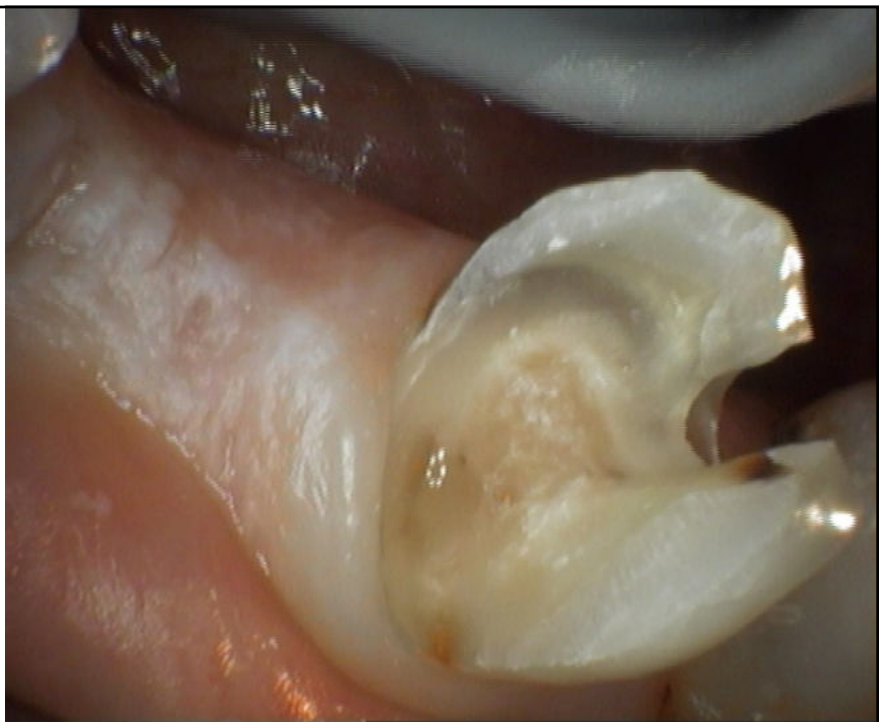


**Ozon in therapy of caries:**



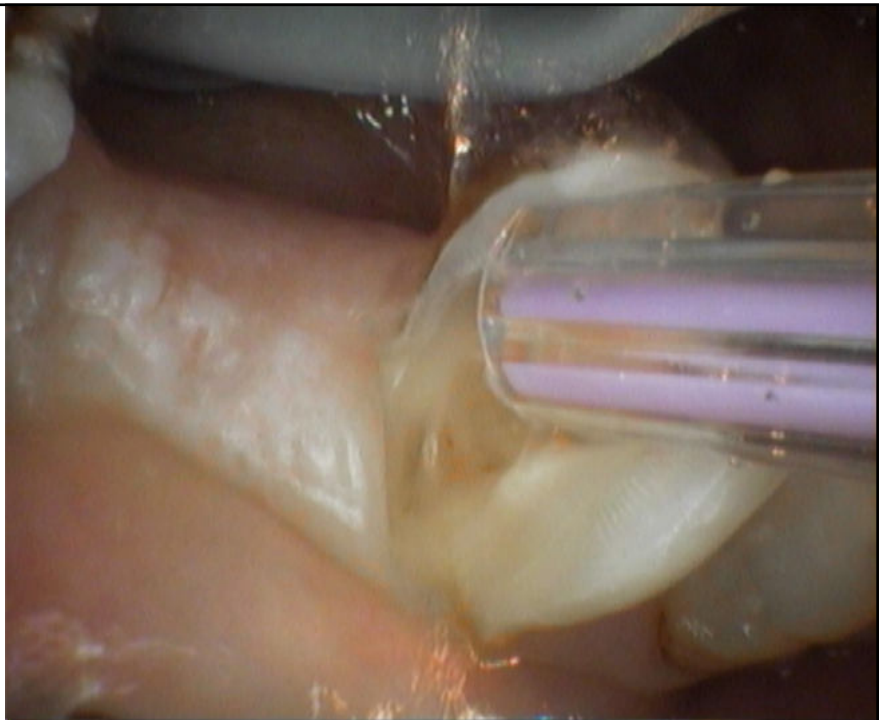
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**Ozonized water can be used as a powerful disinfectant and anti-inflammatory agent in the carious tooth cavity to protect the tooth pulp.**

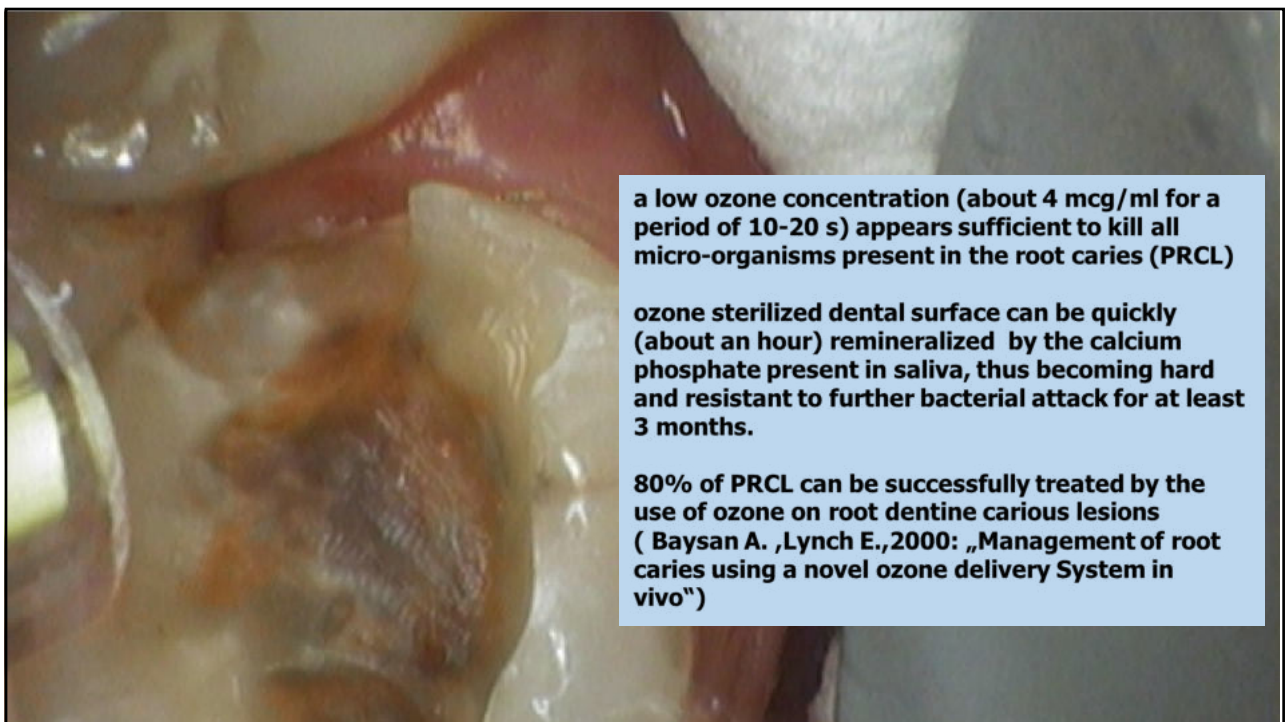


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**For this purpose, after the complete removal of carious dentin, the tooth cavity is intensively rinsed with ozonated water.**



19

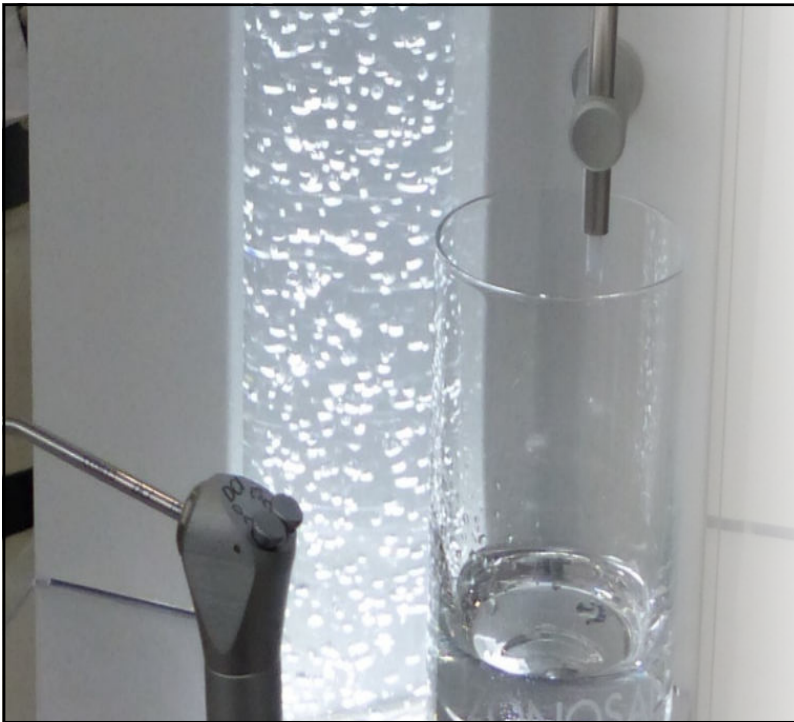


**a low ozone concentration (about 4 mcg/ml for a period of 10-20 s) appears sufficient to kill all micro-organisms present in the root caries (PRCL)**

**ozone sterilized dental surface can be quickly (about an hour) remineralized by the calcium phosphate present in saliva, thus becoming hard and resistant to further bacterial attack for at least 3 months.**

**80% of PRCL can be successfully treated by the use of ozone on root dentine carious lesions ( Baysan A. ,Lynch E.,2000: „Management of root caries using a novel ozone delivery System in vivo”)**

20



**Ozonated water is produced by passing an oxygen/ozone gas mixture through a column of water**

**The ozone concentration should be 100 mg/l and the time the gas is passed through the water column should be 5-6 minutes.**

**The water quality and temperature are crucial for the maximum ozone saturation in the water.**

**Bidistilled laboratory water is suitable.**

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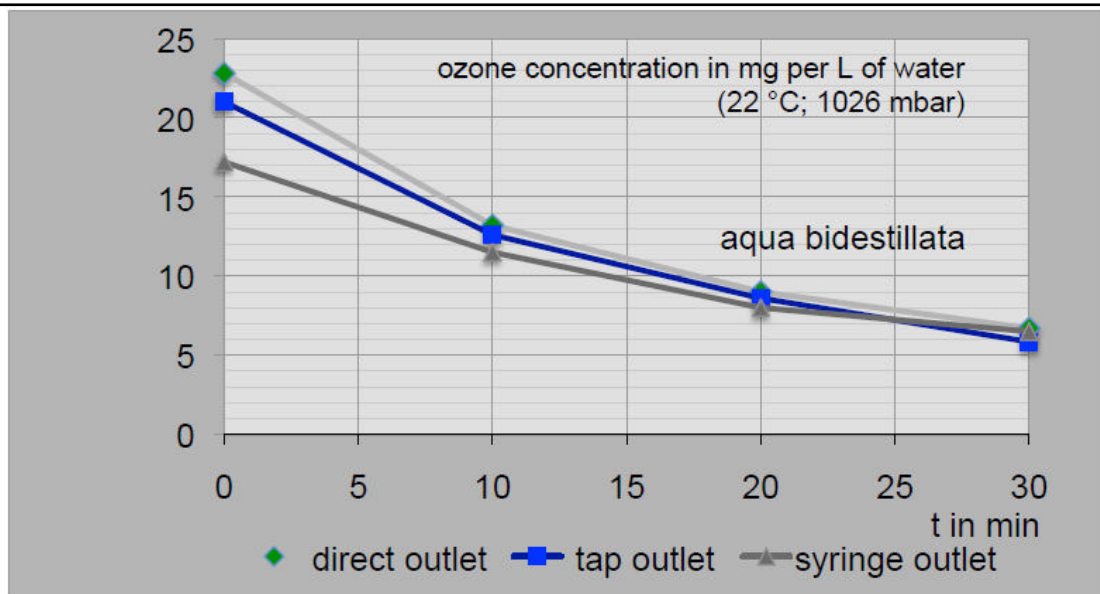
**After 5-6 minutes, the concentration of ozone dissolved in the water can reach 25% of the ozone concentration of the gas mixture.**

**Thus, an ozone concentration of 20-25 mg/l can be achieved, which is more than sufficient for optimal disinfection in medical use.**

**This ozonated water can be used, for example, in all dental and oral surgery applications.**



22



Viebahn-Hänsler 2016

Taking into account the degradation of ozone, one remains in the safe range of action in all dental and surgical applications.

23



The ozonated water is used as a rinsing medium, e.g. in the ultrasonic device.

Ozonated oils can be instilled in gum pockets, for example.



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**Ozonated olive oil can be poured into a hypodermic syringe and inserted into gum pockets, fistula ducts, etc. can be instilled.**



25

#### **Ozone in endodontics:**

**Ozonized water can be used for flushing during sewer preparation.**

**„Ozone was found to be effective against endodontic pathogenic microorganisms like E.Faecalis, Candida albicans, Peptostreptococcus micros and Pseudomonas aeruginosa for disinfecting of root canals and dentinal tubules.“**

**„When the specimens was irrigated with sonication, ozonated water had nearly the same antimicrobial activity as 2.5% NaOCl and also it demonstrated the antimicrobial activity of ozone in root canal treatment without any tissue toxicity.“**

**„Ozonated oil.....was efficient in canal sterilization .....“** Naik S. 2016



**E.g. the self-adjusting file system:**

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**„Ozone also eliminates the distinctive anaerobic odor associated with some chronically infected teeth.“**

**„The following steps should be added before the final biomechanical preparation:**

**The files are coated with ozonated olive oil for lubrication and disinfection.**

**The canals are prepared & .... irrigated with ozonated water and dried.**

**Before filling, a slow insufflations (45-60sec) into each canal with moderate/high concentration of ozone gas.**

**Insufflation of ozone electrochemically travels into the lateral canals and dentinal tubules killing the microbes. “**

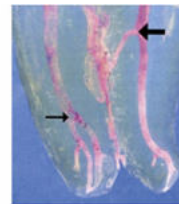
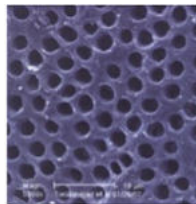
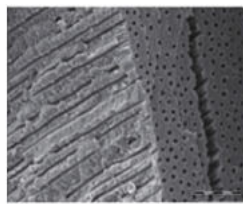
**„Ozone will also penetrate through the apical foramen and enter into the surrounding and supportive bone tissue, encouraging healing & regeneration...”** Naik S. 2016



27

#### **Sensitization to the protein decay products mercaptans and thioethers:**

**Devitalized teeth and derived organic intermediate products such as mercaptans and thioethers can also be a focus for immunological inflammatory reactions, regardless of their toxic effects.**



**Even with the most perfect methods of root canal preparation, it is not possible to completely remove organic tissue and microorganisms from the root canal.**

**Thus, the action of resident anaerobic bacteria such as Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum or Treponema denticola inevitably produces hydrogen sulfide compounds such as methyl mercaptans and thioether compounds such as dimethyl sulfides and diethyl sulfides.**

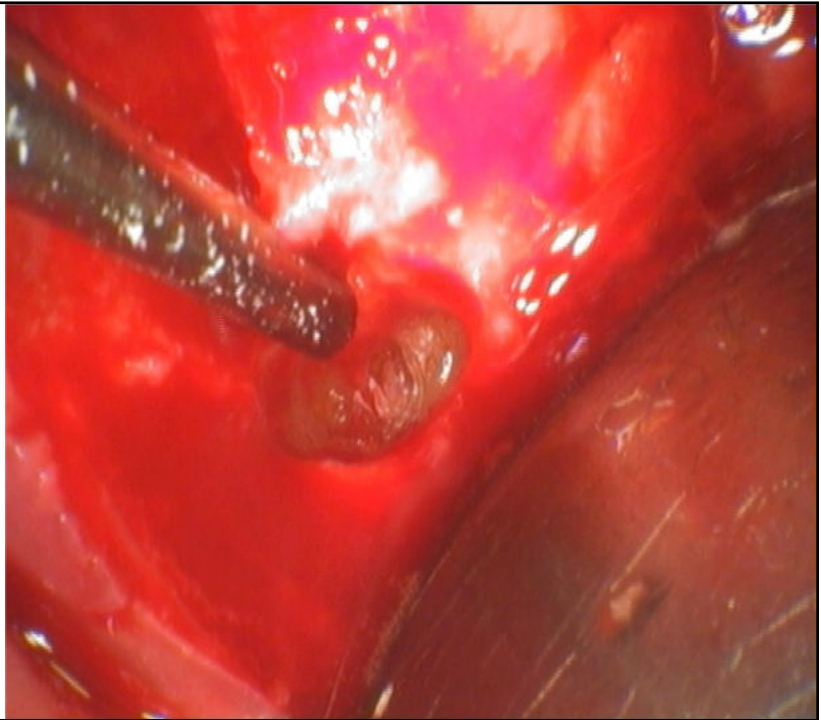
**The toxicity of these products has been known for more than 30 years. However, toxic effects alone cannot usually explain the described local and systemic inflammatory reactions and the individually different symptoms of the patients.**

**Studies have shown that, in addition to toxic effects, protein decay products can also cause pathological immune reactions. In these cases, there is no direct correlation to the dose (i.e. to the amount of toxin), but an individually shaped sensitivity, which, however, can be amplified by other inflammatory processes.**

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### Ozon in implantology:

**„When Ozone therapy is used in implants, prevention of infection and enhancement of bone regeneration is seen when ozone is bubbled into the socket about 40sec, followed by placement of implant into the socket.“** Naik S 2016



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### Ozon in oral surgery:

**„This solution is suitable for treating heavily infected wounds in order to eliminate pus, necrotic materials and bacteria.**

**Ozonized water-oxygene-jet-spray** is useful for removing thick pus from purulent abscesses, empyemas and osteomyelitic infections.

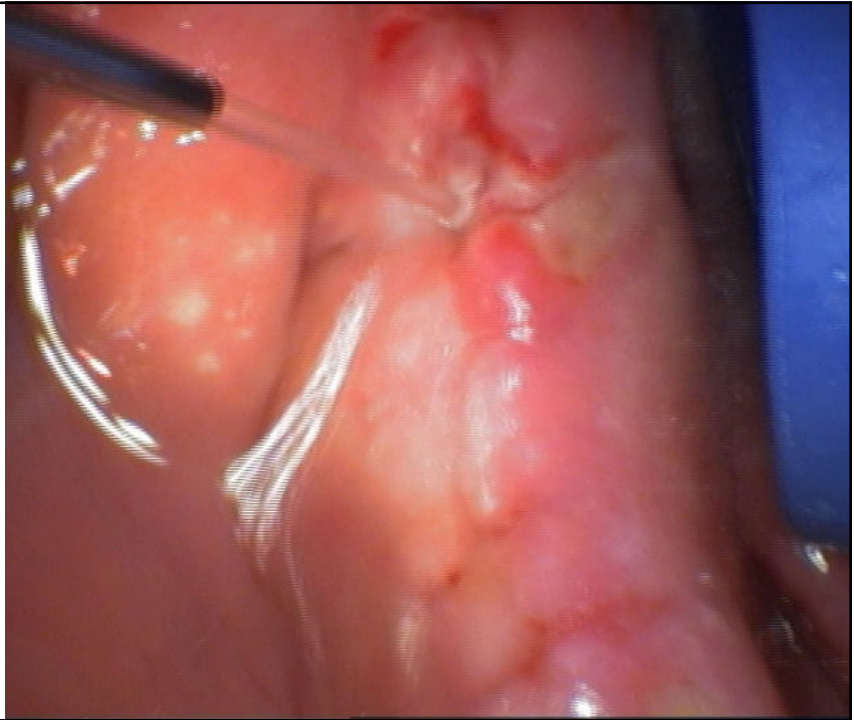
**It is feasible to eliminate hopeless infections by only using the combination of ozonized water[..] and ozonized oil.“** Naik S 2016



30

The ozonated water can be flushed directly from the cytozon device into wound dehiscences.

For this purpose, blunt cannulas are used, which are available in different diameters.



31

#### **Ozone for wound treatment:**

„Ozone has been reported to accelerate the healing of soft tissue conditions i.e. aphthous ulcers, herpes labialis. ANUG and other gingival infections, because ozone encourages physiological healing rate as well as it controls opportunistic infections.“

Naik S 2016

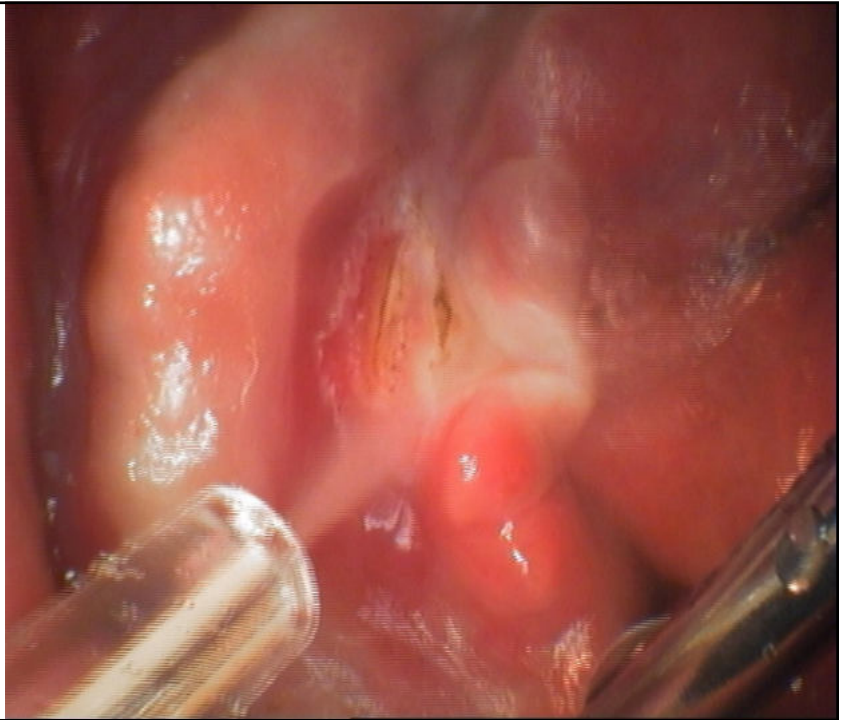
**Example image:**  
Surgical treatment of an ulcer in the anterior mandibular region:



32



During and after the surgical procedure, the treatment area is intensively rinsed with ozonated water.



33

To continue the treatment at home, the **ozonized water** must be maintained in a glass bottle, filled 2/3, tightly closed and has to be transported and stored in an upright position.

It must be stored in a refrigerator, at ca. 5°C.

Under these conditions, the ozone concentration may be halved within ca. 10h.



Advice your patients, never to take a breath, while opening the bottle, because there will be **gaseous ozone** in the supernatant, that **must not be inhaled**.

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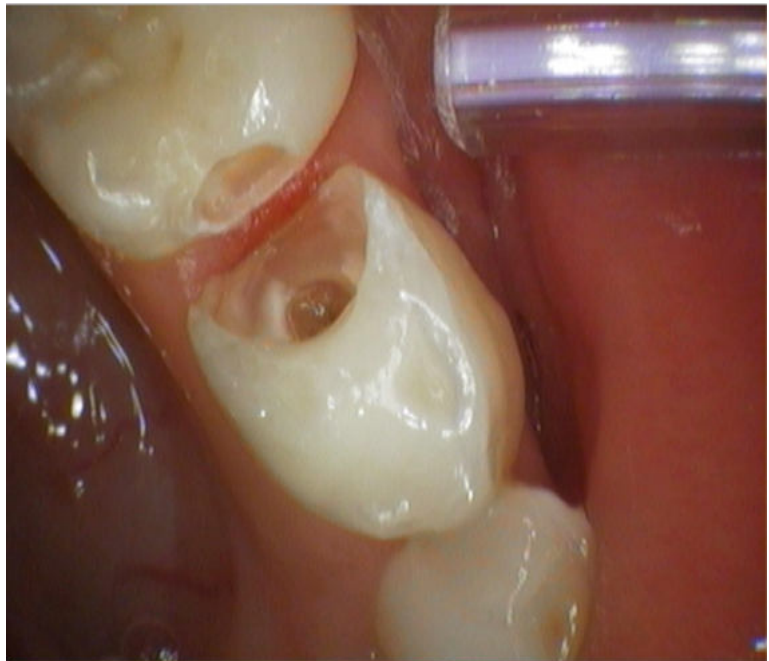
**Ozone in paediatric dentistry**



35

**Preparation:**

**Flushing of the entire treatment area with ozonated water.**

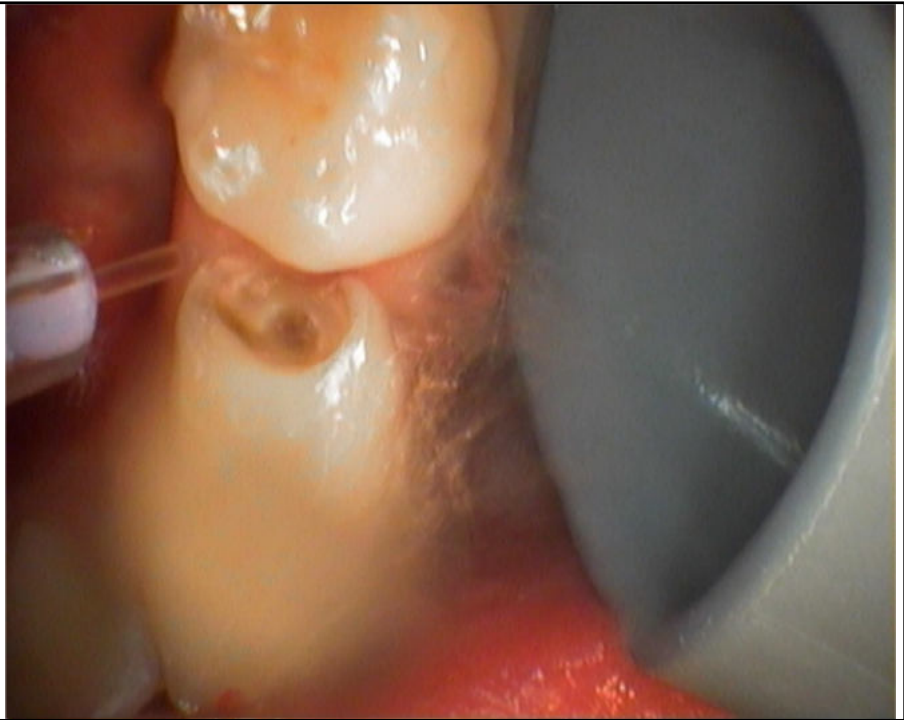


36

As **O<sub>3</sub> inhalation** is accompanied by dangerous side-effects and since O<sub>3</sub> is a gas, its benefits are limited under the circumstances of the oral cavity.

To increase the effectiveness and the safety of ozone treatment, ozone may be dissolved in water.

This is advantageous as **ozonized water** is easier to administer and safer than ozone gas.



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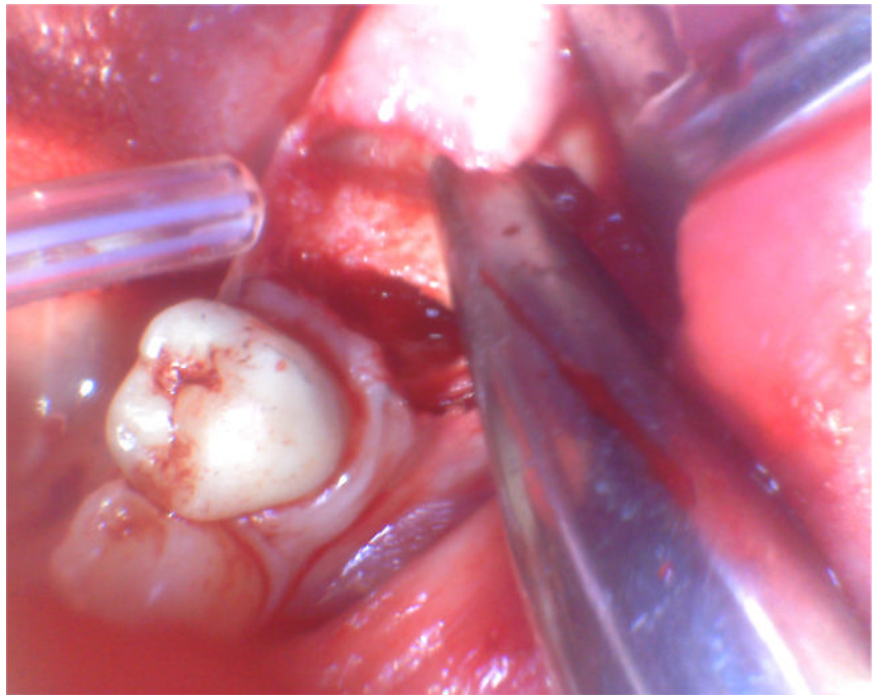
The postsurgical therapy by **ozonized water** rinsing of the site



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**Ozone in the  
treatment of  
alveolitis:**

**Removal of tooth  
36 under ozone  
water flushing:**



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**„Application of ozonated  
water and ozonated oil daily  
accelerate the healing  
rate....“ Naik S 2016**

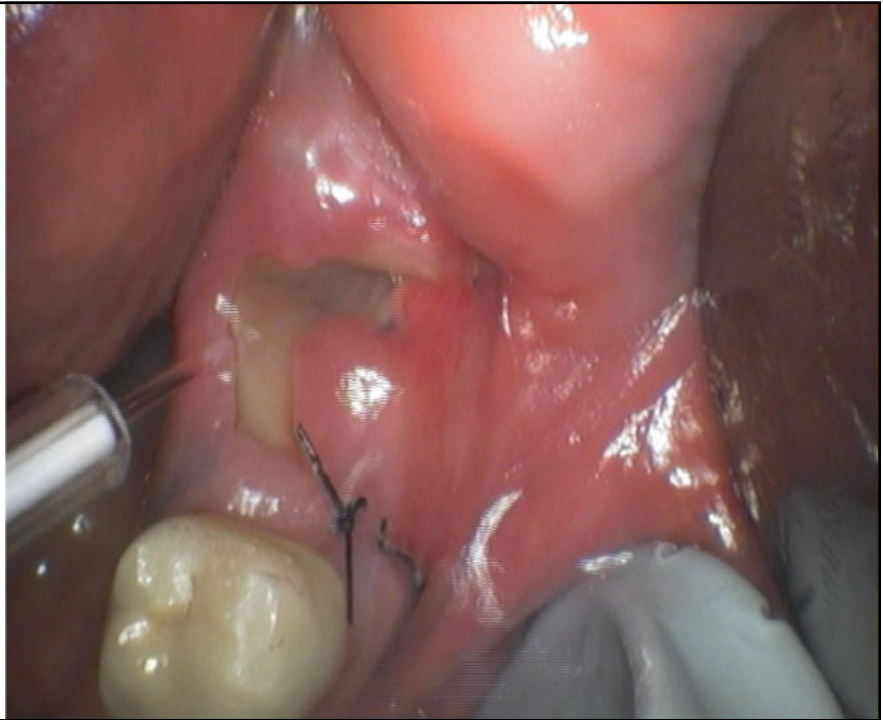


40



**„....it also reduces the post extraction healing time by forming a pseudo-membrane over the socket and protecting it from any physical and mechanical insults.“** Naik S 2016

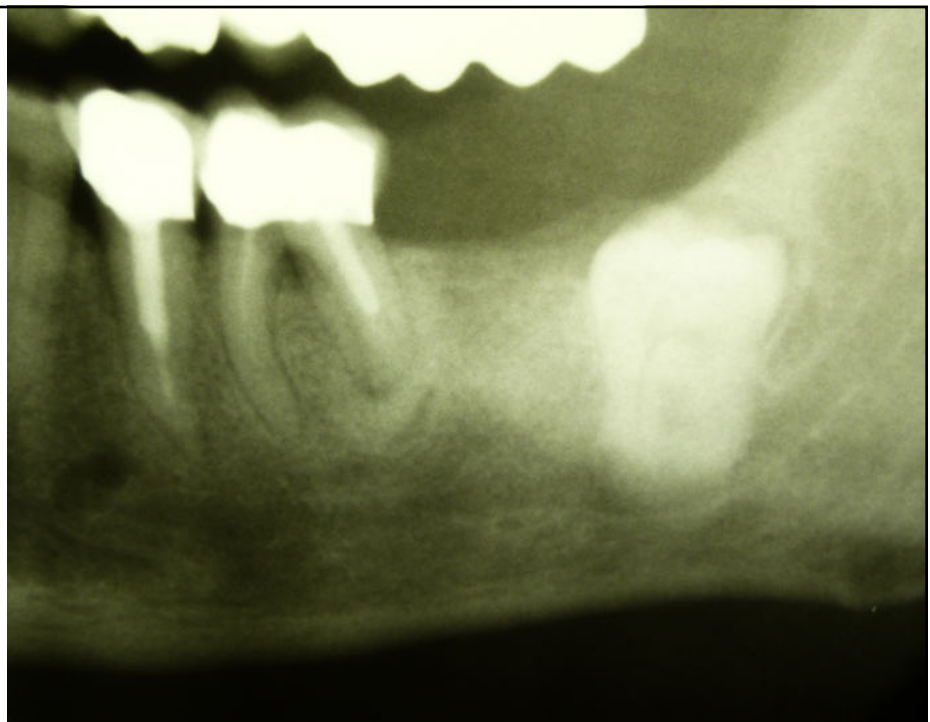
**Despite seemingly irritating healing, the patient continued to complain of pain in the jawbone.**



41

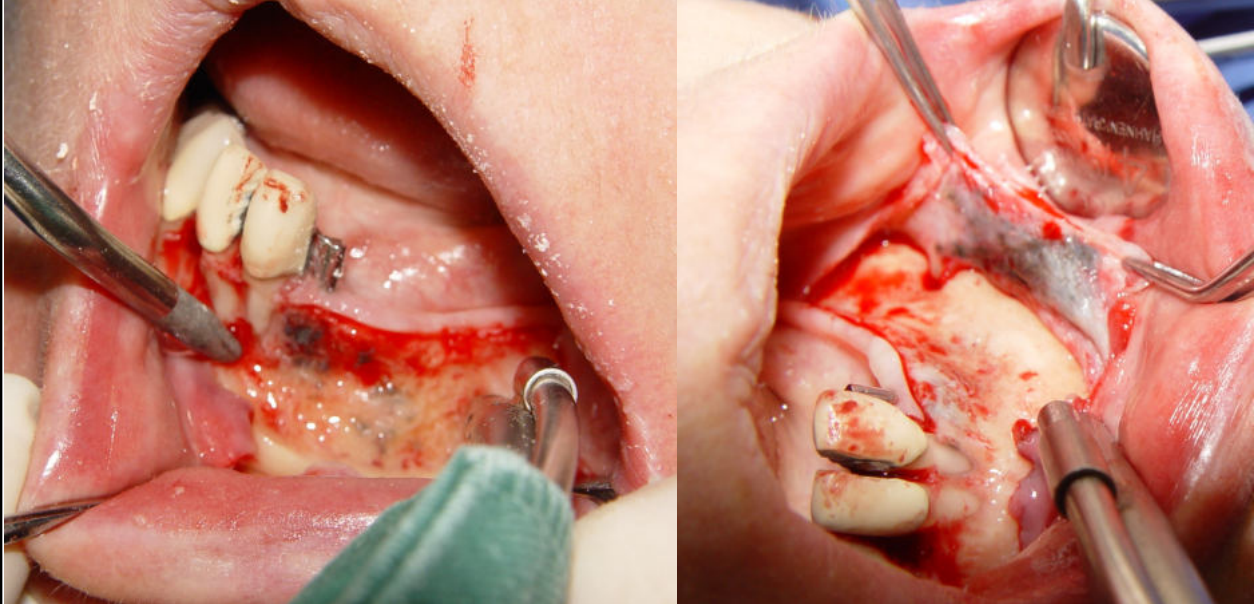
**The X-ray image shows further findings that can explain the pain.**

**Often, microbial infections  
In the roots of the devital teeth,  
metabolic products are  
scattered in the  
jawbones.**



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How far toxins from dental infections can spread into the jawbone marrow spaces can be shown by the example of a metal tattoo in the jaw tissues of the left lower jaw:

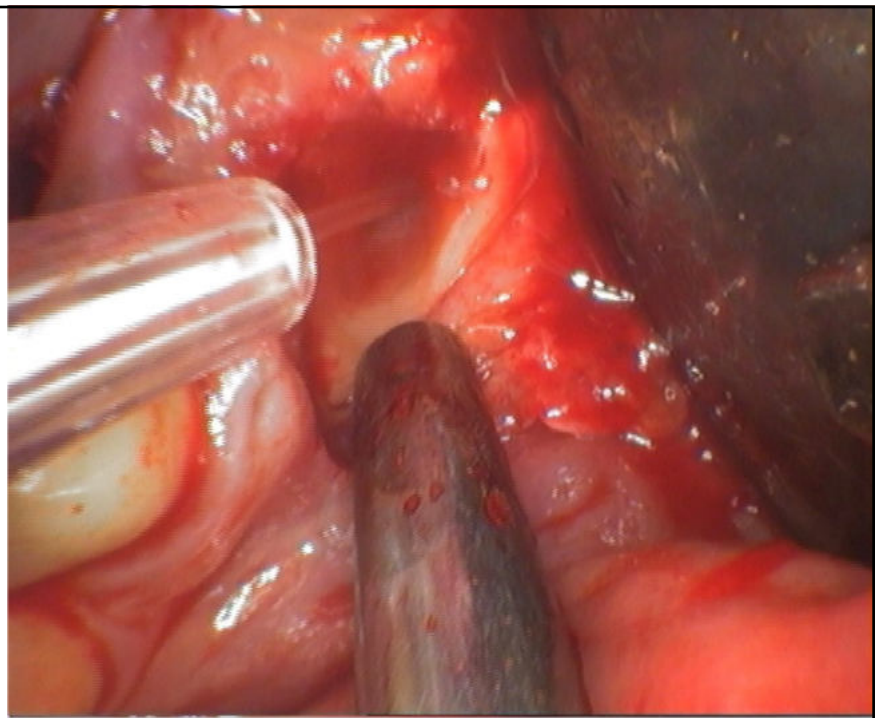


43

In order to remove the microbial metabolites scattered into the medullary spaces, a surgical procedure is performed under ozone water flushing.

„In alveolitis, there is accelerated healing by irrigation with **ozonated water** after removal of the necrotic plug and debris....“

Naik S 2016

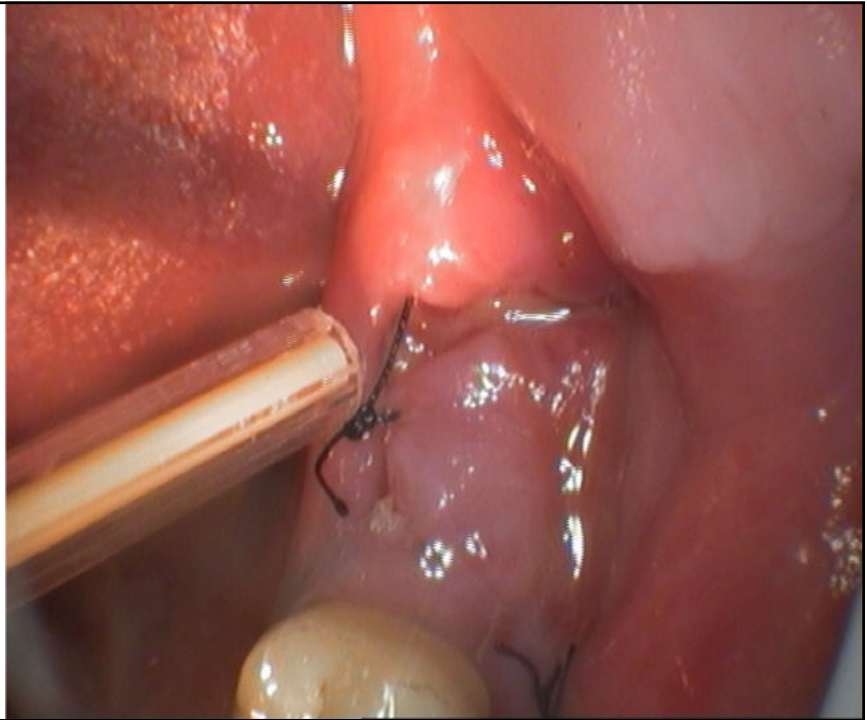


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**In this case of the therapy of alveolitis, the primary wound healing took place again.**

**Now, however, there was pain in tooth 35.**

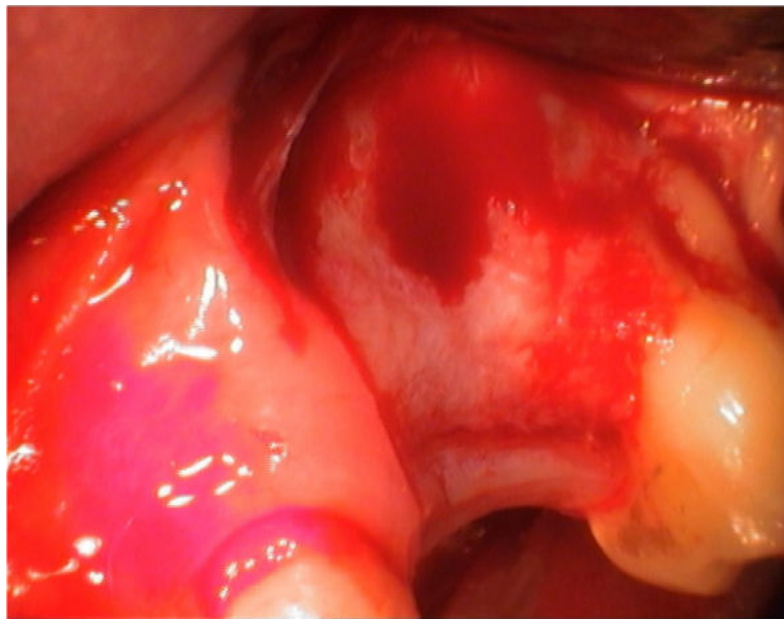
**The focal disease does not heal until the last focus is removed.**



45

**In oral surgery, ozonized water is used to promote haemostasis,**

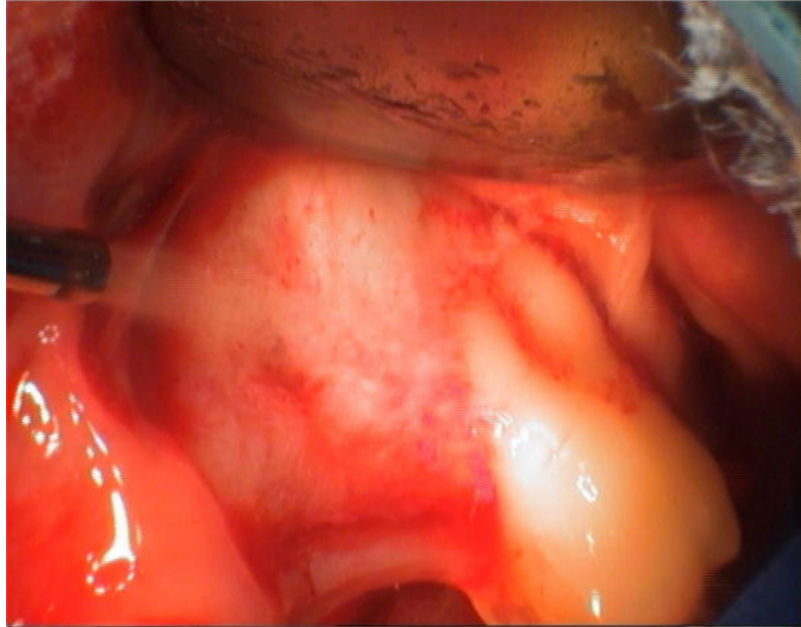
**or rather to blow free the surgery site from blood in cases of poor visibility.**



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**Ozonized water-, oxygen-jet-spray** delivered by the cytozone is used during surgery, to keep the site free from bleeding:



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**Ozone in oral surgery and maxillofacial surgery:**

Filippi A 1995

**Ozonized water** in oral surgery:

**I.a. Prewashing and disinfection of the whole mouth.**

Prewashing of the surgical sites by professional dental cleaning under irrigation with **ozonized water**

**I.b. Rinsing the whole surgery region with **ozonized water**.**



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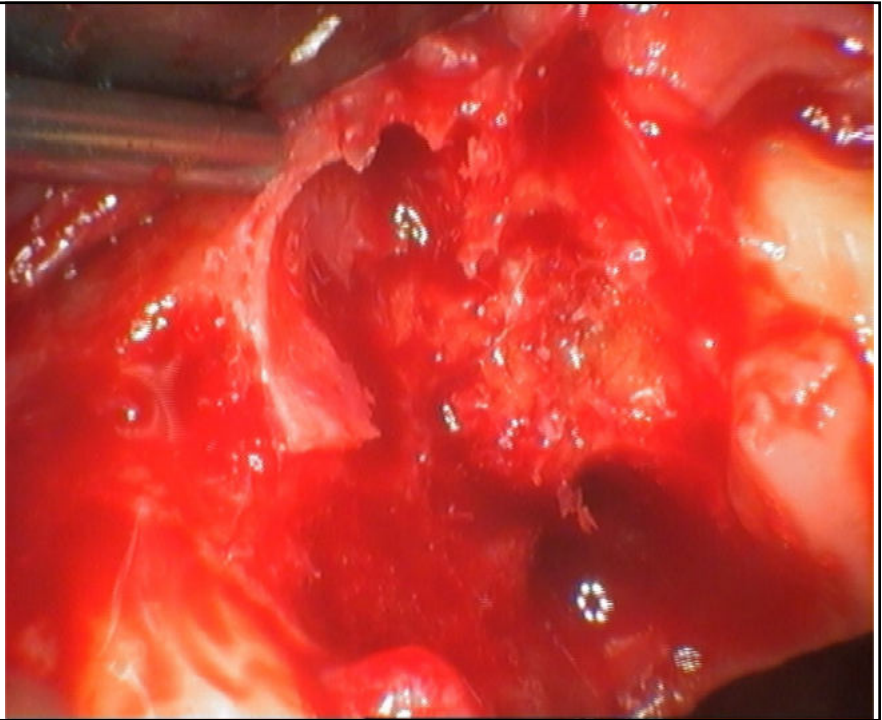


**During surgery:**

**Toxine and hypoxia related fatty degeneration of the alveolar bone in the trifurcation of the removed upper molar are present:**

**Fat-soluble toxins can be stored in fat cells, where they are protected from the body's detoxification systems.**

**In the fatty degenerated bonemarrow of the jaw bone, specific cytokine expressions of CCL5 (RANTES) have been shown.** Lechner 2010



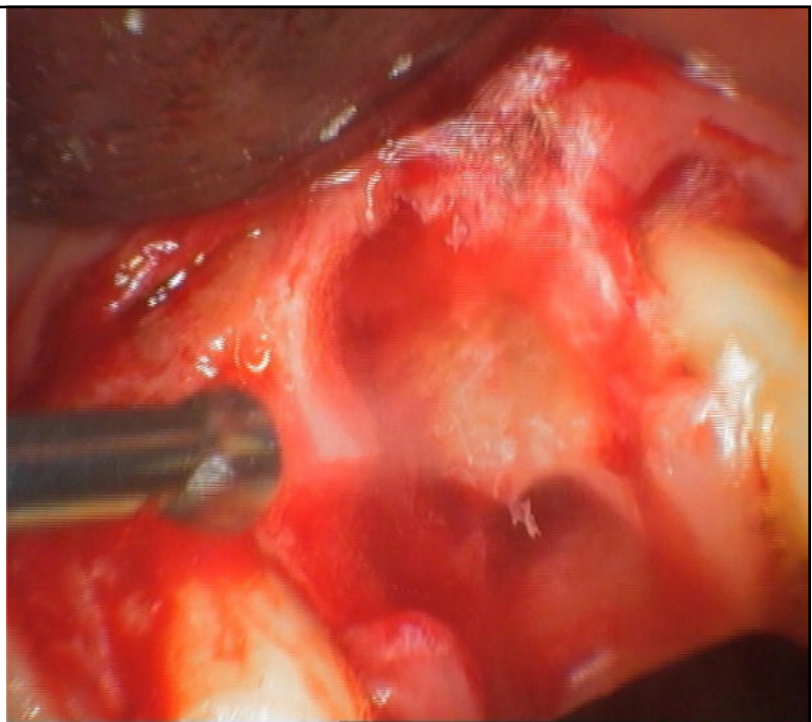
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**II. Dissolving of the fatty degenerations and**

**III. Degradation of toxins**

**by the [ozonized water-oxygene-jet-spray](#).**

**The success is controlled by organoleptical detection of toxins and their degradation products, such as sulfones, sulfoxides, sulfonic acids, etc.**



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**Sinusitis maxillaris and osteosinusitis maxillaris can be treated by the surgical removal of the toxins and of the inflamed tissues at the border between sinus and jaw bone.**

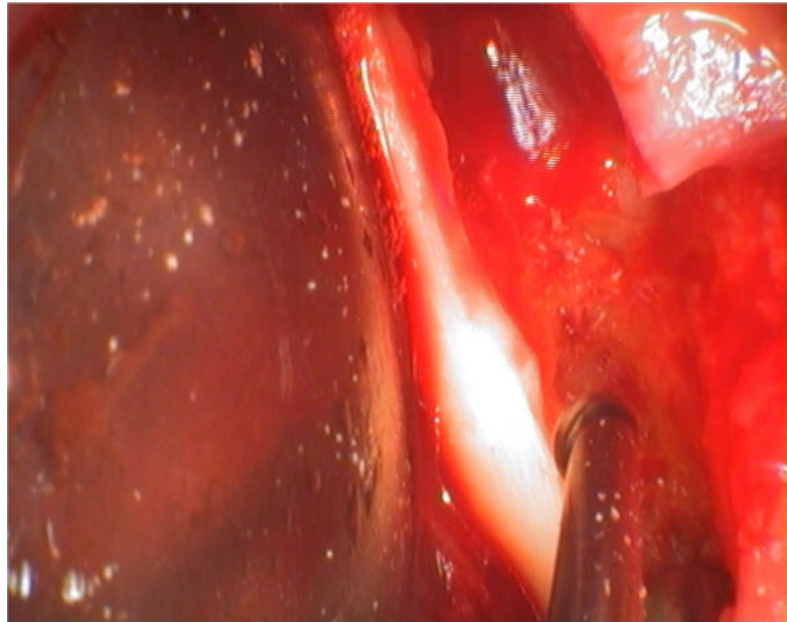
**The sinus is thoroughly rinsed and filled with [ozonized water](#), before suturing.**



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***Focus surgery in the lower jaw bone area:***

**Toxic, fatty degenerated bone material often surrounds the nervus alveolaris inferior.**



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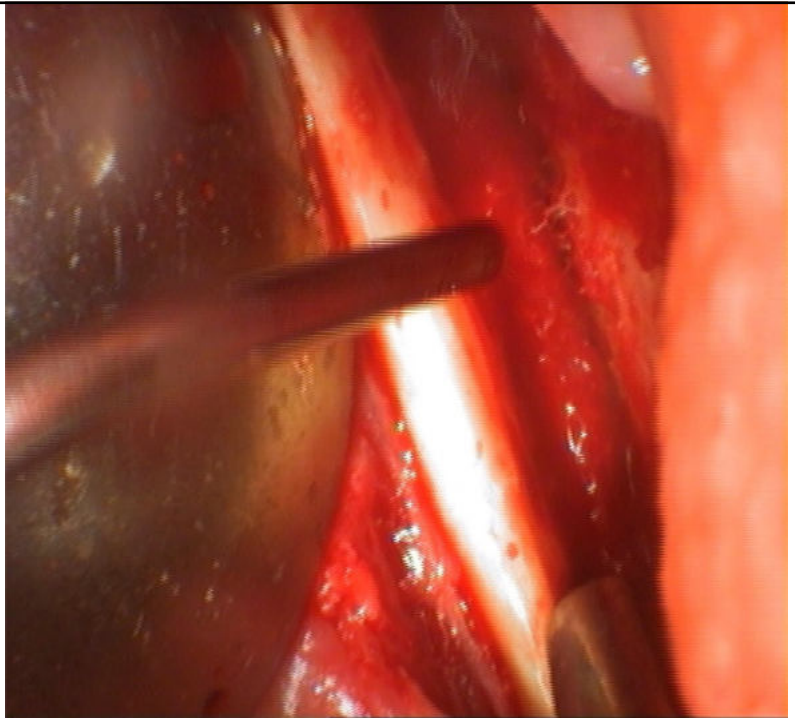
**Dissolving of the fatty degenerated tissues and Degradation of the toxins around the nervus alveolaris inferior by the use of the [ozonized water-oxygene-jet-spray](#).**

**Currently this seems to be the only way to reach these toxin-deposits.**

***Detoxification of xenobiotics in two phases (Williams RT 1947)***

**By the way ozone acts locally as a phase 1 activator of the detoxification process.**

**Additionally surgery itself acts as drainage of toxins from their deposits in the jaw bone.**



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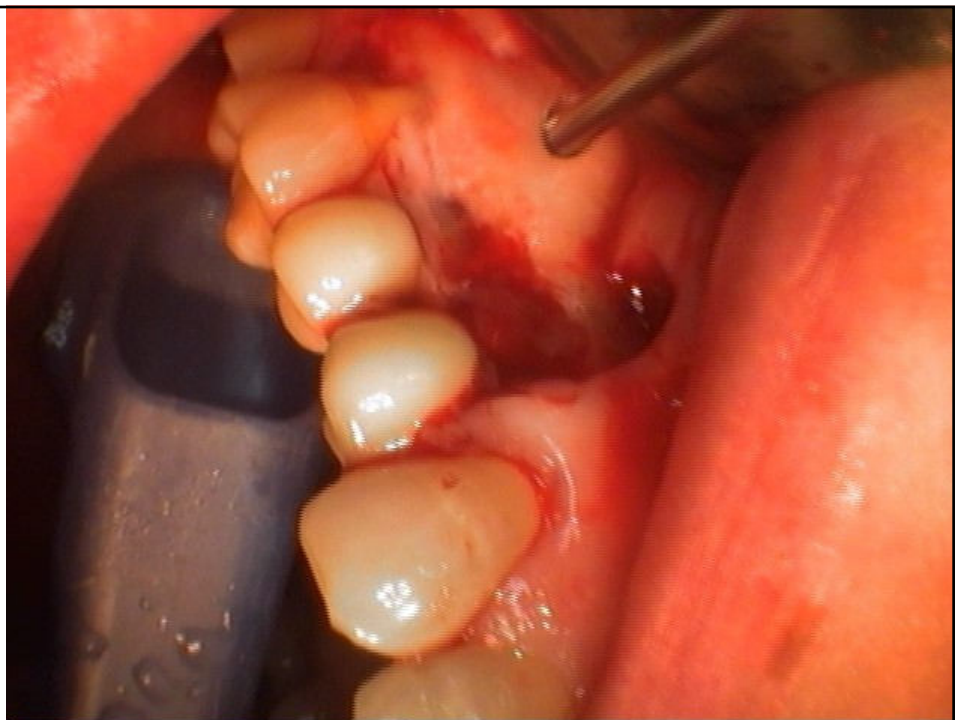
**Ubi pus ibi evacua**

**After degradation of toxins by the [ozonized water-oxygene-jet-spray](#),**

**the degradation products are immediately sucked off, by the strong dental vacuum suction system.**

**This is intended to avoid toxic hazard to the dental staff.**

**There might be produced toxin-degradation products, e.g., which become more toxic than the original toxins.**



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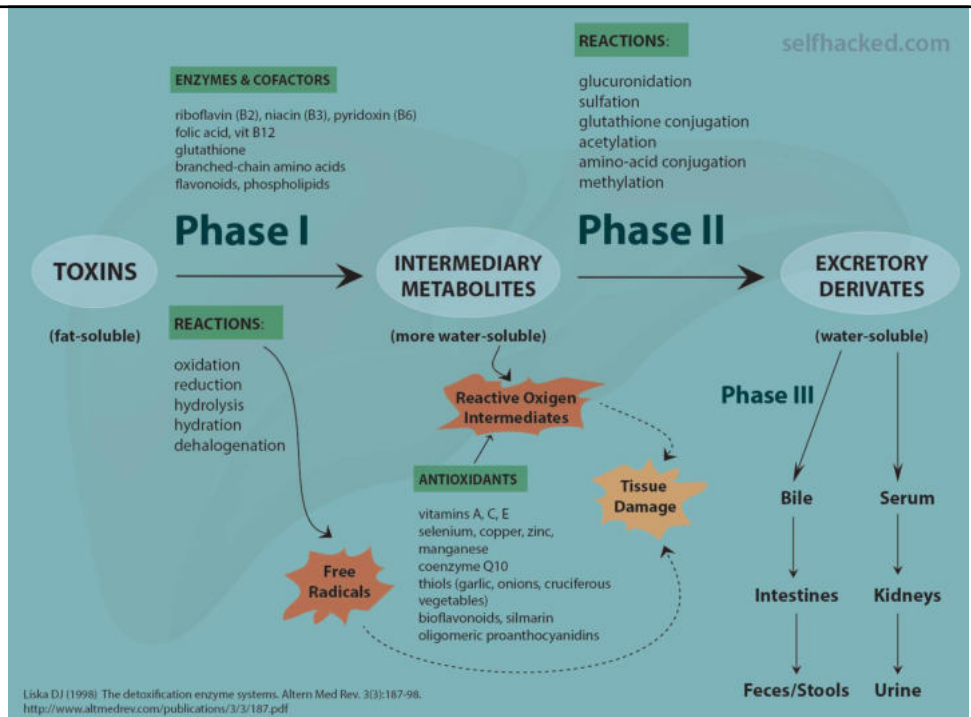


In the following phase 2 of the detoxification process, toxins become conjugated.

The conjugation enzymes like Glutathion-S-transferase are provided by the systemical ozone therapy.

That is why, systemical ozone therapy in form of low dose MAHT a/o RI are obligate.

Cofactors, namely vitamins, trace elements and n-acetylcysteine are substituted.

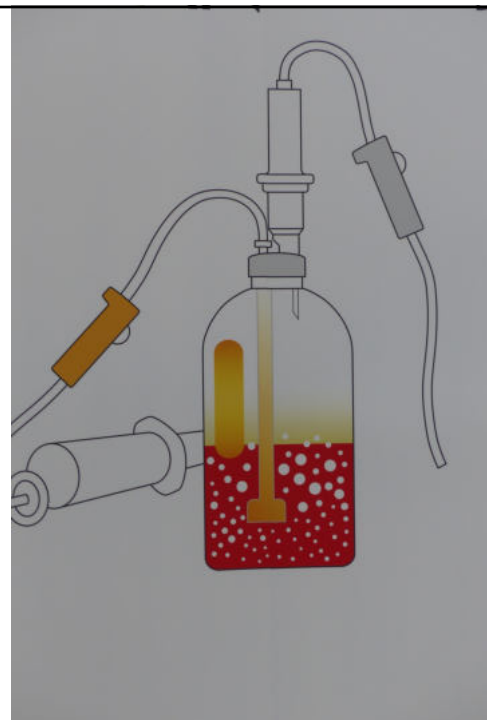


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Without the parallel activation of the phase 2 of the detoxification process, accumulation of toxins and toxic degradation products might occur.

The systemic ozone therapies support the healing, due to their scientifically proven regenerative, immunoregulative, antiinflammatory antihypoxic and analgesic properties.

(Viebahn, Leon, Fahmy, Bocci)



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**Chronic regulation blocking distress in the neurovegetative- and regulative-systems is reduced by the surgical removal of toxine deposits from the oral tissues and the bioregulative stimulus of ozonotherapy.**

**The relief of this chronic distress is the starter of permanent detoxification processes and organoleptic indicators show, that this occurs all over the body.**

**As shown by the examples ozone can only incompletely reach the toxine deposits in the depth of the jaw bone, unless these areas are exposed surgically.**

**Under these circumstances the [ozonized water-oxygen-jet-spray](#) delivered by the cytozone is the indispensable tool for the detection of the toxine deposits by organoleptic analysis and for the removal of these toxine deposits.**

**Because the toxine deposits cannot be diagnosed by x-rays or common clinical diagnostic methods, there is a need of further scientific research with the latest omics analyses.**

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