

Periodontal Health for a Better Life Perio Insight 5 - Autumn 2017

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#### **EXPERT VIEW**

# Current clinical concepts in regenerative periodontal therapy

*Anton Sculean* reviews current knowledge about regenerative periodontal therapy and offers help to clinicians on understanding why, when, and how to use these techniques to improve tooth prognosis.

The main goal of periodontal therapy is to treat the infection caused by periodontal pathogenic biofilm and to arrest or slow down further attachment and bone loss, ultimately preventing tooth loss. Successful treatment is evidenced clinically by a reduction of probing pocket depths (PPD) and a decrease in bleeding scores (i.e. bleeding on probing) along with the reformation of a dentogingival environment that allows effective oral-hygiene measures. These clinical improvements should ideally be accompanied by gain of clinical attachment level (CAL) and radiographic bone-fill.

Even though conventional periodontal therapy – consisting of non-surgical debridement and/or surgical access, including various types of access flaps or tissue-resective techniques – may lead to substantial clinical improvements, residual pockets may either persist or the healing is associated with significant loss of attachment and increase in soft-tissue recessions.

Fig. 1. Histological image depicting periodontal regeneration in an intrabony defect treated with GTR. Formation of cementum (NC), periodontal ligament (NPL), and alveolar bone (NB) coronally to a notch (N) placed on the root at the bottom of the intrabony component, can be observed. Oxone-aldehyde-fuchsin-Halmi staining; x25

It has been shown that deep residual probing depths in treated patients represent a risk indicator for the progression of periodontitis. In addition, deep residual pockets associated with the presence of intrabony defects or Class-II and Class-III furcation involvements have been strongly associated with increased risk for tooth loss. Consequently, one of the clinically most important goals of periodontal therapy is the reduction or complete eradication of deep pockets (i.e. of sites ≥ 6 mm) and elimination of furcation defects.

Ideally, treatment of intrabony and furcation defects should result not only in probing-depth reduction, gain of clinical attachment, and radiographic bone-fill, but also in defect closure via periodontal



regeneration (i.e. formation of root cementum, periodontal ligament, and alveolar bone).

The rationale for integrating regenerative/ reconstructive protocols in the overall treatment concept is supported by findings from clinical studies that show generally larger clinical improvements following such

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**Fig. 2.** Histological image depicting periodontal regeneration in an intrabony defect treated with OFD. The healing is predominantly characterised by a long junctional epithelium (LJE) and limited formation of cementum (C), periodontal ligament (PL), and bone (B), coronally to a notch (N). Hematoxylin and eosin staining; x25





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approaches when compared to conventional treatments, such as open-flap debridement (OFD).

Furthermore, since regenerative periodontal surgery, is a nonresective approach, it may also offer superior aesthetic outcomes when compared to conventional or pocket resective protocols.

In recent decades, a plethora of clinical protocols have been shown to enhance periodontal regeneration and to improve the clinical outcomes in intrabony and in class-II furcation defects. These include:

- the use of various surgical techniques in conjunction with the implantation of bone grafts/bone substitutes;
- ► root-surface demineralisation;
- guided tissue regeneration (GTR);
- growth and differentiation factors;
- enamel matrix derivative (EMD);
- various combinations of the above.

Findings from preclinical and clinical studies have shown that from a biological point of view, the following factors are of pivotal importance for obtaining periodontal regeneration:

 wound stability to allow undisturbed blood clot adhesion and maturation on the instrumented root surface;

- space provision to enable formation and maturation of periodontal tissues;
- uneventful healing (e.g. without bacterial infection), to support maturation of newly formed tissues.

Therefore, treatment concepts aiming to provide a clinical benefit should be based on a sound biological rationale incorporating not only the use of regenerative materials, but also taking into consideration the defect's innate healing potential.

This article presents a brief review on our current knowledge in regenerative periodontal therapy and provides help for the clinician in the decision-making process on why, when, and how to use these approaches to improve tooth prognosis.

#### Bone grafts and bone substitutes

The use of bone grafts or bone substitutes assumes that these materials may facilitate the formation of new connectivetissue attachment and bone regrowth. Indeed, bone grafts or bone substitutes may result in larger PPD reduction and CAL gain compared to conventional periodontal surgery. A recent systematic review of human histological studies confirmed that some small amounts of periodontal regeneration can be achieved after implantation of autogenous bone, demineralised freezedried allogenic bone, and deproteinised bovine bone in intrabony defects.

Furthermore, it has also been recognised that implantation of various types of bone grafts or biomaterials into different types of periodontal defects does not predictably lead to periodontal regeneration but rather to the formation of a long junctional epithelium and encapsulation of the graft/ biomaterial particles in soft connective tissue.

It can thus be concluded that the mere implantation of bone grafts or bone substitutes alone into periodontal defects with the aim of enhancing periodontal regeneration should be avoided despite the possible clinical improvements. At present, the main rationale for using bone grafts or bone biomaterials in regenerative periodontal therapy is to serve as a carrier for biologics (e.g. growth factors, enamel matrix derivative) and/or to prevent a collapse of the mucoperiosteal flap, thereby

ensuring the needed space for the regeneration process.

#### Guided Tissue Regeneration (GTR)

A proven concept that has been shown to result in periodontal regeneration is guided tissue regeneration (GTR), which involves the placement of a mechanical barrier to exclude epithelial cells and gingival connective-tissue cells from the wound area, thus creating a secluded space to be populated by periodontal ligament and bone cells, which can regenerate the attachment apparatus of the tooth. Substantial evidence from animal experiments and human histological studies have validated this concept in intrabony and furcation defects, suggesting that the clinical improvements observed after GTR treatment largely reflect periodontal regeneration (Fig. 1). In contrast, treatment with OFD is predominantly characterised by a long junctional epithelium and limited formation of cementum, periodontal ligament, and bone (Fig. 2).

The first generation of nonresorbable e-PTFE membranes was associated with certain disadvantages, primarily related to the need for a second surgical intervention to remove the barrier, but also to a high risk of membrane exposure and subsequent bacterial contamination or even infection. To overcome these shortcomings, various natural or synthetic bio-absorbable materials have been developed, and comparable histological and clinical outcomes can generally be expected with non-bioresorbable and bioresorbabale membranes.

Evidence from clinical studies indicates statistically significantly higher CAL gains, PPD reductions, and fewer gingival recessions in intrabony and Class-II furcation defects following treatment with GTR,



Fig. 3. Preoperative radiograph of an intrabony defect



Fig. 4. Intraoperative view demonstrating a deep 3-wall defect



Fig. 5. X-ray demonstrates an almost complete radiographic defect fill at one year after therapy with of OFD and EMD.



compared to those achieved following conventional periodontal surgery (openflap debridement, OFD). It has, however, also been demonstrated that the number of residual bony walls significantly influences the outcomes (i.e. the larger the number of residual bone walls the better the clinical result). Generally, narrow and deep defects respond better to treatment than wide and shallow ones.

Moreover, mandibular and maxillary molar class-II buccal-furcation defects benefit more after GTR in terms of horizontal CAL and probing-bone-level (PBL-H) gain than following OFD. Thus, from a clinical point of view, a larger number of Class-II furcations can change to Class I after GTR treatment compared to OFD. This seems to be an important outcome, since it has been shown that teeth with Class-I furcation have an excellent survival rate in the long term similar to that of teeth without furcation involvement. In general, Class-II furcation defects in mandibular molars and buccal sites of maxillary molars respond better to GTR therapy than interproximal furcations. This is most probably because of the technical difficulties in efficiently cleaning interproximal furcations and accurately applying the membrane in the interdental spaces. However, in Class-III furcations, GTR treatment yielded poor results, and they thus represent a contraindication for GTR.

Several studies have demonstrated that the clinical improvements obtained with GTR can be maintained on a long-term basis in intrabony and furcation defects using nonbioresorbable and various types of bioresorbable membranes. Important parameters for longterm stability are not smoking, a high level of oral hygiene, and regular attendance of supportive periodontal therapy.

#### Enamel matrix proteins

The discovery of enamel matrix proteins (EMPs) and their role in the formation of root cementum, periodontal ligament, and alveolar bone during tooth development represents the biological basis for their use in regenerative periodontal therapy. In the clinical setting, EMPs are used in the form of an enamel matrix derivative (EMD) on a prophylene-glycol-alginate carrier. A plethora of studies have demonstrated the biological potential of EMD/ EMPs, suggesting that they may promote periodontal wound healing and regeneration through a wide variety of effects such as cell proliferation and differentiation, biosynthesis of extracellular matrix, angiogenesis, and mineralisation of cementum and bone. Additionally, in vivo and in vitro studies have shown that proliferation of epithelial cells may be inhibited by EMD.

Histological findings in animals and humans have

provided evidence for periodontal regeneration in intrabony defects following the application of EMD in conjunction with access-flap surgery. Clinically, the use of EMD in conjunction with OFD can lead to substantial PPD reduction, CAL gain, and radiographic bone fill in intrabony defects (Figs. 3, 4, and 5). Generally, in twoand three-walled intrabony defects, the obtained clinical improvements are in the range of those obtained with GTR. On the contrary, in one-walled, non-contained intrabony defects. the use of a titaniumreinforced ePTFE barrier yielded significantly higher CAL gains and less residual PPD compared to the use of EMD, which points to EMD's lack of space-providing capacity.

In Class-II mandibular furcations, the application of EMD resulted in clinical improvements comparable to those obtained with GTR, while in interproximal furcations in maxillary molars a significantly

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larger number converted into Class I after EMD compared with conventional surgery. Nevertheless, careful case selection seems important and the presence of proximal bone to the level of the fornix, thick gingival phenotype, and (adequate) keratinsed tissue seem to improve the outcome. Furthermore, EMD does not predictably lead to substantial clinical improvements in teeth with Class-III furcation involvement.

From a clinician's point of view, it is important to point to the fact that fewer postoperative complications were reported following the use of EMD than with GTR. As with GTR, the clinical improvements obtained with EMD can be preserved on a long-term basis. However, the combination of EMD and GTR has failed to show any additional benefit compared to the use of EMD or GTR alone.

## Combination approaches

Several experimental and clinical studies have indicated that the success of regenerative periodontal therapy is limited by the available space under the mucoperiosteal flap. Particularly in non-contained intrabony defects, various combination protocols including the use of bone grafts or bone biomaterials combined with either GTR or EMD has been proposed. Evidence from preclinical and clinical studies indicates that combination approaches may offer certain advantages in non-contained or large intrabony defects and Class-II furcations. It should, however, be kept in mind that in cases where a combination approach is adopted, the main rationale for the use of bone grafts or bone biomaterials is to ensure space provision, while periodontal regeneration is promoted using a membrane, EMD, or other biologicals (e.g. growth factors).

# GDFs and autologous blood concentrates

During the last three decades, a variety of growth and differentiation factors (GDFs) – such as plateletderived growth factor (PDGF), acidic and basic fibroblast growth factors (a/bFGF), and bone morphogenetic proteins (BMPs) – and various formulations of autologous blood concentrates have been evaluated for their potential to support periodontal wound healing and regeneration.



"The clinical improvements after regenerative treatment can be preserved on a long-term basis in most treated sites"

Human histological studies have shown periodontal regeneration in intrabony defects treated with either GDF5 or rhPDGF-BB on a beta-tricalcium phosphate (b-TCP) carrier while the combination of rhPDGF-BB and DFDBA resulted in robust and consistent periodontal regeneration.

Platelet Rich Plasma (PRP) is an autologous concentration of growth factors derived from typical platelets following centrifugation to reach super-natural concentrations. PRP has been utilised for several decades by clinicians for various indications in periodontal and oral surgical procedures. As PRP possesses limited space-provision potential, it has been used mainly in combination with bone grafts or substitutes. At present, the available data do not seem to support a clinical benefit following the use of PRP in regenerative periodontal therapy.

Recently, novel preparations of autologous blood concentrates (e.g. platelet-rich fibrin) have been suggested as being more beneficial - compared to PRP - in enhancing periodontal wound healing and regeneration. The preparation of platelet-rich fibrin (PRF) is easier as it does not require the use of anticoagulant, bovine thrombin, or calcium chloride. A recent systematic review including meta-analysis has evaluated the clinical outcomes following the additional use of L-PRF alone (e.g. without any addition of bone graft or membrane) in conjunction with OFD in intrabony and Class-II furcation defects as compared to OFD alone (Castro et al. 2017). The results have shown statistically significantly higher PD reductions, CAL gains, and bone-fill when L-PRF was used, thus pointing to the positive effect of this approach on periodontal



#### Fig. 7. Decision tree for regenerative therapy in furcation defects

wound healing. However, it should be noted that there is, at present, no histological evidence demonstrating periodontal regeneration following the use of PRF.

Even though from a biological point of view the use of GDFs and autologous blood concentrates are of potential interest, further controlled clinical studies are needed to evaluate their potential benefit over the already established protocols.

# Decision-making process

The most important steps to be considered when performing regenerative periodontal therapy in intrabony and furcation defects are summarised in Figures 6 and 7.

Several factors such as level of oral hygiene, smoking, and baseline tooth mobility have been shown to negatively influence the outcomes of regenerative therapy GTR. Therefore, besides controlling for oral hygiene and smoking status, mobile teeth should be splinted before regenerative treatment. It has been also shown that endodontically treated teeth are not a contraindication for a regenerative approach, provided that the root-canal treatment is of an optimal quality.

The selection of the appropriate surgical approach including various modifications of papilla-preservation flaps such as the modified or simplified papilla-preservation flap (MPPF/SPPF), single buccal flap, or minimally invasive surgical techniques (MIST) - and the use of microsurgical instruments and optimal magnification ensures access to the defect and thorough removal of calculus and bacterial biofilm from the root surfaces. At the same

time, this minimises the risk of traumatising the soft tissues. The decision for selecting the appropriate regenerative material or various combinations is made after careful evaluation of defect anatomy (i.e. non-contained or contained defects) to ensure space provision and wound stability. The selection of the appropriate suturing technique to obtain tensionfree primary wound closure and postoperative infection control (including the use of antiseptics) are mandatory steps that decisively influence the early wound healing and, consequently, the final outcomes.

The clinical improvements after regenerative treatment can be preserved on a long-term basis in most treated sites, provided patients do not smoke, maintain high oral-hygiene standards, and regularly attend supportive periodontal treatment.

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#### Anton Sculean

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**FOCUS** 

# **Søren Jepsen** describes challenge of creating EuroPerio9 scientific programme

The EuroPerio9 congress, which takes place in Amsterdam in June 2018, is expected to attract up to 10,000 people to hear the latest insights in periodontal research and clinical practice. Søren Jepsen, scientific chair of EuroPerio9, outlines a scientific programme that features more than 100 speakers in the main programme and many innovations including live surgery, a debate, and the "nightmare session".

What have been the main challenges in putting together a programme with so many speakers?

First, it must all be new, and it is quite a challenge to avoid repeating what has been done before. Second, the EFP is a federation, so all 30 national societies were invited to send their proposals for topics and speakers according to criteria we had provided. They submitted about 400 proposals, but we could accommodate only about 100. We have such a big pool of talented speakers in Europe, and – unfortunately - we cannot take them all. We also wanted to have more women speakers and more younger speakers, but without neglecting the well-established experienced speakers – the stars. It is very painful to leave out people who deserve to be there. Also, we have to invite speakers from smaller countries as well the big ones. And, of course, we invite various speakers from

outside Europe - so we end up with having most of the best speakers in the world. So, for me and the fantastic team that makes the EuroPerio9 organising committee, it's all a huge balancing act.

How have the EuroPerio congresses evolved and what have you learnt from the previous ones? What has changed most is the size of the meeting – from less than 6,000 in Madrid (EuroPerio5, 2006) to almost 10,000 in London (EuroPerio8, "We wanted to have more women speakers and more younger speakers"

2015). Also, we now have a global audience – there were people from 106 countries at EuroPerio8 – so it is no longer a pure European congress. And we see more and more young people in the audience.

#### WEDNESDAY, JUNE 20, 2018

preliminary programme overview as per July 2017





- Sponsor Workshop
- Sponsor Session





Members of the EuroPerio9 organising committee

There are now so many abstract submissions from people who want to present their work in short oral presentations or posters. This is something we have learnt from London, where there were many more than anticipated and it was difficult to accommodate all of them. So, this time we are scheduling twice as many sessions for this type of presentation. By the December 5 deadline, a record 1,746 abstract submissions had been received, compared to 1,614 three years ago.

We are following the same structure used in London and in Vienna (EuroPerio7, 2012) with four parallel tracks of presentations. And we are keeping the balance between perio and implant topics the same – about two thirds to one third, although some sessions combine the two. What we did not continue is the separate track for dental hygienists. We had meetings with hygienists' societies and they told us "we feel ourselves to be part of the team". So, we have created the Team Session track instead it's more inclusive. We have also expanded the programme by

having more sessions on the Wednesday afternoon (before the official opening ceremony), and we have added some new formats.

What are these new formats? There are eight new formats, starting with the joint meeting with the Japanese Society of Periodontology on the opening day. Our Japanese colleagues approached us about having a special session with us, so this is a way to reach out to the East and attract more people from that part of the world. There will be two sessions - one on biofilm and antiinfective therapy, the other on regenerative periodontal and implant therapy.

Also on the Wednesday is the EFP Alumni Symposium with the Perio Talks given by alumni and current students of the EFP-accredited postgraduate programmes in periodontology. This will be the first formal gettogether of the EFP Alumni and the talks will be very attractive to younger people – the future of European periodontology.

Then we have the debate about the use of antibiotics.

As well as the two sides of the arguments – presented by Andrea Mombelli and David Herrera – there will be engagement with the audience, most likely through a special congress app that allows your smartphone to function as a voting device.

Next is live periodontal/ peri-implant surgery, which has not been done before at a EuroPerio congress. This will be carried out by Giovanni Zucchelli and Martina Stefanini at the ACTA dental school and transmitted in real time to the audience in the auditorium. You need a surgeon who is selfconfident and self-composed and willing to do this - and I am very confident with this team. The type of surgery is most likely to be a new procedure on implants that has not been performed very often.

Another important innovation is the interdisciplinary treatment-planning session, where cases will be shown and different options for treatment will be discussed by experts from different speciality areas of dentistry. This is interactive too – we will get the audience onboard with their opinions, via some voting. There will be a 3D session on reconstructive surgery at teeth and implants. We tested 3D at Vienna, but here we will have a much bigger auditorium. It's like an old movie theatre, with very comfortable chairs. It will be packed, for sure.

On the final day there will be the EFP Perio Contest, a new part of the programme proposed by Journal of Clinical Periodontology editor Maurizio Tonetti, in which presentations will be judged not only by an expert jury but also by social-media voting before



EuroPerio9. The three final contestants will then be invited to present their work on stage in Amsterdam and the winner will be selected – once again with the audience involved.

Finally, we have the dramatically named "Nightmare Session" in which Mario Roccuzzo, Giulio Rasperini, Jean-Louis Giovannoli, and Caroline Fouque will explore treatments that went badly – in periodontal plastic surgery, regenerative surgery, and in the treatment of peri-implantitis. You need to be an outstanding clinician - someone with a lot of experience and selfconfidence – to stand and up show your failures. But there is so much you can learn from your mistakes. This is going to be fantastic. Let's go for it!

# Latest research

### Clinical Periodontology

#### PERIODONTAL DISEASES

#### Association of flossing and inter-dental cleaning and periodontitis in adults

The aim of this cross-sectional study was to assess the association of flossing with periodontitis, using the National Health and Nutrition Examination Survey (NHANES) for 2011-2014. It used the CDC definition of periodontitis and three categories of flossing: those who did not floss or who flossed only one day during the previous week, those who flossed on two to four days, and those who flossed on five or more days.

The study included 6,939 adult subjects, of whom 35% flossed once or more each week and 40% had periodontitis. After adjustment, the odds of periodontitis were 17% lower for subjects who flossed more than once a week than for subjects who flossed less often (odds ratio=0.83, 95% CI 0.72-0.97). A dose response was not observed.

Researchers concluded that flossing was associated with a modestly lower prevalence of periodontitis. Older age, being male, smoking, low income, and less-frequent dental visits were associated with a higher prevalence of periodontitis. Flossing between two and four days a week could be as beneficial as flossing more frequently.

Authors: M. Soledad Cepeda, Rachel Weinstein, Clair Blacketer, Michael C. Lynch.

Published in Journal of Clinical Periodontology, Volume 44, Number 9 (September 2017)

S Full article: http://onlinelibrary.wiley. com/doi/10.1111/jcpe.12765/full

#### PERIODONTAL THERAPY

#### Clinical and microbiological effects of the adjunctive use of probiotics in the treatment of gingivitis: A randomised controlled clinical trial

This placebo-controlled clinical trial evaluated the efficacy of a probiotic combination in the treatment of gingivitis and assessed its impact on the subgingival microbiota. The trial took place over six weeks with 59 patients (29 tests, 30 placebos). Test treatment consisted of the administration of two oral tablets per day containing the probiotic strains Lactobacillus plantarum, Lactobacillus brevis, and Pediococcus acidilactici; the control group received similar tablets but without live bacteria.

Both treatment groups experienced a statistically significant improvement in mean GI (p < .0001), but no differences between treatment groups were found for any clinical index. A significantly higher reduction in the number of sites with higher GI scores (GI = 3 at baseline) was observed in the test group,

while in subgingival samples, a significant reduction in *T. forsythia* was significant only in the test group (p<.008).

The trial concluded that using probiotic tablets did not lead to significant changes in mean GI. However, a significant reduction occurred in the number of sites with severe inflammation and the adjunctive use of this probiotic promoted a significant microbiological impact.

Authors: Eduardo Montero, Margarita Iniesta, Marta Rodrigo, María José Marín, Elena Figuero, David Herrera, Mariano Sanz.

Published in Journal of Clinical Periodontology, Volume 44, Number 7 (July 2017).

S Full article: http://onlinelibrary.wiley.com/ doi/10.1111/jcpe.12752/full

in the XCM group and 1.2 ± 0.3 mm in the CTG group,

with a significant difference favouring the control

group (0.3 mm; p = .0001). Both procedures resulted in similar final KT amount with no significant

difference between treatments. In conclusion, CTG

was more effective than XCM in increasing buccal

Authors: Francesco Cairo, Luigi Barbato, Paolo

Tonelli, Guido Batalocco, Gabriella Pagavino,

Published in Journal of Clinical Periodontology,

S Full article: http://onlinelibrary.wiley.com/

peri-implant soft-tissue thickness.

Volume 44, Number 7 (July 2017).

doi/10.1111/jcpe.12750/full

#### **IMPLANT THERAPY**

Xenogeneic collagen matrix versus connective tissue graft for buccal soft-tissue augmentation at implant site. A randomised, controlled clinical trial

This randomised clinical trial compared xenogeneic collagen matrix (XCM) with connective tissue graft (CTG) for increasing buccal soft-tissue thickness at implant sites.

Soft-tissue augmentation with XCM (test) or CTG (control) was performed at 60 implants in 60 patients at the time of implant uncovering. Measurements were performed by a blinded examiner at baseline, three, and six months. Outcome measures included buccal soft-tissue thickness (GT), apico-coronal keratinized tissue (KT), chair time, and postoperative discomfort. Visual Analogue Scale (VAS) was used to evaluate patient satisfaction.

After six months, the final GT increase was  $0.9 \pm 0.2$ 

Partners





Michele Nieri.







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**Ukraine** Асоціація лікарів-пародонтологів

et d'Implantologie

Ассоциации

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	<b>France</b> Société Française de Parodontologie et d'Implantologie Orale
	<b>Germany</b> Deutsche Gesellschaft für Parodontologie
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	Hungary Magyar Parodontológiai Társaság Ireland Irish Society of Periodontolgy
	Ireland Irish Society of Periodontolgy
\$	<b>Israel</b> Israeli Society of Periodontology and Osseointegration
	<b>Italy</b> Società Italiana di Parodontologia e Implantologia
	<b>Netherlands</b> Nederlandse Vereniging voor Parodontologie
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	Poland Polskie Towarzystwo Periodontologiczne
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	<b>Romania</b> Societatea de Parodontologie din Romania
ġ	Serbia Udruzenje Parodontologa Srbije
÷	<b>Slovenia</b> Združenje za ustne bolezni, parodontologijo in stomatološko implantologijo
<u>å</u>	<b>Spain</b> Sociedad Española de Periodoncia y Osteointegración
-	Sweden Svenska Parodontolog föreningen
+	Switzerland Société Suisse de Parodontologie / Schweizerisch Gesellschaft für Parodontologie / Società Svizzera di Parodontologia
C+	Turkey Türk Periodontoloji Dernegi
×	United Kingdom British Society of Periodontology
EFF	associate-member societies
(1	<b>Azerbaijan</b> Azərbaycan Parodontologiya Cəmiyyəti
	Lithuania Lietuvos Periodontolog Draugija
*	Morocco Société Marocaine de Parodontologie