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REVIEW

Annual review of selected scientific literature: A report of the Committee on Scientific Investigation of the American Academy of Restorative Dentistry

Terence E. Donovan, DDS,[a] Riccardo Marzola, DDS,[b] Kevin R. Murphy, DDS, MS,[c] David R. Cagna, DMD,[d] Frederick Eichmiller, DDS,[e] James R. McKee, DDS,[f] James E. Metz, DDS,[g] Jean-Pierre Albouy, DDS, PhD,[h] and Mathias Troeltzsch, MD, DMD[i]

ABSTRACT

Problem. There are countless numbers of scientific studies published in countless scientific journals on subjects related to restorative dentistry.

Purpose. The purpose of this article is to review pertinent scientific studies published in 2017 on topics of interest to restorative dentists.

Methods and materials. The authors, considered to be experts in their disciplines searched the scientific literature in 7 different areas (prosthodontics, periodontics, dental materials, occlusion and temporomandibular disorders, sleep-disordered breathing, oral medicine and oral and maxillofacial surgery and dental caries). Pertinent articles were either identified and referenced or reviewed.

Results. A total of 437 articles in 7 disciplines were identified or reviewed.

Conclusions. An impressive amount of scientific literature related to restorative dentistry was published in 2017. The evidence presented in this article can assist dentists in the practice of contemporary evidence-based dentistry. (J Prosthet Dent 2018;120:816-78)

PROSTHODONTICS

In 2017, professional literature germane to the clinical practice of prosthodontics was published at an astounding rate. The annual content of over 50 professional journals was searched in its entirety to arrive at this review intended to provide readers with a general clinical update. For convenience, prosthodontics has been divided into 8 subtopics: general prosthodontic considerations, conventional removable complete prosthodontics, conventional removable partial prosthodontics, conventional fixed prosthodontics, general implant prosthodontic considerations, implant removable prosthodontics, implant-fixed prosthodontics, and prosthodontic materials. In addition to the articles selected for review, a sizable volume of excellent general reviews, systematic reviews, meta-analyses, and helpful clinical descriptive materials were also published on topics of prosthodontic interest. Although it would be impractical to provide detailed comments on this voluminous additional material, it is listed here for the reader's convenience: clinical processes,[1-7] anatomy and physiology,[8-20] biomechanics,[21] bruxism,[22-25] conventional complete dentures,[26-28] conventional fixed prosthodontics,[29-33] conventional removable partial prosthodontics,[34-36] diagnosis,[37-43] digital dentistry,[44-47]

[a]Chair for Committee on Scientific Investigation (AARD), Professor, and Chair for Biomaterials, Department of Operative Dentistry, University of North Carolina School of Dentistry at Chapel Hill, NC.
[b]Private practice, Ferrara, Italy.
[c]Private practice periodontics and prosthodontics, Baltimore, Md.
[d]Associate Dean, Professor, and Director, Advanced Prosthodontics, University of Tennessee Health Sciences Center, Memphis, Tenn.
[e]Executive Director, Delta Dental, Stevens Point, Wis.
[f]Private practice, Downers Grove, Ill.
[g]Private practice, Columbus, Ohio.
[h]Private practice, Montpellier, France.
[i]Private practice oral and maxillofacial surgery, Ansbach, Bavaria, Germany.

esthetics,[48-55] evidence-based dentistry,[56-68] general topics in implant dentistry,[69-81] general topics in prosthodontics,[82-85] geriatrics,[86-99] implant-supported fixed prosthodontics,[100-108] implant-assisted removable prosthodontics,[109-117] implant surgery,[118-122] maintenance,[123] mastication,[124-126] materials science,[127-137] occlusion,[138] pathology and disease,[139-152] peri-implant conditions,[153-170] pharmacology,[171-177] practice considerations,[178-181] preprosthetic surgery,[182-192] radiology,[193-195] statistics,[196-208] temporomandibular disorders (TMDs) and orofacial pain,[209-219] and treatment success/survival.[220-222] Readers may also be interested to know that a ninth edition of the Glossary of Prosthodontic Terms was published in 2017.[223]

General prosthodontic considerations

The accurate use of interocclusal registrations in prosthodontic therapy is essential. Much has been taught and written about best practices (techniques and materials) for the accurate and precise mounting of dental casts in an articulator. Unfortunately, limited evidence and consensus exists to drive such procedures. To clarify the impact of materials on registration procedures, Ghazal et al[224] evaluated articulator condylar element displacements related to various interocclusal recording materials, record storage time, and the interocclusal recording technique used on the condylar element displacements.

Seven groups of 6 different interocclusal recording materials were investigated: Aluwax (aluminum-impregnated wax, double thickness, warm), Beauty Pink Wax (hydrocarbon wax compound, double thickness, warm), Futar D Fast and Futar Scan (polyvinyl siloxane [PVS]), Ramitec (polyether), LuxaBite (composite resin), and LuxaBite corrected with Aluwax (warm). To establish a patient analog, standardized dentate casts were anatomically mounted on a reference articulator (SAM-ASP 350) at maximal intercuspal position. Teeth in maxillary and mandibular right posterior sextants of the patient analog were prepared for occlusal coverage restorations and fixed partial dentures (FPDs). A second articulator (SAM-MPI 515M, a condylar position indicator) was equipped with 6 highly sensitive digital gauges capable of recording 3D condylar element displacements (0.010-mm resolution).

With the casts mounted on the reference articulator, interocclusal registrations were made in the right sextant (using the prepared teeth) at the occlusal vertical dimension. Eight records of each material group were made. All records were stored at room temperature in closed containers. Dental casts were then transferred to the condylar position indicator articulator. At 1 hour and again at 48 hours of storage, interocclusal records were transferred to the casts, and condylar displacements were measured. Two-way ANOVA was used to determine influences of recording materials and each of the following factors: region (record versus nonrecord side), storage time, and recording technique.

At 1-hour storage, vertical condylar displacement on the record side ranged from 0.29 mm (Aluwax) to 0.14 mm (Futar Scan). Lateral displacement ranged from 0.13 mm (Aluwax) to 0.02 mm (Ramitec), whereas anterior-posterior displacement ranged from 0.15 mm (Ramitec) to 0.04 mm (Futar Scan). Generally, reduced displacements were seen with the corrected resin records (0.03, 0.02, and 0.07 mm). In comparison, displacements on the nonrecord side were reduced. For all materials, condylar displacements increased after 48 hours of storage. Both storage time and recording technique had a significant influence on displacement of the articulator's condylar elements.

Within the limitations of the experimental design used, the authors concluded that casts mounted using the materials, techniques, and times investigated may reflect inaccuracies, particularly in a vertical dimension. Elastomers yielded significantly better results, whereas waxes and uncorrected composite resin underperformed. Corrected composite resin records showed the best accuracy. Consideration should be given to mounting casts on the articulator as soon as possible after the clinical interocclusal registration procedure.

Initial diagnostics in complicated prosthodontic rehabilitations often start with an esthetics assessment and concurrent evaluation of the orientation of the planned occlusal plane. In this regard, the transverse occlusal plane (TOP), as viewed from a frontal perspective, is typically paralleled with horizontal references such as the horizon, interpupillary line, and/or commissure line. Diagnostic and visual conflicts may occur when these key reference planes are not coincident. This is particularly true when the smile frame (that is, lip orientation as defined by commissure line) is canted. To address this esthetic concern, Silva et al[225] conducted an online survey of patient preferences (51% women, aged 18 years and older) regarding TOP orientation in faces that display a decided cant of the commissure line as viewed from a frontal perspective.

A digital image of an attractive, facially symmetrical, dentate, smiling, female (control model) was developed to include the TOP and commissure line parallel to both the interpupillary line and horizon. This image was then digitally manipulated to reorient the lips/commissure line to 3-degrees off parallel with the interpupillary line. Then, the dentition/TOP was digitally reoriented to produce 3 distinct experimental models: TOP parallel to interpupillary line; TOP parallel to commissure line; and TOP oriented to the mean between the interpupillary and commissure lines. The 4 images (1 control and 3 experimental) were organized into 6 pairs for direct comparison. Survey participants were asked, "Which face is more attractive?"

The results indicated that most participants considered the control image most attractive. For images displaying a canted commissure line, most participants preferred the TOP cant as well, particularly when the TOP paralleled the canted commissure line. Although dentists may have their own thoughts and strong opinions on appropriate esthetics, a detailed understanding of public perspectives on this issue is most helpful to arrive at congruent plans and mutually acceptable treatment results.

Conventional removable complete prosthodontics

The successful performance of maxillary conventional complete dentures relies, in part, on the prosthesis support, stability, and retention derived from the denture base. Dimensional errors and the potential for suboptimal denture base retention resulting from classical compression molding of heat-activated poly(methyl methacrylate) is well known. Comparison of computer-aided design and computer-aided manufacturing (CAD-CAM) milled to compression-molded poly(methyl methacrylate) denture bases with regard to the critical clinical endpoint of retention would be of interest. AlHelal et al[226] carried out an in vivo investigation to make this direct comparison using a rather unique denture base dislodging protocol.

Twenty maxillary edentulous participants were recruited. Definitive PVS impressions were made using standard procedures. Impressions were scanned, and standard tessellation language (STL) files were exported for CAD-CAM, milled denture base fabrication. The impression was then cast in Type III dental stone. Definitive casts were used to fabricate compression-molded acrylic resin denture bases using a long polymerization cycle. All denture bases were fitted intraorally using standard clinical procedures. A stainless-steel hook was attached to the geometric center of the palate on the cameo surface of each denture base. This hook provided a consistent means of denture base engagement for retention testing. A custom-designed testing device (with digital force gauge, motorized stand, force transmission mechanism, and a facebow) applied a direct vertical dislodging force 3 times at 10-minute intervals to the denture bases in situ.

The results indicated significantly increased retention for milled denture bases compared with conventionally manufactured denture bases. The average retention for the milled bases was approximately 75 N, whereas the average retention for the conventional bases was 55 N.

The authors concluded that the retention offered by complete maxillary denture bases milled from prepolymerized poly(methyl methacrylate) resin was significantly greater than that offered by conventional compression-molded, heat-polymerized denture bases. Milled denture bases might be an appropriate choice when increased retention is desired. The authors identified the short testing interval as a potential limitation of the study. In addition, testing mandibular denture bases using the same protocol might be hampered by the lack of an easily available central dislodging point.

The phrase "computer-engineered complete dentures" (CECD) includes digital and CAD-CAM dentures with fabrication typically initiated by acquiring scan data for design and application, followed by computer numerical control milling and rapid prototyping followed by conventional processing or rapid prototyping followed by printing. The concept of CECD originated in Japan with the first English-language article appearing in the mid-1990s. Although this form of complete denture manufacturing has gained momentum in recent years and reports continue to appear on a regular basis, consensus on clinical outcomes and clinical applications is still lacking. Kattadiyil and AlHelal[227] conducted a systematic review of available professional literature to determine applications and outcomes of CECDs.

The Population, Intervention, Comparison, and Outcome (PICO) questions formulated included the following two questions: What are the clinical outcomes associated with CECD? and Are there specific clinical applications and significant advantages of CECDs? Electronic searches of English-language literature from January 1984 to May 2016 initially yielded 926 titles. Upon application of relevancy and exclusion criteria, 4 articles were identified to address the first PICO question, and 10 articles were identified for the second question.

A review of the acquired articles related to clinical outcomes revealed the potential for significantly better complete denture initial fit and retention, as well as reduced clinical appointment time for milled CECDs, compared with conventional complete dentures. An additional advantage associated with CECDs is the possibility of electronically archiving digital manufacturing directives for future rapid refabrication when needed. Applications reported in the literature with CECDs include remanufacture of denture teeth due to wear, removable-to-fixed conversion prostheses, custom orientation jigs, implant conversion components, monolithic fixed complete dentures, electronic superimposition on cone beam computed tomography (CBCT) to precisely relieve mental foramen impingement, wax trial denture with excellent fit-support-stability-retention during esthetic evaluations, and digitally planned immediate complete dentures.

The authors concluded that although better initial fit and retention, reduced appointment time, and digital archiving are all positive outcomes associated with advancing CECD clinical technology, long-term controlled clinical trials are necessary before definitive conclusions can be reached on CECDs. With continued

clinical implementation of CECDs, the list of clinical applications will undoubtedly grow as well.

Conventional removable partial prosthodontics

Although conventional removable partial dentures (RPDs) provide an affordable and predictable treatment alternative for partial edentulism, they can represent a risk to the remaining dentition, particularly the abutment teeth, if the RPDs are poorly designed, inadequately fitted, undersupported, or inappropriately maintained. Teeth adjacent to RPD components are at increased risk of biofilm, plaque, and calculus formation, as well as unfavorable biomechanical load transmission. However, regular biofilm control and denture hygiene can maintain periodontal health in RPD wearers. Most reports on the periodontal status of abutments and nonabutments in RPD patients focus on clinical parameters. Costa et al[227] addressed both clinical and microbiological parameters of healthy patients after RPD rehabilitation.

Eleven women (mean age: 53.3 years) with dentate maxillae and healthy Kennedy class I or II mandibular residual dentitions were enrolled. RPDs, designed and fabricated using standard procedures, were made incorporating cobalt-chromium frameworks, infrabulge clasps on distal abutments, circumferential clasps on other selected abutments, and lingual or palatal bar major connectors. All participants received pretreatment prophylaxis and dental hygiene instructions.

Abutments that served in direct or indirect prosthesis retention were identified as experimental teeth, whereas all other mandibular and maxillary teeth served as controls. Microbiologic sampling (subgingival paper point biofilm collection) was related to clinical data collection (probing depth, gingival recession [GR], bleeding on probing [BOP]) that occurred at 5 different time points (prosthesis placement and 7, 30, 90, and 180 days of functional loading). Checkerboard DNA-DNA hybridization was used to identify and quantify up to 43 different microbial species from subgingival biofilm samples.

The total and individual microbial genome counts significantly increased at 180 days with no significant differences between experimental and control teeth. *Prevotella melaninogenica* presented the highest incidence in all the sampling periods. *Streptococcus* species, *Aggregatibacter actinomycetemcomitans*, and other species associated with periodontitis (*P anaerobius*, *P nigrescens*, and *Tannerella forsythia*), as well as opportunistic *Candida* species, were recovered in moderate counts. Experimental teeth demonstrated greater GR than control teeth, irrespective of sampling time. No significant BOP or probing depth differences were found between groups over time.

In summary, both total and individual microbial counts increased after 6 months of wearing the denture in abutment and nonabutment teeth, with no differences in microbial profiles over time. The increased microbial count at 6 months highlights the need for continued hygiene instruction and controlled oral and denture hygiene maintenance over time. No differences in BOP or probing depth were identified between the groups over time, whereas GR increased for abutment teeth. The authors cautioned against generalizing these results due to the small number of study participants, the inclusion of only 2 different RPD types, and the limited duration of experimental observation.

The profession's initial foray into computer-engineered RPDs suffered because early CAM methods relied exclusively on subtractive processes. When milling processes were used, the fabrication of complex RPD frameworks resulted in the deformation or fracture of relatively thin elements. More recently, rapid prototyping additive manufacturing has been successfully applied to RPD metal framework fabrication. The coincident development of compatible CAD software has rendered CAD/rapid prototyping systems capable of resin pattern development for conventional casting and direct fabrication of metal RPD frameworks. Unfortunately, comparisons of CAD/rapid prototyping metal frameworks with conventionally manufactured metal frameworks are lacking. With this in mind, Ye et al[228] explored the CAD/rapid prototyping RPD framework processes and compared outcomes with conventional processes.

Fifteen relatively healthy, partially edentulous patients (6 men and 9 women, age: 41-79 years) were enrolled in the study. The planned RPDs had the following design characteristics: 6 maxillary, 9 mandibular, 8 Kennedy class I, 3 class II, 3 class II, 1 class IV, and a total of 40 occlusal rests. After standard tooth preparation for planned prostheses, 2 PVS definitive impressions were made and cast in dental stone. Casts were randomly distributed to the CAD/rapid prototyping experimental group (scan plus digital survey and design plus selective laser metal melting) or the conventional control group (manual survey and design plus wax-invest-heat metal casting). All frameworks were manufactured from the same cobalt-chromium alloy and then finished and polished using standard techniques. A single, blinded prosthodontist was responsible for all framework evaluations and adjustment clinical appointments.

Primary fit evaluation was accomplished by 3 additional prosthodontists who visually assessed and scored framework fit using established criteria. Secondary fit evaluation used low-viscosity PVS to disclose potential vertical space between rests and rest seats on complete framework placement. Resulting PVS fit records were evaluated under low-power stereomicroscopy to identify record perforations (indicative of rest-to-rest seat contact) or record thickness (indicative of rest-to-rest seat noncontact).

Experienced observers judged all frameworks to have clinically acceptable fit, with rests visibly contacting rest seats and critical framework elements appropriately related to corresponding anatomic surfaces. Framework movement could not be detected on clinical force application to rests. Based on PVS fit records, acceptable rest-to-rest seat fit (<50 μm) was identified in 42.5% of the CAD/rapid prototyping frameworks and 72.5% of the conventional frameworks. The mean thickness of rest-to-rest seat fit records for CAD/rapid prototyping frameworks (174 μm, range: 41 to 546 μm) was significantly greater than that for conventional frameworks (108 μm, range: 17 to 369 μm).

The authors concluded that CAD/rapid prototyping using selective laser metal melting is a viable alternative to conventional RPD manufacturing. Despite statistically inferior fit dimensions, clinically acceptable fit, as judged by expert observers, may indicate good use in the future. Additional clinical trials and improvements in CAD/rapid prototyping processes are necessary.

Conventional fixed prosthodontics

Traditionally, conventional fixed prosthodontic restorations may be predictably retained when tooth preparations provide optimal resistance and retention form, restorations are well adapted to the preparation surfaces and finish lines, a suitable cement is appropriately used, and complete restoration seating is achieved during placement. The profession has decades of experience with lost-wax casting and the expectation of exceptional fit for conventional cast metal–fixed prosthodontic restorations. However, a fit comparison is lacking between conventional metal complete-coverage frameworks and frameworks manufactured with newer CAD-CAM technologies. Using cement space as an indicator of crown fit, Dahl et al[229] carried out an in vitro comparison between traditional lost-wax cast metal frameworks and frameworks produced with 5 different digital technologies.

The left central incisor on a maxillary dentate model was prepared to receive an esthetic crown. The model was scanned, and the resulting STL file was exported for CAD-CAM processing. From the single STL file, 3 experimental framework replicates from 5 different manufacturing processes were made: milled presintered zirconia; milled hot-isostatic-pressed zirconia-dioxide; milled lithium disilicate–reinforced glass-ceramic; milled cobalt-chromium metal alloy; and laser-sintered cobalt-chromium metal alloy. Then, 3 PVS impressions were made of the maxillary model, and standard lost-wax laboratory processing was used to produce 3 control cobalt-chromium single crown metal frameworks (no veneering porcelain was applied). A total of 18 frameworks were available for comparisons. Using a triple-scan experimental protocol, scans were made of the master model, each framework on the master model, and the intaglio surfaces of each framework. Scans were digitally combined using an appropriate software program, and cement space was evaluated.

The results indicated that all restorations made with CAD-CAM technology had significantly greater cement space than conventional frameworks produced by lost-wax metal casting. The greatest average maximum cement space was calculated for the milled presintered zirconia group, and the lowest maximum cement space was seen in the cast cobalt-chromium group.

The authors concluded that the accuracy of fit for single-unit complete coverage frameworks, as indicated by minimal cement space, appears to be improved for conventional lost-wax metal casting compared with newer CAD-CAM technologies. Of the 3 different production technologies investigated, the least cement space was identified for lost-wax metal casting, followed by laser sintering and milling. Studies involving a greater number of specimens are needed. In addition, further investigation is required to establish the triple scan protocol as a preferred methodology to assess restoration adaptation.

The decision to provide prosthodontic replacement for a single missing mandibular first molar is based on several factors including the condition of available hard/soft tissues, condition of adjacent teeth, available restorative space, hygiene access, and patient wishes. Unfortunately, limited data are available, indicating whether masticatory performance or patient satisfaction is a factor that should be considered. The objective of a study published by Kumar et al[230] was to determine whether masticatory performance and patient satisfaction differed when a single missing mandibular first molar was replaced by a FPD or a single implant crown.

One hundred and twenty healthy participants missing only mandibular right first molars and who fulfilled inclusion criteria were enrolled in the study. After obtaining consent, 60 individuals were randomized to the tooth-supported FPD group (treatment duration: 2 to 3 weeks) and 60 to the implant crown group (treatment duration: 26 weeks). Three months after restoration placement, data collection was accomplished using a Likert-scale, self-developed, close-ended, bounded, prevalidated, satisfaction questionnaire, and the evaluation of right-side masticatory performance and efficiency using a functional sieving protocol was performed. Satisfaction was assessed on 7 items: overall satisfaction, esthetics, speech, function, cleansability, treatment duration, and willingness to undergo similar treatment again. Masticatory performance was calculated as the volume percentage of peanuts, at 20 mastication strokes, pulverized to finer than 1700-μm particles. After determining the number of additional strokes required to achieve a predefined masticatory performance norm, a masticatory efficiency percentage was calculated.

The results indicated no significant differences in masticatory performance or efficiency between tooth-supported FPD and implant crown groups. Consolidated satisfaction scores in the 2 groups were not significantly different. However, overall satisfaction with the prosthesis and satisfaction with function were significantly greater in the implant crown group, whereas satisfaction with treatment duration was significantly greater in the tooth-supported FPD group.

The authors suggested that greater overall prosthesis satisfaction in the implant crown group could be related to easier maintainability or to a feeling that a more advanced treatment was provided without compromising adjacent natural teeth. A better functional rating for the implant crown might be associated with the more natural feel of the restoration. More obvious is patient satisfaction with the shorter treatment duration associated with the FPD. The relatively short follow-up period was identified as a potential limitation of this study.

General implant prosthodontic considerations

Most implant restorations require the use of a screw fastener during the restorative phase of treatment. Unintended screw loosening during functional loading of the definitive restoration occurs frequently and has significant mechanical and biological consequences. One etiology for unintended implant retention screw loosening is the failure to achieve recommended retention screw insertion torque and the all-important screw preload, at initial placement. Albayrak et al[231] investigated retention screw insertion torque by evaluating the reliability of currently available mechanical and electronic torque-control devices and by comparing the percentage of absolute deviation among manufactures and device types.

Five new torque-control devices from 5 different manufacturers were included for evaluation: 2 spring-type mechanical devices (Straumann and Implance), 2 friction-type mechanical devices (Biohorizons and Dyna), and 1 electronic device (Megagen). Each device was used to load a torque-testing machine 5 times after appropriate calibration of the machine. The target torque application levels used were those prescribed by the manufacturer of each torque-control device (range: 25 to 35 Ncm). Mean torque values and the percentage of absolute deviation from target torque values were calculated for each manufacturer/device.

The results revealed that recorded torque values for each device were significantly lower than intended target values. The percentage of absolute deviation from target torque for the Megagen electronic device was significantly the highest at 28.33%. The percentage of absolute deviation from the target torque did not differ significantly among Straumann (13.26%), Dyna (7.82%), Biohorizons (7.31%), and Implance (8.43%) devices.

The authors concluded that none of the torque-control devices evaluated were capable of achieving their intended torque values. This translates to suboptimal implant retention screw preload and perhaps increased likelihood of unintended screw loosening during functional loading. Although all devices were incapable of achieving target torque values, spring-type and friction-type mechanical torque-control devices performed significantly better than the electronic device tested. The authors cautioned that the devices tested in the present study were new. A future investigation using the same experimental protocol should look at devices subjected to clinical use and sterilization procedures and should investigate the need for periodic wrench recalibration. The inclusion of additional electronic torque-control devices in future research was also suggested.

Outcomes research is an important element in the armamentarium of evidence-based dentistry. Dental therapeutic interventions are likely influenced by existing systemic diseases, particularly for patients suffering from chronic and poorly controlled systemic conditions. Given the current prevalence of systemic disorders in typical dental patient populations, a better understanding of potential impacts on the provision of implant dentistry might facilitate patient and practitioner understanding, as well as subsequent clinical decision-making. Carr et al[232] sought to identify associations between implant failure and concomitant systemic conditions/diseases in a consecutive series of patients who received dental implants between October 1983 and December 2014 in a single treatment facility.

Data were gathered from a clinical database of electronic health records to identify patient demographics, implant-specific characteristics, medical profiles, and time to first implant failure. Demographic information included the era of first implant (1983-2000 and 2001-2014) to reflect substantial implant surface characteristic changes in the latter half of the investigation. Data were abstracted for the following diseases/conditions: autoimmune, cardiovascular, bone, immunosuppressive, inflammatory, neuropsychiatric, and metabolic conditions; malignant neoplasms; chemotherapy/radiation therapy; and postmenopausal status (over 20 specific diseases/conditions in total). No attempt was made to abstract management of the disease/condition. Patient-level implant survival was estimated using the Kaplan-Meier method. Demographic-systemic disease/condition associations with implant failure were statistically evaluated.

This cohort consisted of 6358 patients, with a median age of 53 years at first implant placement; of the 6358, 713 experienced implant failure at a median of 0.6 years after placement. For the 5645 patients who did not experience implant failure, the median follow-up duration was 5.8 years. The rate of survival free of implant failure at 5 years was 90%, 87% at 10 years, 84% at 15

years, 83% at 20 years, and 81% at 25 years. More than 20 systemic diseases/conditions were identified for the assessment, of which 15 comprised more than 50 patients and 5 comprised more than 500 patients. All associations were adjusted for age, sex, and era of implant, given the strong influence of these factors on implant failure. After adjustment, no systemic disease/condition was shown to increase the risk for implant failure in the population and setting studied.

The authors concluded that the decision-making process for patients in need of complex dental rehabilitation can be challenging. Patients considering oral reconstruction involving dental implants in the setting studied do not appear to risk implant loss because of the systemic diseases/conditions identified here. Dentists who can offer similarly derived information can help patients better manage complex therapeutic decision-making.

Implant-assisted removable prosthodontics

The use of fixed implant-supported restorations to restore Kennedy class I partial edentulism is generally considered a positive concept. However, because of the cost of such treatment, the need for surgical intervention, and the need for adequate hard and soft tissue, this treatment can be impractical, if not impossible, for some patients. Optimizing functional mechanics and esthetics using a removable partial overdenture (RPOD) by strategically incorporating appropriately sized and positioned dental implants may improve restorative prognosis and, in turn, patient satisfaction. Jensen et al[233] published a medium- to long-term retrospective investigation assessing the performance and complications associated with restoring mandibular Kennedy class I partial edentulism with implant-assisted RPODs.

This analysis included all patients treated between 1999 and 2014 in a private practice setting and a general hospital who received 2 dental implants and a mandibular Kennedy class I implant-assisted RPOD. The 23 patients (6 men and 17 women; mean age: 59 years) retrospectively enrolled had shortened mandibular dental arches with first premolars (8 patients) or canines (15 patients) as the most posterior teeth bilaterally. Typically, 3 denture teeth were incorporated into the prosthesis bilaterally. Implants were placed in the premolar edentulous region in 8 patients (anterior group), whereas molar implants were used in 15 patients (posterior group). Biological and technical complications were identified from a survey of the patients' treatment record. Implants were supplied with ball, Locator, or healing abutments. All patients completed a validated questionnaire for oral health–related quality of life (OHRQoL; OHIP [Oral Health Impact Profile]-NL49), and a visual analog scale (VAS) score was obtained to determine overall satisfaction. Implant survival was calculated by means of the Kaplan-Meier estimate.

Results indicated that patients had an average follow-up period of 8.1 years (range: 3 to 16 years), and the cumulative implant survival rate (ISR) was 91.7%. No anterior group implants were lost; 3 were lost in the posterior group. The mean change in marginal bone level over the observation period was −0.9 mm, with no significant difference between anteriorly and posteriorly placed implants. Biologic complications occurred for 63% of implants, with scores for BOP, plaque, and mucosal health generally low but significantly worse for posteriorly placed implants. Technical complications affected 35% of the participants (prosthesis repair or replacement), with no significant difference between anterior and posterior groups. The mean overall OHIP score was 16.1 (favorable perception of quality), and patients were highly satisfied (VAS: 8.4 out of 10).

The authors concluded that within the limitations of retrospective analysis, the use of implant-assisted RPODs to restore Kennedy class I mandibular partial edentulism is a viable prosthodontic alternative with a high rate of implant survival and patient satisfaction after a maximum of 16 years. Technical and biological complications should be anticipated. Although anteriorly placed implants performed slightly better, other factors (such as bone availability and esthetics) may dictate implant placement in edentulous areas and resultant prosthesis design.

Edentulous residual ridge resorption is chronic, progressive, reasonably uncontrollable, and predictably irreversible. Increasingly severe edentulous ridge atrophy may significantly complicate technical prosthodontic procedures, leading to compromised therapeutic outcomes. In extreme situations, achieving satisfactory prosthesis support, stability, and/or retention may be impossible, even in the presence of integrated dental implants. A basic concern is the impact of mandibular ridge atrophy on masticatory function, particularly during transition from conventional complete dentures to implant-assisted overdentures. To better characterize this transition period, Marcello-Machado et al[234] investigated mandibular function, patient satisfaction, and OHRQoL in atrophic patients before and 1 year after rehabilitation with implant-assisted mandibular overdentures.

Twenty-six healthy conventional complete denture patients were equally distributed to 2 groups based on a radiographic assessment of mandibular atrophies: an AP (atrophic patients) group (atrophic patients: 11 women and 2 men; mean age: 68.4 years) and NAP (nonatrophic patients) group (nonatrophic patients: 6 women and 7 men; mean age: 66.2 years). All patients were subjected to complete the Dental Impact on Daily Life (satisfaction and OHRQoL) questionnaire

and masticatory function (masticatory performance, swallowing threshold, and masticatory efficiency) testing before and after surgical placement of 2 interforaminal implants and prosthesis adaptation. At 3 months after implant placement, overdenture attachments were placed, and the prostheses were readapted. Masticatory function testing was again carried out at 1, 3, 6, and 12 months after overdenture loading, and the satisfaction questionnaire was completed at 3, 6, and 12 months.

The results indicated that mandibular atrophy interfered with masticatory function only in complete denture wearers. This significantly reduced masticatory function was primarily related to a decreased swallowing threshold characterized by the greater number of masticatory cycles needed and impaired masticatory efficiency in APs. However, 6 months after overdenture loading, AP and NAP groups achieved similar masticatory function.

The results also indicated that mandibular atrophy in this patient population did not significantly affect patient satisfaction with their prostheses. However, the AP group required a longer time to adapt to implant overdentures than their NAP counterparts mainly because of the oral comfort parameter over time.

Considering the masticatory performance (ability to pulverize a test food), no differences were identified for APs and NAPs until 12 months after implant overdenture loading. Both APs and NAPs showed significant improvements in masticatory performance throughout the observation period.

Swallowing threshold results indicated that NAPs wearing complete dentures masticated approximately 14% faster than AP counterparts, with no significant difference in the number of masticatory cycles needed. Upon transition to implant overdentures, differences between groups were amplified.

The authors concluded that characterizing transitional adaptation from mandibular complete denture to implant-assisted overdenture was made possible in this investigation by combining objective masticatory function data with subjective assessments of functional capability in atrophic and nonatrophic individuals. Mandibular overdenture rehabilitation appears to affect the objective outcome of masticatory function (as measured by swallowing threshold), with improvements more evident for atrophic patients than for nonatrophic patients. Regarding patient satisfaction and quality of life during transition to implant overdentures, a longer adaptation period was recorded for atrophic patients, ostensibly related to their increased dissatisfaction with oral comfort over a greater period of time. Clinicians may want to consider this when informing patients about expected improvements after mandibular implant-assisted overdenture therapy.

Implant-assisted fixed prosthodontics

Chercoles-Ruiz et al[235] considered the following clinical question: "What is the best treatment option for a pulpally involved tooth?" In reviewing the question, the following statement was offered, "The standard of care for a nonvital tooth is endodontic treatment to preserve the natural tooth." Although naive in scope, this sentiment is at the heart of the diagnostic decision-making, confronting both patients and practitioners on a regular basis. Therefore, the authors developed the following PICO question for systematic review: "In a patient who has a tooth with pulpitis, necrosis with or without a periapical lesion, in the presence or absence of symptoms, and without a radicular fracture, does the conservative treatment (endodontic treatment or retreatment and/or apical surgery) compared with tooth extraction and implant placement achieve higher survival rates?"

The investigation followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines. An electronic search of the professional literature and a manual search of 7 key journals were conducted for articles published between 2006 and 2016. Inclusion criteria limited article selections to randomized clinical trials, prospective or retrospective cohort studies, and cross-sectional studies performed on humans with at least 1 year of follow-up and no language restriction. Strength of Recommendation Taxonomy criteria were used to classify levels of evidence, and data collected for analysis were based on intervention type, outcome (success, survival, and failure rate), assessment criteria, and duration of follow-up.

A total of 1244 articles were identified during electronic and hand searching. Article review and application of exclusion criteria resulted in 45 articles to be included in the systematic review: 2 randomized clinical trials, 22 prospective cohort studies, 17 retrospective cohort studies, 2 cross-sectional studies, and 2 cost-effectiveness analysis studies. The success rate for endodontic treatment was found to range from approximately 42% to 85% after 2 to 10 years. For endodontic retreatment, success ranged from 48% to 89% over 4 to 10 years, and apical surgery success ranged from 59% to 93% after 1 to 10 years. In studies looking exclusively at dental implants, survival rates were reported to vary from 92% to 100% after 1 to 10 years, implant success and complications were rarely reported, and the timing of implant placement (immediate versus early versus delayed) was not a factor. For comparative studies, the survival rate of single-tooth implants was greater than the success rate of endodontic therapy. However, no important differences between treatments were observed until 8 years of follow-up.

The authors concluded that both endodontic and implant treatments are predictable options, and the decision to extract a tooth should be based on current

qualified literature. Although implant survival is comparable with endodontic success, the occurrence of postoperative peri-implant disease (mucositis and implantitis) may require additional interventions, thus confounding results and negatively affecting patient comfort. Although conclusions may be drawn from the data reported, caution should be used because existing comparative studies are retrospective in design. Randomized clinical studies are not available to provide stronger evidence. However, because the different treatment options are comparable in terms of success and survival rates, treatment pursued should be in line with patient preferences and realistic expectations.

Third-party manufacturers offer CAD-CAM custom zirconia implant abutments for fixed prosthodontic restorations. Although attempts are made to develop stable prosthetic interfaces (screw abutment and abutment implant), aftermarket manufacturers must alter abutment design to avoid patent infringement of the original equipment manufacturer (OEM). With limited research to support the mechanical validity of these design alterations, Jarman et al[236] followed an in vitro protocol to compare fracture resistance and failure mode of third-party CAD-CAM zirconia abutments with corresponding OEM zirconia abutments.

Four prosthetic interfaces were selected for investigation: internal conical (Straumann), external hexagon (Nobel Biocare), internal trilobe (Nobel Biocare), and internal hexagon (Biomet 3i). Twenty OEM stock zirconia abutments (5 per group) represented controls. CAD-CAM abutments (Atlantis; Dentsply Sirona) fabricated to match the OEM controls served as experimental specimens. All abutments were screw-fastened to implant analogs. Complete-coverage ceramic crowns were luted to abutments, and completed specimens were mounted in a test frame for static load fracture–resistance testing. Modes of restoration failure were examined by light and scanning electron microscopy.

The results indicated that zirconia CAD-CAM abutments failed at decreased static fracture loads compared with OEM counterparts. Failure modes for internal conical and external hexagon OEM abutments were screw-bending and zirconia fractures, whereas CAD-CAM abutments demonstrated only zirconia fractures. Internal trilobe OEMs failed because of screw-bending, and CAD-CAM abutments showed screw head and zirconia fractures. Finally, internal hexagon OEM abutments demonstrated a zirconia fracture failure, and CAD-CAM abutments suffered screw-head fractures.

Alterations in prosthetic interface designs for the third-party CAD-CAM abutments investigated here appear to have a negative influence on their mechanical performance. A limitation of the study was the use of static rather than cyclic load applications and the absence of wet testing conditions. Given the fracture resistance loads recorded, the authors indicated that careful consideration should be given to the use of alternatively engineered third-party zirconia abutments for anterior restorations and recommended that these abutments should not be considered for posterior single-tooth applications where occlusal forces may exceed 350 to 400 N.

Prosthodontic material science

Yttrium-stabilized tetragonal zirconia has been widely applied in conventional and implant-fixed prosthodontics due to favorable mechanical, biologic, and optical properties. Adhesive placement of zirconia has proven problematic due to the lack of a silica-glass component to facilitate etching and potential structural deterioration upon aggressive airborne-particle abrasion. A hot chemical etching method previously used to surface-condition metals and metal alloys has recently been suggested for zirconia. Generally, this method requires that a heated acid solution (containing HCl and Fe_2Cl_3 at 100°C) be placed in contact with the bonding surface of the zirconia for different durations. An additional bonding tool may be the use of 10-methacryloxydecyl dihydrogen phosphate (MDP) as a primer. Favorable chemical interactions between zirconia ceramic hydroxyl groups and MDP phosphate ester monomer have been demonstrated. Using an in vitro resin-zirconia shear bond strength protocol, Akay et al[237] compared airborne-particle abrasion with hot chemical etching surface treatments and an MDP-containing resin with conventional resin cements.

Sixty zirconia bar specimens (10×5×2 mm) were prepared. Three experimental groups were developed according to surface treatment: 50-μm Al_2O_3 airborne-particle abrasion from 10 mm perpendicular to surface at 0.25 MPa for 15 seconds; 10-minute immersion in a hot chemical etchant comprising 800 mL of methanol, 200 mL of HCl, and 2 g of ferric chloride at 100°C; and 30-minute immersion in the same hot chemical etchant at the same temperature. All 3 surface treatment groups were divided into 2 cementation subgroups containing 10 specimens each. The first subgroup used conventional resin (Variolink II; Ivoclar Vivadent AG) to bond 3×3-mm resin cylinders to zirconia surfaces. The second subgroup used MDP-containing resin (Panavia SA; Kuraray) to bond the same cylinders to zirconia surfaces. After preparation, the specimens were subjected to shear loading in a universal test frame (1 mm/min crosshead speed).

The results indicated that hot chemical etching combined with MDP-containing resin cementation resulted in significantly the highest shear bond strength, whereas airborne-particle abrasion combined with conventional resin cementation yielded the lowest shear bond strengths. Except when combined with long duration,

hot chemical etching and cementation with MPD-containing resin appeared to have an advantage.

The authors concluded that zirconia surface preparation with hot chemical etching for 10 minutes appeared to have promise, regardless of conventional or MDP-containing resin cementation. In addition, as compared with conventional resin, the MDP-containing resin cement (Panavia SA) improved bonding to zirconia when combined with airborne-particle abrasion surface preparation. The lack of thermal and mechanical cycling in this study may have been a shortcoming. In addition, long-term water exposure and subsequent resin hydrolysis is a clinical reality and may influence bond strength results over time. Further study into the question of bonding to zirconia should consider these factors and influences.

To record the fine surface details of wet and hydrated oral hard and soft tissues with a dental impression and faithfully transfer the captured details to dental casts by pouring with gypsum slurries, optimal hydrophilicity and viscosity of impression and gypsum materials must be available. PVS impression materials are inherently hydrophobic, resulting in poor flow along oral tissue and causing poor impression wetting by dental gypsum slurries upon casting. One possible solution used by dental manufacturers is the incorporation of surfactants in PVS. To investigate this possibility, Ud Din et al[238] evaluated experimental PVS impression materials incorporating a novel nonionic surfactant, Rhodasurf CET-2 (ethoxylated cetyl-oleyl alcohol), and compared surface characteristics (contact angle [CA]) with those of commercial impression materials before and after disinfection.

Three hydrophilic commercial PVS materials (Aquasil Ultra Monophase [Dentsply Sirona]; Elite HD Monophase [Zhermack]; and Extrude Medium [Kerr Corp]) and 4 experimental PVS materials (Exp I-IV) were included. Exp I PVS contained no surfactant and served as control. Exp II-IV PVSs contained an increasing amount of a novel surfactant Rhodasurf CET-2. PVS specimen surfaces (40×10×1 mm) were prepared in a standardized metal mold. The drop shape analysis (DSA-100) technique was used to measure dynamic and static CAs between PVS and distilled water drops at specified time periods (droplet spreading at 10, 30, 60, and 120 seconds; immediately after polymerization; 30 minutes after disinfection; 24 hours after disinfection). CAs were measured with and without disinfection of the PVS specimen surface (NaOCl) at 30 minutes and 24 hours.

The results indicated that the CAs of all experimental materials were within the range of those obtained for the commercial materials, with the exception of Exp IV PVS, which demonstrated the significantly lowest CAs at all 3 static time points. The control (Exp I) PVS was hydrophobic at all 3 time points (hydrophobic translates to CAs of approximately 100 or more), as was Elite. Immediately after polymerization, Aquasil demonstrated a relatively low CA that increased significantly after 30 minutes of disinfection and reached near-hydrophobicity at 24 hours. Twenty-four hours after disinfection, the CAs of all experimental and commercial PVSs increased significantly compared with those recorded immediately after polymerization.

The authors concluded that the novel surfactant Rhodasurf CET-2 incorporated at 2.5%wt and 3.0%wt in Exp III and IV PVSs, respectively, appeared to be an effective surfactant-PVS combination, resulting in significantly low CAs that remained after disinfection, compared with other PVS materials studied. The decrease in hydrophilicity with time and disinfection varies with PVS material. Disinfecting the PVS materials investigated for more than 30minutes increased the CAs. Then authors suggested avoiding prolonged (30 minutes or greater) disinfection periods and delayed casting of PVS impressions.

PERIODONTICS, ALVEOLAR , AND PERI-IMPLANT TISSUES

This year's review covered topics relating to the assessment, prevalence, and treatment regimens of periodontal diseases; medication-related osteonecrosis of the jaw (MRONJ); systemic health conditions affecting the periodontium and alveolar bone health; periodontal regeneration; soft tissue augmentation adjacent to teeth and implants; alveolar ridge preservation (RP) and alveolar bone augmentation techniques; and peri-implantitis.

Periodontal disease prevalence, etiology, and treatment

Periodontal disease is a chronic inflammatory disease resulting in the destruction of alveolar bone and the attachment apparatus. Although periodontal disease is classically diagnosed by the use of periodontal probing measurements and radiographs, the use of salivary markers for early and rapid identification of an active periodontal disease state would aid the clinician. Current soft tissue markers for periodontal disease include mucin 4 (MUC4) and matrix metalloproteinase 7 (MMP7). Lundmark et al[239] recently conducted a study to investigate the levels of MUC4 and MMP7 in saliva and gingival crevicular fluid (GCF) of patients with periodontitis. Saliva and GCF samples were collected from patients with periodontitis and healthy controls. The levels of MUC4, MMP7, and total protein concentrations were analyzed using enzyme-linked immunosorbent assay (ELISA) or Bradford assay. They found that MUC4 levels were significantly lower in saliva and GCF from patients with periodontitis relative to healthy controls. MMP7 levels were significantly higher in saliva and GCF from those with periodontitis. However, multivariate analysis revealed that MUC4 was significantly associated

with periodontitis after adjusting for age and smoking habits and that the combination of MUC4 and MMP7 accurately discriminated periodontitis from healthy controls. The combination of MUC4 and MMP7 may be used as a possible novel biomarker for periodontitis, facilitating an accurate screening test for periodontal disease.

Furcation involvement has been identified as a negative prognostic factor for the maintenance of attachment levels and long-term tooth retention. Although supportive periodontal therapy can improve outcomes, less is known about the fate of furcation-involved (FI) teeth in a population not receiving regular periodontal treatment. Nibali et al[240] assessed the association between FI and tooth loss for individuals not undergoing regular periodontal treatment.

Data from 2333 participants at baseline and at 11-year follow-up of the Study of Health in Pomerania (SHIP) were used. All participants had half-mouth periodontal examinations, including FI in 1 maxillary and 1 mandibular molar, at baseline. A total of 1897 participants and 3267 molars were included in the final analysis. The main strength of this study lies in the large sample size and in the analysis of a population not undergoing regular periodontal therapy.

In total, 375 participants (19.8%) lost molars during the follow-up period. Respectively, 5.6%, 12.7%, 34.0%, and 55.6% of molars without FI, degree I FI, degree II FI, and degree III FI were lost. Initial probing pocket depth and clinical attachment loss (CAL) were also associated with molar loss. Baseline degree I FI was associated with a 1.73 incidence rate ratio of tooth loss, whereas degree II-III were associated with a 3.88 incidence rate ratio of tooth loss compared with molars without FI at baseline. This study provides evidence for an increased risk of molar loss because of periodontal furcation involvement in a general population not undergoing regular periodontal care therapy.

An initial periodontal treatment frequently consists of nonsurgical debridement, followed by reevaluation for possible surgical therapy. The patient may present with deep probing depths (PD), which makes nonsurgical therapy, such as scaling and root planning (SRP), less effective. For these patients, the potential benefit of local drug delivery has been suggested. Metformin (MF), a biguanide used in the treatment of diabetes mellitus type 2 as an oral hypoglycemic drug, has shown a stimulating effect on osteoblastic cell lineages. Indigenous delivery of MF has been shown to be successful in early clinical trials. Pradeep et al[241] investigated the efficacy of MF 1% gel as an adjunct to SRP in the treatment of moderate and severe chronic periodontitis (CP). Seventy participants were divided into 2 treatment groups: SRP plus 1% MF and SRP plus placebo. The clinical parameters of the plaque index (PI), modified sulcus bleeding index, PD, and CAL were recorded at baseline and at 3, 6, and 9 months. Radiologic assessment of intrabony defects (IBDs) and percentage defect depth reduction (DDR%) was done at baseline and at 6- and 9-month intervals using computer-aided software. PD, CAL, and DDR% were evaluated in 2 subgroups in both the placebo and MF group: initial PD of 5 to 7 mm and initial PD of greater than 7 mm. It was demonstrated that the mean PD reduction and mean CAL gain was found to be greater in the MF group than the placebo group at all visits. Clinical parameters (PD and CAL) within both test subgroups showed significant improvement in the 1% MF group as compared with the placebo group. The mean probing depth-reduction difference between test and control groups was almost 2 mm, which is clinically relevant. A significantly greater mean DDR% was found in the MF group than the placebo group at 6 and 9 months in both test subgroups. The authors also suggested that the slightly lesser DDR% in the MF group seen in the subgroup with baseline PD greater than 7 mm compared with baseline PD of 5 to 7 mm may be attributed to the difficulty of penetrating MF gel to a deeper PD.

The use of systemic antibiotics has been incorporated into several periodontal treatment regimens. The advantage of systemic antibiotics is the enhanced delivery of the antibiotic to the deeper portions of the periodontal pocket. However, this advantage must be weighed against the problems inherently associated with the delivery of systemic antibiotics such as side effects, allergic reactions, and the development of resistant organisms. Preus et al[242] evaluated whether the administration of systemic antibiotics in addition to SRP therapies was beneficial in the long term. They examined the 5-year clinical outcome of therapy between groups of patients treated with conventional over-weeks SRP or same-day full-mouth disinfection (FDIS), with or without adjunctive metronidazole (MTZ). After a 3-month oral hygiene phase, 184 patients with periodontitis were randomly allocated to 1 of 4 treatment regimens: FDIS+MTZ, FDIS+placebo, SRP+MTZ, and SRP+placebo. After active treatment, the patients received biannual maintenance. One hundred sixty-one patients completed the 5-year follow-up maintenance and examination, where CAL, probing pocket depth, presence of plaque, and bleeding were registered. They found that MTZ increased the highest CAL recording by an average of 0.17 mm, whereas FDIS decreased it by an average of 0.12 mm. Both results were statistically insignificant. Single-level analyses showed statistically significant results, but likely no clinical differences. The authors demonstrated that these results could not be confirmed with more appropriate analyses and were too small to recommend MTZ, with its risk of side effects and environmental consequences, for the treatment of patients with severe periodontitis.

Medication-related osteonecrosis of the jaw

The effectiveness of management strategies used for the treatment of MRONJ remains poorly understood and has remained a controversial topic within the oral and maxillofacial surgery community. Therapeutic management has focused on the symptomatic treatment and can be divided into surgical therapy and nonsurgical therapy. Nonsurgical therapies may include long-term use of local antimicrobials, both systemic and local, drug "holidays"; hyperbaric oxygen therapy; low-intensity laser therapy; teriparatide; ozone; and combinations of pentoxifylline and tocopherol therapies. Surgical treatments range from conservative to aggressive, such as curettage, sequestrectomy, and alveolar resection as a final resort. El-Rabbany et al[243] conducted a systematic review examining the effectiveness of treatments for MRONJ. The authors conducted a comprehensive search of MEDLINE, Embase, the Cochrane Library, and Scopus to identify randomized controlled trials (RCTs), non-RCTs, and prospective cohort studies to evaluate comparatively the effectiveness of management strategies for the treatment of MRONJ. They found 13 studies with a medium-to-high risk of bias which met the inclusion criteria of this review. Compared with medical treatment with local antimicrobials with or without systemic antimicrobials, the study investigators associated surgical treatment with higher odds of complete resolution of condition (2 studies; 76 participants; unadjusted odds ratio [OR]: 3.55). The effectiveness of other therapies, such as bisphosphonate drug holidays, teriparatide, and hyperbaric oxygen, was uncertain. Based on the results of an unadjusted analysis, the results of the studies deemed to be of medium-to-low quality and to have medium-to-low statistical power suggested that the odds of resolving MRONJ with surgical treatment are higher than that of medical treatment.

Studies demonstrating that the overall incidence of tumor patients developing an MRONJ under zoledronate treatment approximates 1%. However, there is a large variation in the reported incidences, up to 20.5%, when level 1 evidence studies are considered. Bone antiresorptive therapy for benign diseases such as osteoporosis must be distinguished from the therapies for tumor patients in this respect, as a less potent medication is required for benign conditions. Consequently, the reported risk of MRONJ among patients treated with either bisphosphonates or denosumab approximates only 0.017%. Despite these rather lower incidences, MRONJ therapy has become more complex recently. This is due in part to the continuous binding by potent nitrogen bisphosphonates to the bone hydroxylapatite. When withdrawing from bisphosphonates, there is a continued effect over years. In addition, a large number of patients who initially received bisphosphonates are being converted to denosumab as there is evidence that denosumab is more effective in the prevention of long bone fractures. This unintended effect results in a double antiresorptive therapy, possibly leading to an increased risk of developing an MRONJ. Unfortunately, studies and even guidelines for MRONJ are inconsistent relating to the question of MRONJ staging and treatment. Hayashida et al[244] conducted a multicenter retrospective study aimed at investigating the treatment methods and outcomes in a large number of patients with MRONJ in Japan by using propensity score–matching analysis. A total of 361 patients with MRONJ at 8 hospitals were retrospectively registered in this study. Various demographic and treatment-related variables were examined and analyzed to determine their correlation with the treatment outcome. After propensity score matching for treatment methods (nonsurgical versus surgical treatment), 176 patients were analyzed by logistic regression. It was shown that those with low-dose administration of an antiresorptive agent and surgical treatment had better outcomes. Furthermore, in 159 patients who underwent surgical treatment, those who underwent an extensive surgery experienced significantly better treatment outcomes than those who underwent conservative treatments. The authors concluded that this study indicates that extensive surgical treatment may be performed as first-choice therapy for patients with MRONJ. These conclusions are not in agreement with the current (2014) recommendations of the American Association of Oral and Maxillofacial Surgeons, which recommends that bone resection be limited to the areas of large sequestra and that elective bone surgery should be avoided.

Relationships between periodontal and systemic health

The association between periodontal disease and the prevalence of diagnosis of cancer continues to be supported by new clinical evidence. Michaud et al[245] prospectively evaluated the association of periodontal disease severity with cancer risk in black and white older adults in a cohort study that included a dental examination. Included were 7466 participants in the Atherosclerosis Risk in Communities study cohort, who at visit 4 (1996-1998) reported being edentulous or underwent the dental examination. Probing depth and GR were measured at 6 sites on all teeth. These measurements were used to define periodontal disease severity. Incident cancers (n=1648) and cancer deaths (n=547) were ascertained during a median of 14.7 years of follow-up. An increased risk of total cancer (hazard ratio [HR]= 1.24) was observed for severe periodontitis (>30% of sites with attachment loss >3 mm) compared with no/mild periodontitis (<10% of sites with attachment loss >3 mm), adjusting for smoking and other factors. Strong associations were observed for lung cancer (HR=2.33), and elevated risks were noted for colorectal cancer for

severe periodontitis, which were significant among never smokers (HR=2.12). Associations were generally weaker or not apparent among black participants, except for lung and colorectal cancers, where associations were similar by race. No associations were observed for breast, prostate, or hematopoietic and lymphatic cancer risk. This study was particularly well done with over 7000 patients examined and an average 15-year follow-up. The study design included full-mouth periodontal probings to determine periodontal disease status. Many previous epidemiologic studies relied on self-reporting for the periodontal disease diagnosis, resulting in underreporting. In addition to the periodontal diagnosis, comprehensive physical examinations and medical histories were obtained every 3 years. This study provides additional evidence that cancer risk, especially for lung and colorectal cancer, is elevated in individuals with periodontitis.

Epidemiologic studies have shown that periodontal disease is now being recognized as a risk factor for cardiovascular disease (CVD). Several mechanisms have been suggested for linking the 2 disease entities, such as spread of infection after bacteremia, injury caused by microbial toxins and inflammation, and endothelial dysfunction. Periodontal disease acts as a source of inflammatory burden, which upgrades production of proinflammatory mediators and adhesion molecules, increasing leukocyte adhesion to the vascular wall. This inflammatory burden acts as an insult to the endothelium, and this disruption in the function of the endothelium predisposes it to the formation of atherosclerotic plaque. Punj et al[246] conducted a study to estimate and compare endothelial function (EF) via flow-mediated dilution (FMD) assessment in periodontal health and disease. A total of 120 patients were selected and categorized equally into 3 groups: healthy (control), CP, and myocardial infarction (MI). Periodontal inflamed surface area and FMD were assessed in all patients. Fasting blood samples were collected to estimate the lipid profile. Comparison of FMD levels among the 3 groups showed statistically significant differences. The value was statistically significant when the healthy group was compared with the CP and MI groups but not when the CP group was compared with the MI group. Lipid profile levels were statistically significant on comparison between the healthy and CP groups and between the CP and MI groups. The authors concluded that EF was impaired in patients with CP compared with healthy patients and that the dysfunction observed was like that observed in the MI group based on FMD values.

Sanz-Miralles et al[247] conducted a similar study, examining the arterial stiffness of the carotid arteries in patients with periodontitis as compared with healthy controls. Intima-media thickness and FMD are commonly used measures of vascular structure and function that serve as surrogate markers for atherosclerosis and have been used in association studies linking periodontitis and atherosclerotic vascular disease. In this study, 80 volunteers were enrolled (39% men; age range: 24-78 years), and 33 pairs were formed of periodontitis patients/periodontally healthy controls, matched by age and sex. A complete-mouth periodontal examination was performed, and the degree of stiffness of the right and left carotid arteries was assessed by measuring pulse wave velocity and the uniformity in pulse wave propagation (R(2)). Patients with periodontitis had a statistically significantly lower uniformity in wave propagation R(2) than controls, but pulse wave velocity did not differ between the 2 groups. A univariate analysis showed a significant negative association between R(2) and periodontitis, body mass index, and smoking; periodontitis remained statistically associated with R(2) in the multivariate analyses. Patients with periodontitis and no established CVD presented with a lower degree of uniformity in the transmission of the pulse wave through the carotid arteries, suggesting an association between periodontitis and arterial stiffness/functional alterations.

The Centers for Disease Control and Prevention estimate that 47% of Americans aged 30 years have periodontitis. Although specific bacterial patterns are essential for disease initiation, some systemic risk factors appear to influence periodontitis progression. Smoking, diabetes mellitus, and interleukin (IL)-1 genetic variations are the strongest validated systemic factors. However, increasing evidence supports the role of obesity and obesity-related traits in periodontitis severity and response to treatment. Central adiposity contributes to inflammation, in part, through activated macrophages in adipose tissues that produce TNF-a (tumor necrosis factor-alpha), IL-1b (interleukin 1 beta), and IL-6, and higher body mass is associated with higher C-reactive protein levels. Given the evidence for elevated IL-1b levels in periodontitis severity and progression, it was postulated that individuals genetically predisposed to overexpress IL-1b may influence the obesity effect on periodontitis progression. Wilkins et al[248] conducted a study evaluating whether specific patterns of IL-1 gene variants, known to affect periodontitis severity, influence the previously reported association between obesity and subsequent periodontitis progression in a longitudinal database. The study population included 292 men (aged 29 to 64 years at entry) from the Veterans Affairs Dental Longitudinal Study from whom DNA and dental and anthropometric endpoints were collected during multiple examinations (approximately every 3 years for up to 27 years). Key variables assessed included periodontitis, body mass index, waist circumference to height ratio for central adiposity, age, smoking, glucose tolerance, and 2 previously reported versions of IL-1 genetic patterns associated with periodontitis severity and progression.

Disease progression was determined using predefined criteria that used a combination of change in classification of disease severity based on alveolar bone loss and tooth loss during follow-up. In HR analyses, men with waist circumference to height ratio greater than 50% at baseline and positive for either IL-1 genotype version were at significantly higher risk (2-fold) for disease progression. Participants positive for IL-1 genotype version 2 exhibited earlier progression (fewer years from baseline to first incidence of progression) than those who were negative (adjusted for age and smoking). This study demonstrated that the observed effect of baseline central adiposity on future periodontitis progression is conditional on proinflammatory IL-1 genetic variations.

The interplay between the functional anatomy of oral cavity and sleep disorders is becoming better understood. Because of its potential to influence systemic inflammation and oxidative stress, sleep duration could be a risk factor for periodontitis. Romandini et al[249] described a cross-sectional study evaluating whether an association exists between periodontitis and sleep duration in a representative sample of the South Korean population. A total of 5812 participants, representative of 39.4 million adults, were examined. Multivariate logistic regressions were applied to control for age, sex, education, smoking status, alcoholism, and consumption frequency of coffee, tea, chocolate, and red wine. Compared with the group sleeping $\leq$5 hours/day, the adjusted ORs for periodontitis prevalence were OR=2.46 in the 6 hours/day sleepers group, OR=2.66 in the 7 hours/day sleepers group, OR=2.29 in the 8 hours/day sleepers group, and OR=4.27 in the $\geq$9 hours/day sleepers group. The association has shown to increase in middle-aged people, women, nonsmokers, the less well educated, those with lower lead and higher cadmium blood levels, and those with higher carotene dietary intake and to be partially mediated by lipid profile alterations, diabetes, serum vitamin D levels, and white blood cell count. This study demonstrated a novel, direct, and independent association between sleep duration and the prevalence of periodontitis. The modification of sleep duration could be involved in preventive and therapeutic approaches to periodontitis.

Periodontal regeneration

The use of autologous blood preparation products such as platelet-rich plasma or platelet-rich fibrin (PRF) has continued to expand in the area of periodontal regeneration. Recent advances have focused on the combination of these products with bone biologics. PRF is a pool of growth-promoting factors and cytokines that promote bone regeneration and maturation of soft tissue. Alendronate (ALN), a bisphosphonate, is known to enhance osteoblastogenesis and inhibit osteoclastic bone resorption, which may promote alveolar regeneration. Kanoriya et al[250] conducted a randomized trial assessing the effectiveness of a PRF and 1% ALN gel combination in the treatment of mandibular degree II furcation defect compared with PRF and access therapy alone. Seventy-two mandibular molar furcation defects were treated with access therapy alone (group 1), access therapy with PRF (group 2), or access therapy with PRF and 1% ALN (group 3). PI, modified sulcus bleeding index, PD, relative vertical attachment level, relative horizontal attachment level, and IBD depth were recorded at baseline and 9 months postoperatively. Radiographically, the defect fill assessed in percentage was evaluated at baseline, before surgery, and 9 months after therapy. The results showed that group 3 had greater PD reduction and relative vertical attachment level and RHAL gain than groups 1 and 2. Moreover, group 3 sites showed a significantly greater percentage of radiographic defect fill (56.01% ±2.64%) than those of group 2 (49.43% ±3.70%) and group 1 (10.25% ±3.66%) at 9 months. This study supports the use of autologous PRF combined with 1% ALN gel which results in significant therapeutic outcomes when compared with PRF and access therapy alone in the treatment of furcation defects. Combining ALN with PRF has the potential to regenerate furcation defects without adversely affecting the healing process.

Periodontal regeneration in the treatment of IBDs is more likely to succeed as compared with the treatment of furcation defects. Patel et al[251] looked at the use of PRF in the treatment of IBDs and assessed the adjunctive use of PRF in the regenerative management of IBDs in comparison with open flap debridement (OFD). Twenty-six bilateral defects (13 per group) in 13 patients were randomized as either PRF (test group) or OFD alone (control group) sites. PD, CAL, and bone PD were recorded. The reduction in defect depth and percentage of bone fill was assessed radiographically. The primary outcomes assessed were changes in PD, CAL, and the percentage of bone fill at 6, 9, and 12 months. A secondary outcome of wound healing using a wound healing index was also assessed. The PRF group showed significant improvement in clinical parameters compared with the control group at 6, 9, and 12 months. The PRF group showed a bone fill of 45.18% ±7.57%, which was statistically significant compared with 21.6% ±9.3% seen in the control group at the end of the study period. The PRF group also showed significant soft tissue healing and reduction in PD. The wound healing index showed significant advantages for the PRF group. Achieving accelerated and more complete surface wound healing is a significant advantage of this procedure as postsurgical GR and loss of interproximal tissue volume is a negative patient-centered outcome regularly seen with all open flap procedures.

A systematic review performed by Castro et al[252] examined the regenerative potential of leukocyte and

platelet-rich fibrin (L-PRF) during periodontal surgery. An electronic and hand search were conducted in 3 databases. Only randomized clinical trials were included. PD, CAL, bone fill, keratinized tissue (KT) width, recession reduction, and root coverage (%) were considered as outcomes. Twenty-four articles fulfilled the inclusion and exclusion criteria, and 3 subgroups were created: IBDs, furcation defects, and periodontal plastic surgery. Significant PD reduction (1.1 ±0.5 mm), CAL gain (1.2 ±0.6 mm), and bone fill (1.7 ±0.7 mm) were found when comparing L-PRF with OFD in IBDs. For furcation defects, significant PD reduction (1.9 ±1.5 mm), CAL gain (1.3 ±0.4 mm), and bone fill (1.5 ±0.3 mm) were reported when comparing L-PRF with OFD. When L-PRF was compared with a connective tissue graft (CTG), similar outcomes were recorded for PD reduction (0.2 ±0.3 mm), CAL gain (0.2 ±0.5 mm), KT width (0.3 ±0.4 mm), and recession reduction (0.2 ±0.3 mm, $P>.05$). This systematic review supports the use of L-PRF in aiding periodontal wound healing, but not when autogenous soft tissue is also used.

In 2 studies, Aslan et al[253,254] described the use of a surgical technique, whereby the entire papilla is preserved in the treatment of deep and wide IBDs (EPP). Primary wound closure and uneventful early wound stability is considered some of the most critical elements of successful periodontal regeneration. Yet, the surgical elevation of the interdental papilla to access deep and wide IBDs entails an impairment of the papillary blood supply that can result in difficult healing due to a lack of primary closure in the early healing period. The technique essentially creates a single papilla tunnel, which is laterally displaced to provide access to the defect. The efficacy of this technique was evaluated in a study of 12 patients with at least 1 isolated deep IBD who received regenerative periodontal treatment. Access to the IBD for debridement was provided by a beveled vertical releasing incision positioned in the buccal gingiva of the neighboring interdental space. After the elevation of a buccal flap, an interdental tunnel was prepared, undermining the defect-associated papilla. Granulation tissue was removed, root surfaces were carefully debrided, and bone substitutes and enamel matrix derivatives were applied. A microsurgical suturing technique was used for optimal wound closure. Early healing was uneventful in all treatments, and 100% wound closure was maintained during the entire healing period. At 1 year, there was significant attachment gain of 6.83 ±2.51 mm. The 7 ±2.8 mm reduction in probing depth was also significant and was associated with minimal increase in GR (0.16 ±0.38 mm). This technique may limit the risk of wound failure, particularly in the early healing phase, thereby preventing exposure of regenerative biomaterials and possibly enhancing stabilization of blood clots in deep IBDs. However, patient selection for this technique is limited by the anatomy of the site and should be used only with defects with wide interproximal distances and deep intrabony components.

Soft tissue adjacent teeth and implants

Clinicians often subjectively relate different facial appearances with dental arch forms. However, evidence for possible associations between facial morphology, attachment loss, and GR is lacking in the literature. Salti et al[255] analyzed whether the facial type, which can be described by the ratio of facial width and length (facial index), is related to periodontal loss of attachment. They hypothesized that a broad face might be associated with less GR and less clinical attachment loss (CAL) than a long face. Data from the 11-year follow-up of the population-based Study of Health in Pomerania were used. Periodontal loss of attachment was assessed by GR and CAL. Linear regression models, adjusted for age and sex, were used to assess associations between specific landmark-based distances extracted from magnetic resonance imaging (MRI) head scans and clinically assessed GR or CAL (N=556). Analyzing all teeth, a higher maximum cranial width was associated with a lower mean GR and a lower mean CAL. Moreover, a long narrow face was significantly associated with an increased mean GR and CAL. Observed associations were more pronounced for incisors and canines than for premolars and molars. This study revealed craniofacial morphology, specifically the cranial width and the facial index, as a putative risk factor for periodontal loss of attachment and may be used as screening tool to identify patients at risk for the development of GR and attachment loss.

Literature describing clinical outcomes after the surgical treatment of recession defects associated with treating large, multiple tooth areas is lacking. In these clinical situations, some clinicians feel that the use of acellular dermal matrix allografts (ACDM) is often required due to the morbidity associated with donor harvesting. Romanos et al[256] conducted a case series evaluating the clinical and patient-centered outcomes when multiple recessions (Miller Class I, II, and III) affecting 5 or more teeth were treated in a single procedure using ACDM in 18 eligible participants. Low mean VAS pain scores (0.7 ±0.8) and analgesic consumption (2.3 ±2.5 tablets) were reported from 0 to 6 days postoperatively. Mean baseline recession depth was 2.1 ±1 mm. One year after surgery, the mean percentage root coverage was 87.1% ±18.3%, and complete root coverage was achieved in 61.7% of recessions with statistically significant differences between smokers and nonsmokers. These results support the use of ACDM in the treatment of large, multiple tooth surgical sites.

The free gingival graft (FGG) is commonly thought to be an effective way of increasing the zone of KG around

teeth. However, there are limited data supporting the use of FGG on implants with limited keratinized mucosa (KM). Oh et al[257] evaluated clinical and radiographic outcomes after FGGs around implants with limited KM during an 18-month follow-up compared with oral prophylaxis without augmentation. This prospective controlled randomized blind clinical study investigated 41 implants displaying lack of KM in 28 participants. After baseline examination, 14 participants in the experimental group received FGGs, followed by oral prophylaxis, and 14 participants in the control group received oral prophylaxis only. The width of KM, the level of mucosal margin, pocket depths, PI, and gingival index were assessed at baseline, 6, 12, and 18 months with changes in crestal bone levels assessed at 18 months. There was a significant gain in KM in the FGG group compared with controls at 6, 12, and 18 months. The mean gingival index was significantly lower for the FGG group at all follow-ups. Crestal bone loss in the FGG group was significantly less than that in the control group at 18 months. This investigation supports the use of an FGG for implants exhibiting lack of KM as a viable treatment option to reduce mucosal inflammation and to maintain crestal bone level in the short term.

Additional evidence supporting the influence of soft tissue thickness upon the maintenance of bone levels adjacent to dental implants was described by van Eekeren et al.[258] The study evaluated crestal bone changes around bone- and tissue-level implants related to initial mucosal thickness. The influence of the location of the abutment on implant interface was also examined. Patients received at least 2 implants: 1 with the prosthetic abutment connection at the crestal bone level (MC) and 1 with the prosthetic abutment connection at 2.5-mm supracrestal level (LC). Flap thickness measurements were made with a periodontal probe after raising the buccal flap. The patients were divided into 2 groups according to the mucosal thickness: group A (thickness, $\leq$2 mm) and group B (thickness, >2 mm). In group A (MC), sites presented with a mean bone change of −0.6 ±0.5 mm. In group B (MC) sites, 20, presented with a mean bone change of −0.2 ±0.4 mm; group A (LC) displayed a mean bone change of −0.1 ±0.5 mm; and group B (LC), 22, displayed a mean bone change of −0.2 ±0.4 mm. A paired-samples *t* test for groups A (MC) and B (MC) yielded a statistically significant difference; no statistically significant difference was found for groups A (LC) and B (LC). This study verifies that if the initial mucosal thickness surrounding bone-level implants is more than 2 mm, there is significantly less crestal bone change than bone-level implants placed in initial mucosal thicknesses of 2 mm or less. This difference was not statistically significant when tissue-level implants were used and when the implant-abutment connection was 2.5 mm above the crestal bone level.

A similar study by Canullo et al[259] specifically addressed the influence of platform-switched implant on abutment interface. They conducted a prospective trial for up to 3 years after implant loading, evaluating the influence of soft tissue thickness on changes in peri-implant marginal hard tissue levels. Any patient who was partially edentulous in the mandible and required at least 2 adjacent implant-supported restorations was recruited. A 3-mm tissue punch biopsy, which corresponded to a diameter slightly smaller than the coronal diameter of the implants, was performed using a circular mucotome. Then, implants with a length of 10 to 13 mm and a diameter of 3.8 mm were inserted. Outcome measures were implant and prosthesis survival rates, marginal hard tissue changes, any complications, and results of morphologic and histomorphometric analyses. A correlation between mucosa width components (epithelium, connective tissue, and epithelium and connective tissue) and radiographic bone loss at 1 and 3 years after loading was performed at the patient level. A total of 26 specimens in 26 patients with 68 implants were analyzed. The specimens were divided into 2 groups: group 1 (16 patients, 40 implants), with thin mucosa ($\leq$2 mm), and group 2 (10 patients, 28 implants), with thick mucosa (>2 mm). None of the implants or definitive prostheses failed during the healing period, and no major biologic or mechanical complications were recorded. The mean epithelium thickness was 0.43 mm; the mean connective tissue thickness was 1.3 mm, and the mean mucosa thickness was 1.75 mm. Comparisons of radiographic bone loss between group 1 and group 2 failed to show any statistically significant differences at the 1-year or 3-year follow-up examinations. The initial mucosa thickness surrounding a bone-level platform-switching implant seems not to influence the pattern of physiologic marginal bone loss. In areas with minimal soft tissue thickness, the use of platform-switched implants or that in combination with soft tissue grafting procedures should be considered.

Applying these findings to the immediate implant placement situation was studied by Canullo et al.[260] They evaluated the 10-year postloading radiological and esthetic outcomes of implants inserted in extraction sites and restored with or without a platform-switching protocol. Twenty-two patients were scheduled for maxillary postextractive implants of 13 mm in length and 5.5 mm in diameter (Global; Sweden & Martina). They randomly received definitive restorations using the platform-switching concept (abutment 3.8 mm in diameter: test group) or standard restoration (abutment 5.5 mm in diameter: control group). Outcome measures were survival rates of implants and prostheses, peri-implant marginal bone loss, and periodontal indices 10 years after prosthetic loading. Moreover, esthetic parameters

including soft tissue buccal peri-implant mucosal recession (REC) levels and mesial and distal papilla height (PH) were made at definitive restoration and after 2 and 10 years. Nineteen implants were analyzed after 10 years of follow-up. No implants or prostheses failed. The postoperative radiographs demonstrated an overall statistically significant mean bone loss of 0.18 ±0.14 mm in the test group and of 0.80 ±0.40 mm in the control group. The test group showed 0.23 ±0.51 mm of REC gain, and PH was of 0.21 ±0.33 mm on average. In contrast, the control group presented an REC of −0.59 ±0.80 mm with PH of −1.12 ±0.55 mm, demonstrating slight, continuous soft tissue shrinkage during the entire follow-up. The mean values were statistically significantly different between test and control group for both REC. This long-term study supports the use of immediate single-implant restorations rehabilitated with a platform-switching protocol, as they provide peri-implant alveolar bone-level stability and avoid continuous soft tissue shrinkage after 10 years of prosthetic loading compared with a platform-matching restoration.

When soft tissue augmentation is required adjacent to an implant, different surgical strategies are useful to improve the amount of KT, including the use of pedicle flaps, soft tissue grafts, ACDM, and xenogeneic collagen matrix (XCM). Mucograft is an XCM and was evaluated for its effectiveness in augmenting tissue-adjacent implants in a study by Cairo et al.[261] They performed a randomized clinical trial comparing XCM versus a CTG in its ability to increase buccal soft tissue thickness at the implant site. 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, 3, and 6 months. Outcome measures included buccal soft tissue thickness, coronal KT, chair time, and postoperative discomfort. A VAS was used to evaluate patient satisfaction. After 6 months, the final buccal soft tissue thickness increase was 0.9 ±0.2 in the XCM group and 1.2 ±0.3 mm in the CTG group, with a significant difference favoring the control group. Both procedures resulted in a similar final amount of KT with no significant difference between treatments. However, XCM was associated with significantly less chair time, less postoperative pain, less analgesic intake, and higher final satisfaction than CTG. Because the tissue thickness is one of the clinical parameters that influence long-term bone height, CTG is more effective than XCM to increase buccal peri-implant soft tissue thickness and enhance the maintenance of bone levels adjacent to dental implants.

In addition to bone level maintenance, patient satisfaction with implant therapy is also dependent on the preservation of interproximal soft tissue volumes in esthetically important sites. Lops et al[262] compared the interproximal papilla stability of restorations supported by computer-aided design and computer-assisted manufacture (CAD-CAM) abutments to those supported by prefabricated stock abutments in anterior areas over a 2-year follow-up. Abutments were selected depending on implant inclination and the thickness of buccal peri-implant soft tissues from the following: zirconia stock, titanium stock, zirconia CAD-CAM, and titanium CAD-CAM. Differences between the height of the papilla tip were measured (REC). They demonstrated that REC values of titanium and zirconia CAD-CAM abutments were significantly lower than those of titanium and zirconia stock. In addition to better interproximal papillae stability, the use of CAD-CAM abutments facilitates cement removal as compared with stock abutments.

Alveolar RP, ridge augmentation, and sinus augmentation procedures

Many studies support the use of some form of particulate grafting in ridge preservation (RP) procedures. It is yet unknown whether all sites require grafting and what technical modifications of the procedure enhance long-term success. Fickl et al[263] examined ridge contour changes after different alveolar RP techniques. An initial total of 40 patients provided a final total of 35 single-gap extraction sites. After tooth removal, the socket was subjected to 1 of 4 treatment modalities: placement of a deproteinized bovine bone mineral (DBBM; Endobon) covered with a soft tissue punch from the palate (Tx1); placement of DBBM without soft tissue punch (Tx2); placement of an adsorbable collagen membrane (OsseoGuard) covering the DBBM (Tx3); and no additional treatment (control). Silicone impressions were obtained before and 6 months after tooth extraction for quantitative-volumetric evaluation on stone cast models. Bone quality and the need for further bone augmentation were also noted. Tx1 and Tx3 resulted in significantly less bucco-oral tissue loss than Tx2 and the control group. Premolar teeth and teeth extracted for traumatic reasons revealed significantly less tissue loss. Using barrier membranes or soft tissue punches in addition to placement of DBBM seems to be advantageous to limit bucco-oral tissue atrophy.

Limited evidence is available evaluating RP and implant placement in molar sites. Walker et al[264] compared alveolar ridge changes with and without RP with CBCT. This parallel, 2-arm randomized clinical trial included 40 patients evenly distributed between 2 treatment groups. After molar extraction, sites were allowed to heal naturally or received RP with freeze-dried bone allograft covered by a nonresorbable dense polytetrafluoroethylene membrane. CBCT scans were made immediately and 3 months after extraction, and then a dental implant was placed. Width and height measurements were made radiographically. Significantly greater

loss in alveolar ridge height was found in molar sites allowed to heal without RP on the buccal aspect of the socket (RP: −1.12 ±1.60 mm versus no RP: −2.60 ±2.06 mm). No significant difference in ridge width loss was found between groups. Two-thirds of ridge width reduction was experienced on the buccal aspect in sites without RP, but width loss was evenly distributed between buccal and lingual aspects when RP was performed. Bone grafting at the time of placement was required in 25% of implants in the group without RP versus 10% of implants in the RP group. In molar extraction sites without RP, significantly more reduction in ridge height occurred, and the majority of ridge width loss was localized to the buccal aspect. When RP was performed, ridge width loss was not significantly decreased, but the loss was evenly distributed between facial and lingual aspects of the extraction site. This study supports site-specific selection for the use of RP procedures.

If RP procedures are not used, a depression often remains in the buccal contour of alveolar bone. Jung et al[265] performed an RCT testing whether small bony dehiscence defects adjacent to implants (≤5 mm) left to heal spontaneously resulted in the same clinical and radiological outcome as defects treated with guided bone regeneration (GBR). Twenty-two patients who received at least 1 implant with a small bony dehiscence defect were enrolled in the study. If the defect height was ≤5 mm, the site was randomly assigned to either the spontaneous healing (SH) group or the GBR group. In the SH group, the defect was left without any treatment. In the GBR group, the defects around the implants were grafted with DBBM and covered with a native collagen membrane. Clinical and radiographic measurements were performed 6 months after implant placement with a re-entry surgery, at the time of crown insertion, and at the subsequent follow-up appointments at 3, 6, 12, and 18 months after loading. The implant and crown survival rate 18 months after loading was 100%, revealing no serious biologic or prosthetic complication. The mean changes of the buccal vertical bone height between implant placement and re-entry surgery after 6 months revealed a small bone loss of −0.17 ±1.79 mm for the SH group and a bone gain of 1.79 ±2.24 mm for the GBR group. Radiographic measurements demonstrated a slight bone loss of −0.39 ±0.49 mm for the SH group and a stable bone level of 0.02 ±0.48 mm for GBR group after 18 months. All peri-implant soft tissue parameters revealed healthy tissues with no difference between the 2 groups. Small bony dehiscence defects left for SH demonstrated high ISRs with healthy and stable soft tissues. However, these same sites revealed more vertical bone loss at the buccal aspect 6 months after implant insertion and more marginal bone loss between crown insertion and 18 months after loading than sites treated with GBR. Considering the incidence of peri-implantitis, this initial compromise of bone height may affect longer term outcomes of nongrafted sites.

The value of adding a bone graft to the gap between the implant fixture and socket wall has been evaluated by Sanz et al.[266] They performed a randomized parallel controlled clinical trial studying the efficacy of grafting with demineralized bovine bone mineral with 10% collagen (DBBM-C) in the gap between the implant surface and the inner bone walls when the implants were immediately placed in the anterior maxilla. The changes between implant placement and 16 weeks later in the horizontal and vertical crestal bone in relation to the implant were evaluated through direct bone measurements using a periodontal probe. The horizontal crest dimension underwent marked changes during healing mainly at the buccal aspect of the alveolar crest where this reduction amounted to 1.1 mm (29%) in the test group and 1.6 mm (38%) in the control group. These findings were statistically significant. This outcome was even more pronounced at sites in the anterior maxilla and with thinner buccal bone plates. The results from this clinical trial demonstrated that placing a DBBM-C bone replacement graft significantly reduced the horizontal bone resorptive changes occurring in the buccal bone after the immediate implantation in fresh extraction sockets.

While numerous recent studies have examined the influence of biomaterials on volumetric stability of the grafted sites when performing sinus floor elevation (SFE) procedures, fewer studies have looked at the influence of the surgical technique on this volumetric stability.

When comparing the lateral window approach to a transcrestal approach, a common perception is that the less invasive technique results in less postoperative discomfort. Temmerman et al[267] performed a study to investigate the influence of various surgical techniques for sinus augmentation on the volumetric changes of graft, membrane, and the postoperative discomfort. Eighteen patients in need of bilateral SFE were assigned to lateral SFE, transcrestal SFE, and intralift procedures. CBCT images made at baseline, 1 week, and 6 weeks were analyzed for volumetric changes in graft and Schneiderian membrane. Questionnaires were used to analyze postoperative discomfort. The overall average graft volume obtained after 1 week was 1.87 cm^3. Volumes decreased after 6 weeks to an overall mean volume of 1.33 cm^3 for an average decrease of 27.6%. After 6 weeks, the amount of graft volume decreased in every treatment option, ranging from −23.13% for the sinus floor elevation: transcrestal approach (tSFE), over −24.55% for the sinus floor elevation: lateral window approach (ISFE), to −33.71% for the IL. Although all treatment options correspond to an increase in Schneiderian membrane volume, no statistically significant

correlation between this increase and loss of graft volume could be obtained for all treatments. It was concluded that all SFE techniques provided sufficient graft volume for implant treatment, provoked a partially transient swelling of the Schneiderian membrane, and resulted in a decrease in graft volume after 6 weeks. However, no significant differences were obtained between treatments. Furthermore, no statistically significant correlation between the postoperative swelling of the Schneiderian membrane and reduction in graft volume at 6 weeks could be found.

A common procedural complication during sinus lift procedures is perforation of the Schneiderian membrane. The possible negative effect of this complication is not well described. Almeida Ferreira et al[268] evaluated ISRs for implants placed in grafted sinuses where a membrane perforation occurred during augmentation using exclusively anorganic bovine bone (ABB) by means of clinical and radiographic examinations. Histologic information of 5 biopsy specimens taken from large membrane perforations was also presented. Details of consecutive patients who underwent sinus augmentation procedures at a private practice setting between 2004 and 2013 were collected from a computer database. The following profiles were selected for data analysis: computed tomography (CT) before treatment; perforated membrane information according to size: not perforated, small ($\leq$5 mm), medium (>5 and <10 mm), or large ($\geq$10 mm); sinuses grafted exclusively with ABB and lateral window covered with a collagen membrane; and implant survival after at least 2 years of functional loading in augmented sinuses. Implants were considered survivals in the absence of infection, mobility, or pain. The sample in this retrospective study comprised 531 patients, of which 214 required bilateral sinus augmentation and 317 required unilateral sinus augmentation (total=745 sinuses). A total of 1588 implants were placed. From 745 augmented sinuses, 237 (31.8%; 523 implants) were perforated during the procedure. Among these, 48 perforations were large (20.2%; 107 implants), 67 (28.3%; 150 implants) were medium, and 122 were small (51.5%; 266 implants). Of 523 implants placed in perforated sinuses, 15 were lost (ISR=97.1%). Comparison of the ISRs for small (97.7%), medium (97.3%), and large (95.3%) perforations with 1065 implants placed in nonperforated sinuses (ISR=97.7%) was not statistically significant. The histomorphometric analysis of the 5 biopsy specimens showed 24.52% ±6.99% of new bone, 24.32% ±6.42% of marrow space, and 51.2% ±3.75% of the remaining ABB. The difference in ISR for implants placed in perforated and nonperforated sinuses was not statistically significant. Within the limits of the histologic data, histomorphometric results with 24.52% ±6.99% of new bone formation in sinuses with large perforations showed similar bone formation compatible with nonperforated sinuses described elsewhere in the literature.

Some augmented sinus sites require a healing period of 6 to 8 months of bone maturation before subsequent implant placement. The addition of biologics to the bone graft material may decrease the time needed before implant placement. Kubota et al[269] evaluated the effect of recombinant human platelet-derived growth factor BB combined with a deproteinized cancellous bovine bone graft for sinus augmentation. The lateral window approach was used for maxillary sinuses with minimal residual bone. Forty-six patients received a total of 105 implants at an average of 13 mm vertical dimension of augmentation within the sinus. After a healing period of 4 months, dental implants were placed and then restored after a 2-month osseointegration period. The result demonstrated increased bone height and implant stability quotient (ISQ) values and a 100% survival rate. This study indicates that the addition of recombinant human platelet-derived growth factor BB to deproteinized cancellous bovine bone accelerated the healing period in maxillary sinuses with minimal native bone.

Peri-implantitis

Titanium is the biomaterial most frequently used to construct implants partly because of the formation of a titanium dioxide (TiO_2), a surface very biocompatible with osseointegration. TiO_2 also has a high resistance to corrosion, although corrosion of dental implants can still happen. Like all metal oxides, TiO_2 is susceptible to acid dissolution. Corrosion-triggering factors include local acidification due to inflammation of peri-implant tissues or by promotion of an acidic environment by bacteria. The resulting corroded implant surfaces may provide microenvironments for secondary colonization. Corrosion of the implant surface is of concern as the result of the corrosion process is the leaching of titanium particles and ions into the peri-implant environment. These corrosion products are not inert and have been associated with the induction of an inflammatory response and bone resorption. Whether an association exists between the presence of titanium dissolution and peri-implantitis is an active area of investigation. Answering this question may further improve our understanding of a possible etiology of peri-implantitis. Safioti et al[270] conducted a study comparing levels of titanium dissolution in submucosal plaque samples collected from healthy implants and implants with peri-implantitis. Submucosal plaque from 20 implants with peri-implantitis and 20 healthy implants was collected with sterile curettes from 30 participants. Levels of titanium were quantified using inductively coupled plasma mass spectrometry and normalized for mass of bacterial DNA per sample to exclude confounding by varying amounts of plaque per site. Implants with peri-implantitis harbored significantly

higher mean levels of titanium (0.85 ±2.47) versus healthy implants (0.07 ±0.19) after adjusting for amount of plaque collected per site. Greater levels of dissolved titanium were detected in submucosal plaque around implants with peri-implantitis than around healthy implants, indicating an association between titanium dissolution and peri-implantitis.

Factors triggering titanium dissolution, as well as the role of titanium corrosion in the peri-implant inflammatory process, were investigated in the following articles. Oliveira et al[271] conducted a systematic review of the literature examining the effects of degradation products on peri-implant tissues, which are released from dental implants as a consequence of therapeutic treatment for peri-implantitis and/or of wear-corrosion of titanium. Seventy-nine relevant scientific articles on the topic were retrieved. The results showed that proinflammatory cytokines, infiltration of inflammatory response cells, and activation of the osteoclasts activity are stimulated in peri-implant tissues in the presence of metal particles and ions. Moreover, degenerative changes were reported in macrophages and neutrophils that phagocytosed titanium microparticles, and mutations occurred in human cells cultured in medium containing titanium-based nanoparticles. Studies have also suggested that debris released from the degradation of dental implants has cytotoxic and genotoxic potential for peri-implant tissues. The authors cited a secondary conclusion that implies dose dependency: the amount and physicochemical properties of the degradation products determine the magnitude of the detrimental effect on peri-implant tissues.

The initiation of the innate immunity pathway is triggered by inflammasomes, large intracellular multiprotein complexes which activate the release of proinflammatory cytokines. Although inflammasome activation has previously been linked to periodontal inflammation, little information on a potential association with peri-implantitis is available. Orthopedic implants are placed in a sterile environment and accordingly should not be exposed to bacteria. However, failing orthopedic implants also induce an inflammatory response such as that seen with peri-implantitis. The loss of orthopedic implants has been described as aseptic loosening, and much research has been carried out during the last 10 years to identify the mechanism of this osteolysis leading to prosthesis failure. From this orthopedic research, an association between inflammasome activation and aseptic loosening has been made. Pettersson et al[272] examined the cytotoxic and proinflammatory effects, including inflammasome activation, of metals used in dental implants, in an in vitro model, as well as from clinical tissue specimens. Human macrophages were exposed to different metals—titanium (Ti), cobalt, chromium, and molybdenum—in a cell-culture assay. Cytotoxicity was determined using the neutral red uptake assay. Cytokine secretion was quantified using an ELISA, and the expression of genes of various inflammasome components was analyzed using quantitative PCR. In addition, the concentrations of interleukin-1beta (IL-1beta) and Ti in mucosal tissue sampled near dental implants were determined. These researchers demonstrated that Ti ions in physiological solutions stimulated inflammasome activation in human macrophages and consequently resulted in IL-1beta release. This effect was further enhanced by macrophages that have been exposed to lipopolysaccharides. The proinflammatory activation caused by Ti ions disappeared after millipore filtration (0.22 μm), which indicated an effect of particles and not the ions alone. The Ti levels of tissue samples obtained near Ti implants were sufficiently high (≥40 μM) to stimulate secretion of IL-1beta from human macrophages in vitro. This study suggests that Ti ions form particles that may act as secondary stimuli for a proinflammatory reaction.

In addition to the chemical corrosion process, additional sources of Ti ions and Ti particles in the peri-implant environment have been suggested. In a review on this topic, Apaza-Bedoya et al[273] suggested the importance of the role of the abutment-to-implant connection in shedding of Ti ions and particles into peri-implant tissues. The aim of this review paper was to report the degradation at the implant-abutment connection by wear and corrosion processes taking place in the oral cavity. Most of the retrieved studies evaluated the wear and corrosion, referred to as tribocorrosion of titanium-based materials used for implants and abutments in artificial saliva. Electrochemical and wear tests together with microscopic techniques were applied to validate the tribocorrosion behavior of the surfaces. Studies also inspected the wear on the inner surfaces of the implant connection as a result of fatigue or removal of abutments. These studies reported increased microgaps after fatigue tests. In addition, data suggest that micromovements occurring at the contacting surfaces can increase the wear of the inner surfaces of the connection. Biofilms and/or glycoproteins act as lubricants, although they can also amplify the corrosion of the surfaces by changes in the pH of the microenvironment. The authors concluded in this review that wear and corrosion debris such as ions, microparticles, and nanoparticles released into the surrounding tissues can stimulate peri-implant inflammation which can lead to pathologic bone resorption. A clinical implication from this review is that the precision of the fit of the abutment, as well as its material makeup, may influence the incidence of peri-implantitis.

The makeup of the implant surface in the development of peri-implantitis continues to be examined. Kim et al[274] studied the occurrence of progressive bone loss

(PBL) around implants with different implant surfaces. This large retrospective study, examining 2517 implants, was performed in 903 patients, including 1147 anodized-surface implants in 454 patients and 1370 resorbable blasting media (RBM)-surface implants in 449 patients. Through regular follow-up radiographs and records, the presence of PBL (up to >50% of fixture length) was investigated. Implant removal for any reason was regarded a failure. In total, 2186 implants (979 anodized implants and 1207 RBM implants) in 793 patients were included in this study. PBL was more frequently observed among anodized implants (n=36 in 21 patients; 4%) than among RBM implants (n=19 in 14 patients; 2%), and this difference was statistically significant. Occurrence of PBL was significantly influenced by surface modification and implant diameter. However, total survival rate was significantly influenced by implant diameter and not by surface modification, although effect of implant diameter was observed to be significant on anodized implants.

The clinician whose patient presents with peri-implantitis is faced with the challenge of determining the best method for chemotherapeutic decontamination of the implant surface. Dosti et al[275] tested the efficacy of commonly used antimicrobial agents in decontamination of multispecies mature oral biofilm on airborne-particle abraded, large-grit, acid-etched (SLA) titanium implants. SLA titanium disks were inoculated with dental plaque and cultured anaerobically for 21 days. The disks were rinsed with 0.9% NaCl; exposed for 2 minutes to tetracycline paste, 1% chlorhexidine gel (CHX), 35% phosphoric acid gel (Etch), or a novel chemical formula (0.3% cetrimide, 0.1% CHX, and 0.5% EDTA [Ethylenediaminetetraacetic acid]); and then rinsed again with 0.9% NaCl. Bacteria were quantified from scanning electron micrographs of the implant surfaces. Living bacteria were quantified with confocal laser scanning microscopy. These results demonstrated that rinsing the surfaces with 0.9% NaCl removed most of the biofilm. However, bacteria persisted in all specimens, and none of the disinfectants was superior to the double saline rinse group. The confocal laser scanning microscopy analysis showed that CHX and Etch groups had a statistically significant reduction of viable bacteria, although small. Overall, the results show that many disinfection agents used in the clinic are ineffective in biofilm removal and leave live bacteria on the surface. Rinsing with saline may also have the desired effect of reducing the chance of titanium surface alteration.

The proper mechanical debridement protocol for the dental implant surface remains controversial. Ronay et al[276] assessed the cleaning potential of commonly used implant debridement methods, simulating nonsurgical peri-implantitis therapy in vitro. One hundred-and-eighty dental implants were ink-stained and mounted in combined soft and hard tissue models, representing peri-implantitis defects with angulations of 30, 60, and 90 degrees covered by a custom-made artificial mucosa. Implants were treated for 120 seconds with the following instruments: Gracey curette, ultrasonic scaler, and an air powder abrasive device with a nozzle for submucosal use utilizing glycine powder. All procedures were repeated 10 times for each instrumentation and defect morphology. Images of the implant surface were made. Micromorphologic surface changes were analyzed on scanning electron microscope images. The areas of uncleaned surfaces (%, mean ±standard deviations) for curettes, ultrasonic tips, and airborne-particle abrasion accounted for 74.70 ±4.89%, 66.95 ±8.69%, and 33.87 ±12.59%, respectively. The air powder abrasive device showed significantly better results for all defect angulations. Scanning electron microscope evaluation displayed considerable surface alterations after instrumentation with Gracey curettes and ultrasonic devices, whereas glycine powder did not result in any surface alterations. Although a complete surface cleaning could not be achieved regardless of the instrumentation method applied, the powder air-abrasive device showed better cleaning potential for all defect angulations with better results at wide defects.

When a significant IBD is associated with the peri-implantitis site, a surgical intervention is often required. Carcuac et al[277] described the results of a 3-year follow-up of patients enrolled in a randomized controlled clinical trial on surgical treatment of advanced peri-implantitis. A total of 100 patients with advanced peri-implantitis were randomly assigned to 1 of 4 treatment groups. Surgical therapy aiming at pocket elimination was performed and, in 3 test groups, supplemented by systemic antibiotics, use of an antiseptic agent for implant surface decontamination, or both. Outcomes were evaluated after 1 and 3 years by means of clinical and radiological examinations. Differences between groups were explored by regression analysis. Clinical examinations at 3 years after treatment revealed improved peri-implant soft tissue health with a mean reduction in probing depth of 2.7 mm, a reduction in bleeding/suppuration (SUP) on probing of 40%, and stable peri-implant marginal bone levels (mean bone loss during follow-up: 0.04 mm). Implant surface characteristics had a significant impact on 3-year outcomes, in favor of implants with non-modified surfaces or turned surfaces. The benefits of systemic antibiotics were limited to implants with modified surfaces and to the first year of follow-up. This study is important as it suggests that surgical intervention may not result in sustainable positive outcomes on implant surfaces designed for more rapid osseointegration. It is suggested that surgical treatment of peri-implantitis is effective and that outcomes of therapy are affected by implant surface characteristics. Also, the

potential benefits of systemic antibiotics are not sustained over 3 years.

The determination of a peri-implantitis site which will benefit for a surgical intervention will depend in part on a radiographic assessment. Serino et al[278] examined the accuracy between intrasurgical and periapical radiographic measurements of bone loss at implants with peri-implantitis. A total of 46 Branemark implants in 24 patients with a diagnosis of peri-implantitis were included in the study. The amount of peri-implant bone loss occurred at those implants was measured during peri-implant surgery and compared with the radiographic bone loss measured by 3 independent examiners. The mean bone loss measured on radiographs underestimated the intrasurgical bone loss at the correspondent sites (0.7 mm at the mesial and 0.6 mm at the distal sites). Only 21% of the radiographic measurements corresponded to the clinical bone loss assessments, whereas an overestimation and underestimation within a range of ±1-2 mm was recorded in 57% of the implants. The radiographic measurements of bone loss at implants affected by peri-implantitis often underestimated the clinical bone loss occurred at the implants.

Food impaction secondary to the development of open proximal contacts between implant support restorations and natural teeth is not uncommon and may contribute to peri-implant bone loss. Pang et al[279] analyzed the prevalence of proximal contact loss (PCL) between implant-fixed prostheses (IFPs) and adjacent teeth and investigated the associated factors. They conducted a study of 150 participants recruited for a prospective study. Two hundred thirty-four IFPs supported by 384 implants for the posterior region were studied. The contact tightness had been recorded using aluminum strips of different thicknesses with a regular interval after delivery. The proximal contact was considered as lost if the contact tightness was over 50 μm, and statistical analyses were performed to estimate the prevalence rate of PCL and its influential factors. Among the total 299 proximal contacts of 234 IFPs, 179 were observed as a PCL (59.9%). Bone level and root configuration of the adjacent teeth and the proximal contact position and jaw position of the implant prostheses were statistically significant factors, when analyzed by the cumulative PCL rate. The proximal contact position and bone level of adjacent teeth and jaw position were revealed to be statistically significant. The authors concluded that PCL should be considered as an implant prosthesis complication to which various associated factors could be related. This study revealed that the lower alveolar bone support level of the adjacent teeth, maxillary position of IFPs, and mesial site of IFPs were significantly associated with a higher incidence of PCL. The clinical implications of these results suggest the use of a retrievable and repairable implant restoration in areas future PCL is expected. Secondarily, the use of removable occlusal appliances may decrease the prevalence of PCL.

Although prevention of peri-implantitis cannot be guaranteed, a preventive maintenance therapy may help to decrease the prevalence of this disease. Factors that affect compliance of preventive therapy are not well defined. Monje et al[280] investigated the association between peri-implant maintenance therapy (PIMT) and the frequency of peri-implant diseases in an attempt to identify factors that contribute to failure of PIMT compliance. A cross-sectional study on patients who were healthy and partially edentulous was conducted. They were grouped in the following categories according to PIMT compliance: regular compliers (≥2 PIMT/year); erratic compliers (ECs) (<2 PIMT/year); and noncompliers (NCs) (no PIMT). Radiographic and clinical analyses were carried out including PD, PI, BOP, mucosal redness, SUP, KM dimension, and marginal bone loss. A multiple logistic regression model was estimated. Two hundred and six implants in 115 patients fulfilled inclusion criteria. At patient level, it was shown that the association between compliance and peri-implant condition was statistically significant. Compliance was associated with 86% fewer conditions of peri-implantitis. The probability of PIMT compliance was substantially associated with the frequency of peri-implantitis. Patients with a history of periodontal disease multiplied their probability of being EC (versus NC) 4.23 times with respect to not having a history of periodontal disease. Moreover, light smokers significantly resulted to be NC compared with regular compliers and EC. Nevertheless, mucositis was not found to be statistically associated with the level of compliance. In addition, PD, PI, BOP, mucosal redness, and SUP varied significantly according to PIMT compliance and peri-implant conditions. Peri-implant maintenance compliance ≥2 PIMT/year seems to be crucial to prevent peri-implantitis in healthy patients. A history of periodontal disease and disease severity and a smoking habit appear to be factors that influence the compliance risk profile.

If an implant must be removed, understanding the likely success of a second implant placed in the same site is an important consideration in the development of a treatment plan. A large retrospective study assessing the survival of dental implants placed in sites of previously failed implants was conducted by Chrcanovic et al[281]. Patients who had failed dental implants, which were replaced with the same implant type at the same site, were included. Descriptive statistics were used to describe the patients and implants; survival analysis was also performed. The effect of systemic, environmental, and local factors on the survival of the reoperated implants was evaluated. One hundred seventy-five of 10 096 implants in 98 patients were replaced by another

implant at the same location (159, 14, and 2 implants at second, third, and fourth surgeries, respectively). Newly replaced implants were generally of similar diameter but of shorter length than the previously placed fixtures. A statistically significant greater percentage of lost implants were placed in sites with low bone quantity. There was a statistically significant difference in the survival rates between implants that were inserted for the first time (94%) and implants that replaced the ones lost (73%). There also was a statistically higher failure rate of the reoperated implants for patients taking antidepressants and antithrombotic agents. This study proposes that implants replacing failed implants have lower survival rates, and the clinician may expect 1 out of 4 replacement implants to fail in the future. It is suggested that a site-specific negative effect may possibly be associated with this phenomenon.

DENTAL MATERIALS

Many studies related to dental materials were published in 2017. This review will discuss studies published on silver diamine fluoride (SDF), stainless-steel crowns, restoration repair and replacement, silver amalgam, resin-based composite, and endodontic materials.

Silver diamine fluoride

One of the more active topics of publication in 2017 has been related to the use of SDF. Of these, valuable guidance was provided by the American Academy of Pediatric Dentistry through its publication of a systematic review and clinical guideline titled "Use of Silver Diamine Fluoride for Dental Caries Management in Children and Adolescents, Including Those with Special Health Care Needs".[282] The expert panel provided graded recommendations regarding the use of 38% SDF for the arrest of cavitated caries lesions in primary teeth, when used as part of a comprehensive caries management program. This last part is an important distinction, as the recommendations do not imply that SDF is intended to replace or displace existing caries preventive and management protocols, but rather to enhance the outcomes of those programs. The recommendations took into account the disparity and morbidity of untreated decay in children and special-needs patients, the growing recognition of risks related to general anesthesia in young children, the high costs of managing early childhood caries, the effectiveness of SDF coupled with its low invasiveness and associated costs, and the lack of reported toxicity or adverse events associated with the SDF use. Practical guidance for use was presented in a series of practical recommendations covering the topics of indications and usage, informed consent, patient protection, lesion preparation, application protocols, application frequency, reapplication, esthetic considerations for black staining of lesions and tissues, and proper CDT coding. This document is the most complete guide available for clinical recommendations on using SDF for the arrest of caries in primary teeth. It is a must-read for anyone considering adding SDF as a component of their comprehensive caries management program.

Several articles reported on the performance of SDF as a caries-arresting medicament in various forms and application protocols. One randomized clinical trial compared 12% SDF with the commercially available 38% SDF, as well as 1 versus 2 annual applications in arresting cavitated lesions in primary teeth.[283] A total of 888 children with 4220 decayed surfaces were randomly allocated to the 4 treatment groups and followed up for up to 30 months. The results showed that 38% SDF was more effective than the 12% SDF solution (OR, 1.98; 95% confidence interval [CI], 1.51 to 2.60, $P<.001$). The frequency of application favored twice annual when the factor of poor oral hygiene was taken into account. Children with a higher visible PI had a lower chance of caries arrest (OR, 0.59; 95% CI, 0.49 to 0.72). The highest performing group was 38% SDF with twice annual application achieving an arrest rate of 75.7% after 30 months. A second paper on performance compared 38% SDF with a tinted water placebo in lesions of preschool children with the outcomes of lesion arrest and plaque microbial composition being assessed.[284] The average proportion of arrested caries was 72% in the SDF versus 5% in the placebo group, demonstrating a strong treatment effect. An interesting finding was that there was no consistent change in the abundance of caries-associated microbes in either the treatment or placebo plaque samples. Plaque samples were collected 14 to 21 days after treatment; so apparently, the SDF treatment had no sustained impact on the adjacent plaque microbial biome. No adverse responses were reported.

Another article looking at mechanisms of action for SDF performed a literature search resulting in 29 articles related to the effect of SDF on cariogenic bacteria and alteration of dental hard tissues.[285] Eleven of the articles concluded that SDF was bactericidal to cariogenic bacteria, primarily *Streptococcus mutans* and that it inhibited the growth of cariogenic biofilms on teeth, mostly in laboratory models. This discrepancy in findings with the prior clinical study is an example of how laboratory models often do not predict or replicate actual clinical biology. This same review reported that SDF use was associated with enamel and dentin remineralization, a higher resistance of treated lesions to subsequent demineralization, and the formation of a mineral-rich surface in arrested lesions. Four of the cited studies reported that SDF inhibited collagenases and protected dentin collagen from damages.

A systematic review of clinical trials was published which evaluated the efficacy of SDF in controlling caries progression in children when compared with active controls or placebos.[286] Eleven articles were included in the final review and meta-analysis. Caries arrest at 12 months was 66% higher than that with other active materials and 154% higher than that with placebos. Overall caries arrest was 89% higher (95% CI, 49% to 138%; $P<.001$) than that when using either active materials or placebo, and the quality of the evidence was graded as high.

A second systematic review included 19 studies, 16 in the primary dentition and 3 in the permanent dentition.[287] Eight contributed to a meta-analysis, and the overall proportion of arrested caries was 81% (95% CI, 68% to 89%). No adverse effects were noted other than the black staining of lesions, and the overall conclusion was that 38% SDF is effective at arresting caries in children, but there was no consensus on the number and frequency of applications needed at this time.

Three articles reported on perceptions and acceptance of the SDF treatment. The first was a clinical study of 32 preschool children with 118 active caries lesions in primary teeth.[288] The patients were enrolled at a community dental clinic in Oregon, and the lesions were treated with 1 or 2 applications of 38% SDF. Patients were assessed over 3 months, and parents surveyed regarding subjective feelings about SDF. The clinical outcomes were that all assessed lesions were arrested with no associated adverse effects or incidences of pain or infection. The parental impressions were favorable for ease of application, taste, and esthetics, but one has to question as to how a parent can assess the impression of taste in their children.

A second Web-based survey assessed parent's perceptions to photographs of SDF-treated lesions and the acceptability within different behavior management scenarios.[289] Most parents (67.5%) judged staining in posterior teeth to be esthetically tolerable, but only 29.7% had the same judgment as it related to anterior teeth. As scenarios were presented with increasing behavioral barriers, the level of acceptance by parents increased, and when faced with the scenario of general anesthesia, acceptance of SDF increased to 68.5% on posterior teeth and 60.3% on anterior teeth.

A third article investigated the perceptions of dental hygienists practicing in alternative settings with regard to using SDF.[290] A survey tool was distributed to 222 California hygienists practicing in alternative settings treating underserved populations. The response rate was 46% (103), and just over half (54%) reported being familiar with SDF. Highly favorable responses were recorded for the features of being noninvasive, less expensive than traditional treatment, more time efficient, and not requiring local anesthesia. Although 56% thought that parents would object to the permanent black staining, 88% still felt that the advantages outweigh the disadvantages for underserved patient populations.

Two articles investigated the use of SDF in older populations for root caries control. The first was a cost-effectiveness study modeling patient treatment scenarios over 10 years.[291] The model included 4 treatment scenarios of no treatment, daily fluoride rinses, chlorhexidine varnish 2 times per year, and SDF 2 times per year. Data from systematic reviews of these scenarios were used to infer the relative efficacies of the treatments, and the outcomes were annualized cost and years of teeth being caries free. As in most preventive scenarios, in populations with 16 teeth considered at low tooth-level risk, the least costly, but also least effective was no treatment (130 Euro, 144 years). SDF ranked second at 180 Euro and 151 years, and both chlorhexidine or fluoride rinse were not cost-effective for preventing new root caries. When scenarios were tested with more than 16 teeth and higher tooth-level risk, SDF was the most effective and least costly alternative (8.3 Euro per caries-free tooth-year).

The second article was a systematic review of SDF effectiveness in older adults.[292] Three RCTs of root caries preventive fraction and arrest rates found that both outcomes were significantly higher than a placebo treatment. The preventive fraction at 3 years was found to be 71% for SDF compared with placebo, and all 3 studies reported significant preventive fractions at all time points with no observed adverse effects. The overall conclusion was that the existing reports on SDF support its effectiveness for root caries prevention and arrest.

Evidence continues to support the efficacy of SDF in primary teeth and root caries in older adults. There are still very few studies investigating treatment of occlusal or proximal lesions in permanent teeth, so it is uncertain if the arresting phenomena experienced in primary teeth and root lesions will convey to permanent dentition. The fact that protocols cannot establish evidence-based recommendations on frequency and timing of reapplication indicates that SDF is similar to most preventive regimens in that it is risk-based, requiring good clinical assessment of risk and intelligent judgment for establishing the individual frequency of treatment and monitoring. One outstanding model demonstrating the impact of SDF as part of a caries-management program was recognized with the American Dental Association's Presidential Citation of Dr Frank Mendoza, a pediatric dentist with the Indian Health Service Dental Clinic in Warm Springs, Oregon.[292] Dr Mendoza was able to demonstrate over 3 years a dramatic reduction in both restorative treatment needs and treatment under general anesthesia in a very high–risk population. What is important to realize, however, is that this success was due in large part to the establishment of a comprehensive caries-management

program in which SDF played a pivotal role but also relied on good pediatric medical collaboration, community acceptance, patient navigation, parental support, and a host of other components that are part of a system, and not simply a treatment. What is becoming more and more apparent is that SDF is successful as a treatment, but caries management requires a much broader system approach to be successful.

Stainless-steel crowns

Stainless-steel crowns have been a mainstay for the treatment of extensive caries in primary teeth. The material is well proven, but as is often the case it is how this material is used that may play a bigger role than the material itself. It has been 20 years since Dr Norna Hall, a general practitioner in Northern Scotland, first started managing caries on primary teeth by placing stainless-steel crowns over unprepared teeth using glass ionomer cement, thus sealing in carious tissue. The Hall Technique became popular 10 years ago, and evidence for the success of this method continues to grow. A 2017 article in the British Dental Journal provides a good summary of evidence from randomized clinical trials completed or underway.[293] These studies have reported success rates (no pain or infection) in the high 90% ranges over the normal functional service life of the primary teeth. This article also describes many of the common questions regarding the technique and its outcomes.

Two additional articles described clinical outcomes using this technique. The first followed 246 children aged 4 to 9 years and treated in a United Kingdom specialist hospital setting.[294] A retrospective comparison was made between conventional caries removal and preparation for stainless-steel crowns and crowns placed over unprepared teeth using the Hall Technique. The outcomes were described as success, minor failure, or major failure in the categories of clinical, radiographic, and final tooth condition. There were 836 teeth receiving conventional crowns and 388 teeth with the Hall Technique. The majority of primary teeth in both approaches remained asymptomatic over a period of up to 77 months with an overall success rate of 95.3% in the conventional group and 95.8% in the Hall Technique.

A second article described a retrospective study of Hall Technique crowns placed on primary molars at the University of Iowa College of Dentistry from 2011 to 2015.[295] The outcomes were categorized as clinical and radiographic success or failure, with clinical failure defined as the need for pulp therapy or extraction and radiographic failure as any new visible pathology. The study included 293 crowns with a mean follow-up of 9.9 months at the first recall and 20.1 months at the second recall. The overall clinical success rates were 98.9% at the first recall and 97.4% at the second recall. Radiographic success was 97.7% at the first recall and 94.9% at the second recall.

This evidence demonstrates that the biological management of caries is a viable option and can provide a less invasive, yet equally effective, outcome to traditional caries removal in primary teeth. It is also another example where advances in treatment were not due to improved materials, but rather by a more effective use of proven, traditional materials in a nontraditional way. This is a proof that we all need to keep an open mind when faced with nonconventional approaches to innovation.

Sealants

Another active area of publication in 2017 has been the topic of pit and fissure sealants. Several articles addressed cost-effectiveness of sealants, with the first comparing sealants to fluoride varnish on first molars with the measured outcomes being the proportion of children developing caries into dentin on treated teeth and the cost-effectiveness of both preventive modalities after 36 months.[296] The results from 835 treated children, aged 6 and 7, divided into the 2 treatment arms showed that 17.5% of the fluoride varnish and 19.6% of the sealant children developed subsequent decay, but there was no statistically significant difference between the 2 preventive modalities. Similar results were seen at the tooth level of analysis. Retention data showed that 74% of maxillary sealants and 93% of mandibular sealants remained intact at 36 months. The difference in mean cost, including intervention costs, between the 2 modalities was £68.13 (95% CE, £5.63-£130.63; P=.033), with the fluoride varnish having the lower cost.

A second article made a similar cost comparison of pit and fissure sealants to fluoride varnish but modeled the simulated progression of caries over a 9-year period.[297] This model found that pit and fissure sealants were less expensive and more effective than fluoride varnish in preventing occlusal lesions. The incremental cost-effectiveness ratio for sealants was $156.87 per first lesion averted when the assumption was made that 100% of sealants placed would require replacement at some time over the 9 years. The cost per first lesion averted dropped to $113.00 if the assumption were that half of the sealants initially placed would require replacement. Another study evaluated the downstream costs for nearly a million Medicaid-enrolled children who were 3 to 6 years old using claims data from several southern states.[298] The findings were that in all states, the Medicaid expenditures were much lower over the subsequent 5 years for children who received topical fluoride and dental sealants before caries development. The per-member per-year difference in costs ranged from $88 for Alabama to $156 for Mississippi. The total cost savings across all 6 states ranged from $1.1 million per year in Mississippi to $12.9 million per year in Texas

when assuming a 10% sealant treatment penetration level. Finally, a systematic economic review of school-based sealant programs updated the cost and benefit information from a previous 2002 review.[299] The new evidence included 14 studies added to the original 4 in the 2002 review and found that the median one-time cost per tooth sealed was $11.64, with a median economic benefit of $6.29. The authors noted that over 4 years, the benefit would exceed costs by $11.73 per sealed tooth. The economic benefits of school-based sealant programs and sealants in general are well justified by evidence and become even greater in high-risk populations.

There were also articles published on the clinical performance of pit and fissure sealants. One study from Germany used public health records to assess the effect sealant placement on caries prevalence in 505 elementary school students over 4 years[300] The records indicated that 34.9% of children had at least 1 sealant and 10% had 4. Children without sealants had a 2 times higher caries rate than those with sealants. Children with 4 sealants showed the lowest decay rates, and children with earlier application of sealants were also showed lower decay rates than those with later or missing application. Students with less than 4 sealants were also at higher risk for developing caries in their permanent dentition than students with 4 sealants (OR=4.36).

A randomized clinical trial compared fissure sealing with fluoride varnish in preventing caries in the first permanent molars of 6 and 7 year olds.[301] The population was from a mobile clinic program servicing schools in areas of social and economic deprivation in South Wales. A total of 1016 children were randomly assigned to receive either fissure sealants or fluoride varnish (6 months intervals). The primary outcome was the proportion of children developing caries into dentin. The difference between the 2 preventive regimens was not statistically significant when analyzed on the child, tooth, or surface basis. The semiannual application of fluoride varnish was equivalent to the placement and maintenance of fissure sealants at 36 months in caries prevention.

An interesting article presented a case series of pit and fissure sealants that were evaluated after 22 years in service.[302] Ten patients with 41 teeth sealed with either resin-modified glass ionomer (RMGI) cement (Vitrebond or Fuji II LC) or a polyacid-modified resin composite (VariGlass VLC) were recalled, and retention of the sealant material was evaluated by visual inspection, photography, and scanning electron micrographs of epoxy replicates. Retention was classified as fully retained, partially retained, or fully lost. No caries (NC) or history of caries was found in any of the sealed fissures. Although visual and photographic assessments resulted in some sealants being classified as partially or totally lost, the scanning electron micrographs showed evidence of sealant retention in all teeth regardless of the material used as the sealant. This case series shows that the protective features of sealants can be present even when visually the material can appear partially or fully lost. It also demonstrates that sealants can remain present in fissures for more than 20 years.

Two systematic reviews were also published related to sealants. The first was an update that compared different types of sealants in preventing decay on the occlusal surfaces of permanent teeth in children and adolescents.[303] Thirty-eight trials involving 7924 children were included, 7 trials being new for the update. Fifteen trials evaluated resin-based sealants versus no sealant, 3 evaluated glass ionomer sealants versus no sealant, and 24 trials compared 1 type of sealant to another. For resin-based sealants and based on moderate-quality evidence, if the control decay rate were assumed to be 16%, the application of sealants would reduce that rate to 5.2% at 24 months. Similarly, if the control decay rate were assumed to be 40%, sealants would reduce it to 6.25%, and if the control decay rate were 70%, the sealants would be expected to reduce that rate to 9.63%. For glass ionomer sealants, the quality of evidence was very low and inconclusive. The comparisons of different sealant materials also suffered from low-quality evidence, and no conclusions could be drawn. Only 4 trials recorded adverse events with none being reported. The overall conclusion was that there was moderate-quality evidence that resin-based sealants reduce caries between 11% and 51% compared with no sealant at 24 months.

The second systematic review assessed the relative clinical performance of sealants in different teeth.[304] This review included 16 randomized clinical trials with 2778 patients at an average age of 8.4 years. No difference was noted in sealed teeth or sealant retention in relation to left versus right side, maxilla versus mandible, first versus second permanent molar, or permanent molars versus deciduous molars. The only difference of significance was that compared with first permanent molars, sealed permanent premolars were less likely to develop caries (RR=0.12; 95% CI, 0.03 to 0.44; P=.001) and less likely to experience loss of sealant (RR=0.33; 95% CI, 0.20 to 0.54). This was based on low- to moderate-quality evidence. The implications of this are that sealants can be placed with confidence on any deciduous or permanent teeth without having the location adversely impact their clinical performance.

One rather interesting sealant study assessed the efficacy of sealing occlusal carious lesions in permanent molars and premolars.[305] This randomized clinical trial included teeth with carious lesion depth to the middle third of dentin and randomly assigned the teeth to either sealant or conventional restorative treatment. No caries removal was performed before sealant placement, and the teeth were followed up for 3 to 4 years. Of 28 sealed

lesions, 2 sealants were totally lost, 1 was partially lost and repaired, and 1 showed radiographic caries progression. In the restored lesions, 1 restoration required repair. Although the overall success rate was higher for restorations, the fact that only 1 lesion showed progression over a 3- to 4-year period indicates that there was potential to control disease progression but regular monitoring would be essential to maintain the integrity of the sealed lesions.

Two articles reported on the performance of resin infiltration on the progression of proximal lesions. The first compared fluoridated toothpaste plus flossing plus resin infiltration to a control of fluoridated toothpaste plus flossing alone on the progression of proximal lesions in primary molars.[306] Surface lesions were randomly assigned to the 2 treatment groups in a split-mouth design and followed up for 1 year after the treatment. Fifty high– to medium–caries risk children were included, with 42 available for follow-up. Caries progression was observed radiographically in 11.9% of the infiltration lesions and 33.3% of the control lesions ($P<.05$). No side effects were noted, and the mean time required for infiltration was determined to be 11.29 minutes per tooth.

The second study evaluated an infiltrating resin on caries progression in noncavitated pit and fissure lesions.[307] Eighty-six teeth with noncavitated occlusal caries were randomly assigned to either a commercial pit and fissure sealant (Alpha Seal-DFL) or Icon infiltrant (DMG). Caries progression was monitored at 12-month intervals for 3 years by laser fluorescence and radiographs. Results showed no difference in lesion progression regardless of the evaluation time, and both materials remained stable after 2 and 3 years of evaluation. These results show that infiltrating resins can be used interchangeably with conventional sealants for preventing the progression of early occlusal lesions.

Overall, both the efficacy and cost-effectiveness of sealants continue to be supported by a growing body of evidence. The impact can be seen in public health programs and school-based programs, as well as in the continuing observations of improved oral health in private practices. However, Dental Quality Alliance measures around sealant program performances still show that there is a significant portion of at-risk children not receiving the benefit of sealants on first molars and an even larger deficiency on second molars; thus, in spite of the evidence, we still have a long way to go.

Restoration repair and replacement

The topic of repair and refurbishment of restorations continues to gain evidence for effectiveness, utilization, and training. A follow-up report of a 12-year clinical trial evaluated the survival of composite resin and amalgam restorations that had undergone refurbishment.[308] Forty-eight composite resins and 126 amalgams with suitable defects were originally assigned to either a control group of replacement or a treatment group of refurbishment by polishing and/or margin repair. Quality was assessed using USPHS criteria, and after 12 years, both the refurbished amalgam and composite resin restorations had similar clinical performance and longevity to the control replacement restorations.

A similar article with a much larger sample size looked at the success and failure of repaired restorations in 11 Dutch general dental practices.[309] Nearly 60 000 class II amalgam and composite resin restorations were included over a 12-year observation time. At 10 years, the combined survival rate of the unrepaired original restorations was 65.92%, whereas the survival rate for repaired restorations was 74.61%. Risk factors that were identified as being tied to failure were molars, multisurface restorations, presence of endodontic treatment, and an RPD being present. Identifying these risk factors from a large sample of restorations placed in general practice provides valuable information to consider when deciding upon repair versus replacement.

A survey of the teaching of repair and replacement was published for 16 dental schools in Oceania.[310] Thirteen schools reported teaching the repair of composite resin restorations as an alternative to replacement. All 13 agreed that the primary driver for repair was tooth preservation, with the main clinical indications being margin defects and secondary caries. The 13 schools also reported high patient acceptability, but only 3 reported having a recall system in place after repair and none of the schools were documenting longevity of the repaired restorations.

A published systematic review and meta-analysis of the management and teaching of repairs included 29, mainly qualitative, studies that encompassed 7228 dentists and 276 dental schools.[311] The proportion of dentists claiming to perform repairs was 71.5% (95% CI, 49.7% to 86.4%), and 83.3% (95% CI, 73.6% to 90.0%) of dental schools taught repairs. The meta-analysis of 30 172 restorations showed that 31.3% (95% CI, 26.3% to 36.7%) of failed restorations had been repaired rather than replaced. Some of the barriers identified to repair included payment systems and regulations, and facilitators of repair were practicing in public health settings and were the dentists who placed the original restoration.

There is a considerable body of long-term evidence supporting both the teaching of restoration repair and the performance of repaired restorations. One often cited factor is the lack of reimbursement for repaired restorations due to the inability to code for the procedure. A proposal was put before the American Dental Association's Code Maintenance Committee in 2017 for a new code for the repair of direct restorations, but in spite of the evidence, it was soundly defeated. We continue to

teach what is appropriate while setting the wrong example.

Silver amalgam

The decline in use of amalgam continues. A 2017 query of a large payer database of more than 27 million direct restorations placed in 11.8 million patients enrolled in private benefit programs shows that 14% of those restorations were filed in claims data as amalgam and 86% as composite resin.[312]

In spite of this decline, research on amalgam continues to be published, and the material continues to draw attention. The Environmental Protection Agency ruling on the mandatory installation of amalgam separators was delayed until late 2016 but officially went into effect on July 14, 2017, with a compliance deadline of July 14, 2020. The rule covers all dental facilities within the United States with a few exceptions: Dentists who practice in oral pathology, oral and maxillofacial radiology, oral and maxillofacial surgery, orthodontics, periodontics, and prosthodontics are exempt from the rule; Dentists who do not place amalgam and only remove amalgam in unplanned or emergency situations (estimated at less than 5% of removals) are also exempt; Mobile dental units are exempt; Dentists who already have separators are grandfathered for 10 years.

A few articles continued to investigate the risks associated with amalgam use. One analyzed the hair sample levels of mercury in dentists practicing in Sri Lanka.[313] Fifty dentists were compared with 50 non-dental controls showing that although the dentists had a slightly higher average level of hair mercury, both groups were well below the 10 ng/mL (10 ppb) level, which is considered as normal and that no occupational hazard was present.

A review of occupational hazard literature was published which included 15 publications between 2002 and 2015.[314] In several references, dental personnel had higher mercury levels in biological fluids and tissues than controls, but in all cases, these exposure levels were below recommended guidelines as in the previously cited study.

One large study using a nationwide population-based database looked at the association between amalgam restorations and attention deficit/hyperactivity disorder (ADHD) in children and adolescents.[315] A population of 88 068 individuals having a history of at least 1 restoration in the 2002 to 2010 time period and no prior ADHD medical history were followed up through 2011 to determine the possible association of amalgam restorations with the risk for ADHD diagnosis after placement. Other factors considered were age, sex, and number of amalgam restorations. During the 2002 to 2011 study period, the incidence rate of ADHD was 32.4 per 100 000 person-years, and those with 6 or more amalgam restorations had a higher risk (HR=1.20; 95% CI, 1.04 to 1.38; P=.015) than those receiving composite resin or glass ionomer restorations. This finding of increased risk, however, was determined to be due to the confounding factor of age and not restoration type. The final conclusion was that there was no association observed between receiving amalgam restorations and future ADHD diagnosis.

Composite resin

With the growing dependence on composite resins for direct restorations, there was a wide variety of subject matter included in the 2017 literature. Several articles looked at applications in children and special-needs patients. The first evaluated the survival and risk factors associated with composite restoration failures in primary teeth.[316] A total of 212 restorations in the primary teeth of 76 high–caries risk children were followed up for up to 6 years. The mean survival time was 4.3 years, with an annual failure rate of 18.8%. This overall high failure rate was even higher in teeth that had received pulp treatment (HR=2.16; 95% CI, 1.02 to 4.58).

A second article similarly evaluated the longevity and factors related to failures of adhesive restorations in deep carious lesions of permanent molars in children.[317] This study compared composite resin and RMGI using both complete and selective caries removal as part of the restorative procedure. The overall survival rate at 36 months was 57.9%, with a high annual failure rate of 16.7%. There was no difference in restoration longevity between composite resin and RMGI; however, teeth restored with RMGI had a lower survival rate than those restored with composite resin (HR=4.11; 95% CI, 1.91 to 8.81). The conclusions were that adhesive restorations performed in the permanent molars of young, high–caries risk children had limited survival regardless of the caries-removal technique used.

A third article assessed the cumulative 3-year survival of atraumatic restorative treatment (ART) and conventional resin composite restorations in patients with disabilities.[318] Treatment was provided to 66 patients (13.6 ±7.8 years) both with and without general anesthesia and in both primary and permanent teeth. In all, 182 ART and 116 composite resin restorations were placed and followed up for 3 years resulting in cumulative survival rates of 94.8% for ART and 82.8% for resin composite. These results are more encouraging than the previous 2 papers and may have been due to more consistent and comprehensive follow-up of these special-needs patients. It was noted that the special-needs patients in this study were seen a minimum of every 6 months after the treatment.

One study conducted within a practice-based research network of 24 general practices looked at a large set of anterior composite resin restorations over a

period of up to 13 years.[319] A total of 72 196 restorations were placed in 29 855 patients between 1996 and 2011. The overall annual failure rate at 5 years was 4.6% (95% CI, 4.5% to 4.6%). Age was a significant patient factor with both younger (<13 years) and older (>65 years) patients having a 17% and 81% higher risk of failure than the age 25 to 35 cohort. Fillings in central incisors were the most prone to failure, and there were significant outcome differences noted between operators.

The evaluation time for composite resin restorations continues to grow longer as longitudinal studies receive additional follow-up. One article describes the 5 to 20 years follow-up of 103 light-activated composite resin restorations placed in posterior teeth by a single operator.[320] The mean survival time of restorations still in function was 11.7 years, with 98% still being in function and 95.1% rated being clinically acceptable.

Another retrospective study reported 18-year findings of 204 composite resin sandwich restorations restored using a glass ionomer base and Herculite XRV.[321] The reported survival rates were 92.6% at 10 years and 82.4% at 18 years. The most common failure mode noted was secondary caries at 69.4%. The caries risk was also a significant factor, but not the type or location of tooth or class I versus class II restorations.

An interesting review of studies of composite resin restorations in vital posterior teeth compared results from 2 different time periods, 1995 to 2005 and 2006 to 2016.[322] Overall survival rates for studies from the 1995 to 2005 period were 89.4% compared with 86.9% for the 2006 to 2016 period, showing little difference between the periods. Secondary caries was reported at similar frequencies between the 2 periods, 29.5% in 1995 to 2005 versus 25.7% in 2006 to 2016, but the frequency of both composite resin and tooth fracture was significantly higher in 2006 to 2016 than that during 1995 to 2005. The authors speculate that this may have been due to composite resins being used in larger restorations during the later time period.

A systematic review investigated the outcomes of single-unit restorations in posterior permanent vital teeth as a function of restoration type and size.[323] Fourteen articles of low to moderate quality were included with a mean follow-up of at least 3 years and outcomes of clinical or radiographic failure. Included were 358 crowns, 4804 composite resin, and 303 582 amalgam restorations. Data from the randomized clinical trials showed that amalgams outperformed composite resin regardless of the restoration size, and observational studies showed that crowns outperformed amalgams in teeth with fewer than 2 remaining walls. The remaining tooth structure was the strongest predictor of treatment success.

Another review compared direct with indirect composite resin restorations on posterior teeth with or without cusp involvement.[324] Nine studies were included, with 6 being used in a meta-analysis of longevity. The results showed no difference in clinical longevity between direct and indirect composite resin restorations or between restorations in molars or premolars. Although the first review showed crowns to outperform direct restorations, those were not composite resin crowns, which this review showed to only be equivalent to directly placed composite resin restorations. This indicates that one must not make the assumption that all crowns are created equal.

Few articles also described technique variables related to the placement of composite resin restorations. One reported on the 36-month outcomes of bulk fill versus a nanofill composite resin.[325] This was a split-mouth study in which 50 patients received at least 1 restoration of each of the 2 materials. Outcomes were evaluated using USPHS criteria, and 81 restorations were available at 36 months. The bulk-fill material showed better margin adaptation and discoloration ($P<.05$), but all restorations were retained and none showed postoperative sensitivity, secondary caries, or loss of anatomic form.

Another article reported on a comparison between sonic and conventional incremental placement of composite resin in posterior molar teeth.[326] This was again a split-mouth trial with 30 patients receiving 2 class I restorations, 1 with a conventional composite resin (Herculite Ultra; Kerr Corp), and 1 with a sonic placement system (SonicFill; Kerr Corp). After 2 years, there was no difference noted between materials using the USPHS-modified evaluation criteria.

A third article presented a systematic review comparing the use of flowable composite resins to traditional ones in restoring noncarious cervical lesions.[327] Eight studies were cited with follow-up times of 1 to 3 years concluding that there is moderate-quality evidence that resin viscosity does not influence retention at 3 years and that the quality of evidence indicating better margin adaptation for flowable resins was doubtful.

Three articles published in 2017 looked at the comparative performance of composite resin and amalgam. The first was a retrospective cross-sectional review of patient records from 600 randomly selected military patients.[327] All direct posterior restorations placed within the prior 2 years were included. Of the 2117 restorations reviewed, 67.5% were initial restorations, 32.5% were replacement restorations, 64% were amalgam, and 36% were composite resin. Mandibular first molar restorations were the most frequently replaced at 23.1%, and mandibular premolar restorations were the least frequently replaced at 0.9%. Replacements increased with patient age, and there was no significant difference in the frequency of replacements between amalgam and composite resin.

A second article was a similar retrospective review of electronic patient records in 25- to 30-year-olds receiving

care in the Helsinki City Public Dental Service.[328] A total of 5542 two- and three-surface amalgam and composite resin restorations were followed up via records from 2002 to 2015. Of these, composite resins made up 93%, and amalgam made up the remaining 7%. The median survival time for all restorations was 9.9 years with no significant difference between composite resin and amalgam. Replacement restoration were more frequent in the mandible, and not surprisingly, median survival time was greater in premolars than molars and greater in 2-surface than 3-surface restorations.

The third article comparing materials took an interesting look at individual genetic markers for matrix MMP as one of many factors associated with the failure of direct restorations.[329] The hypothesis was that failure of composite resin restorations could be uniquely associated with the genetic expression of MMPs. The data were obtained from the University of Pittsburgh School of Dental Medicine Dental Registry and DNA Repository project. The patient records were recovered for all restorations of posterior teeth from 4856 patients, and the restoration status was tracked for 1, 2, and 5 years after placement. Restoration failure was defined as any necessity for replacement due to fracture, discoloration of composite resin, or secondary caries. For the genetic analysis, 412 records of patients with extensive anterior composite resin restorations were tracked for both restoration failure and the expression of 20 single nucleotide polymorphisms in 4 genes with known functional MMP activity. Of the 6266 amalgam and 2010 composite resin posterior restorations monitored over 5 years, the survival probabilities showed no differences between the 2 materials. Of the 443 complex anterior composite resin restorations monitored, 9% were considered failures with the main reason being secondary caries. Most interesting was that the case-control analysis of gene expression in patients with these anterior restorations showed a strong association between 4 of the 20 genetic variants. This provides early evidence that genetic variations tied to the degradation of collagen could have a role in composite resin restoration failures. It may also provide a potential explanation as to why some patients do not respond to preventive measures as predictably as others.

Endodontic materials

Two articles compared the performance of mineral trioxide aggregate (MTA) with the calcium silicate–based Biodentine (Septodont). The first was an 18-month retrospective record review of 30 patients, 15 of which received direct pulp capping with MTA and 15 with Biodentine.[330] The success rates for both materials were statistically similar at 84.6% for MTA and 92.3% for Biodentine, and radiographic dentin bridging was observed in 69.2% of MTA treatments and 61.5% of Biodentine-treated teeth. Two noted adverse events were the higher incidence of diffuse calcifications within the pulp chamber and the occurrence of coronal discoloration in MTA treatments.

A systematic review of in vitro studies focused on the occurrence of coronal discoloration with silicate-based cements.[331] Twenty-three studies were cited, and results showed that some gray and white MTA products had a strong potential for staining, whereas products such as Biodentine, Portland cement, and several other MTA-based materials had a low potential to stain. Apparently this indicates that composition alone cannot be used to predict the potential for discoloration as different MTA-based products were listed as having both high and low staining of hard tissues. Manufacturers will certainly need to address this issue.

An article was published that presented evidence-based guidance on the use of vital pulp therapies for deep lesions in children.[332] This guidance was based on a recent systematic review and meta-analysis that included 41 articles on the subject of vital pulp therapy in primary teeth.[333] The panel developing the guidance recommended the use of MTA and formocresol in pulpotomy and indirect pulp treatments based on moderate-quality evidence at 24 months. There were no firm recommendations regarding direct pulp capping as the data were either low-quality or very low–quality evidence, and success appeared to be independent of the medicament used. They did, however, recommend against the use of calcium hydroxide as a pulpotomy medicament.

OCCLUSION AND TMD

Structural changes in the TM joint

Ahn et al[334] authored an article discussing the relationships between TMJ disk displacements and condylar volume. Several articles have described the changes that occur when there are structural alterations in the TMJ. Many studies have reported that one of the common signs of TMJ disc displacement (TMJ DD) is facial deformity caused by loss of posterior mandibular vertical dimension, decreased condylar height and condylar process, and a steep mandibular plane, resulting in a retrognathic mandible with hyperdivergent skeletal patterns. The results of this study indicate that these specific dentofacial characteristics may be explained by decreased condylar volumes associated with TMJ DD.

A cross-sectional study was designed. All candidates were suspected clinically of having TMJ problems. Inclusion criteria were men older than 18 years and women older than 17 years to avoid growth-related size differences; consent to a bilateral high-resolution MRI examination of the TMJs in the sagittal (opened and closed) and coronal (closed) planes; and consent to TMJ multidetector computer tomography (MDCT) or TMJ CBCT

within 3 months before or after the MRI examination. Exclusion criteria were any systemic disease, history of trauma involving the TMJs, and juvenile rheumatoid arthritis. A total of 122 joints from 61 adult patients (17 men and 44 women) were used. The age of men ranged from 18 to 24.8 years (mean: 22.2 ±3.9 years) and that of women ranged from 17.3 to 43.3 years (mean: 25.0 ±6.8 years). For volumetric analyses, total condylar volume and its components (condylar cortical and trabecular volumes) were calculated from the CT data. TMJ MRIs were made to evaluate disk status, which was divided into 3 categories. The first category as normal disk position (NR), which was defined as the intermediate zone of the disk, was interposed between the condyle and the posterior slope of the articular eminence, with anterior and posterior bands equally spaced on either side of the condylar load point. The second category was disk displacement with reduction (DDR): In the closed-mouth position, the disk is in an anterior position relative to the condylar head, and the disk reduced upon opening of the mouth. The third category was disk displacement without reduction (DDNR). In the closed-mouth position, the disk is in an anterior position relative to the condylar head, and the disk does not reduce with opening of the mouth.

Of the total 122 condyles, 33 (27%), 34 (27.9%), and 55 (45.1%) were NR, DDR, and DDNR, respectively. Twenty-two of 34 male condyles (64.7%) and 67 of 88 female condyles (76.1%) had TMJ DD. Because TMJ MRIs were made for patients who were suspected of having TMJ problems, the prevalence of TMJ DD was higher than that of NR. The results showed that TMJ DD correlated significantly with condylar volume, regardless of sex, and there were sex differences as well. All condylar volumes tended to decrease as TMJ DD progressed from DDR to DDNR, but the decreasing patterns were different among the 3 condylar regions. There were significant differences in both total condylar and trabecular volumes among the 3 DD status (NR>DDR>DDNR; $P<.01$, respectively). Cortical volumes were significantly different between NR and DDNR or between DDR and DDNR.

All 3 volumetric measurements were significantly influenced by TMJ DD. Total condylar volumes and trabecular volumes were significantly reduced in patients with TMJ DD (NR>DDR>DDNR), whereas cortical volumes were significantly different only when TMJ DD progressed to DDNR (NR/DDR>DDNR). These findings indicate that total condylar volume and its components significantly associated with TMJ DD status and condyles with DDNR showing the smallest condylar volumes with the smallest cortical and trabecular volumes. The results are supported by previous studies reporting that osseous change of the mandibular condyle is significantly influenced by TMJ DD and that altered condylar morphologies become more severe as TMJ progresses.

Kang et al[335] discussed the dental and skeletal maturation in female adolescents with TMJ osteoarthritis (OA). Early onset of diseases particularly in the circumpubertal phases, as well as female predominance, has already been described well in previous epidemiological studies of TMJ OA. Moreover, in certain situations, TMJ OA during adolescence shows different patterns from those of adult TMJ OA. Despite the lack of consensus on the definition and pathogenesis of such a condition, rapid progressive degenerative bony changes resulting in decrease in condylar mass and abnormal condylar shape in juvenile females and young female adults are widely observed and described as idiopathic condylar resorption. Severe destruction of TMJ due to OA results in a typical hyperdivergent facial profile even in adults and more prominently in juveniles, thereby affecting the ongoing growth of the maxillomandibular complex. The studies about the relationships between facial profiles and extent of skeletal and dental maturation in adolescent have been reported previously.

The relationship between craniofacial growth and development of TMJ OA in adolescents has been controversial. TMD during adolescence may have potential effects on future masticatory function, growth of the mandibular condyle, and finally on facial morphology. Retruded maxilla and mandible, clockwise mandibular rotation, and increased horizontal overlap have been observed in adolescent TMJ OA patients. Moreover, a decreased occlusal force has been described in patients with steeper mandibular plane angles, skeletal open occlusal relationships, and TMDs. Furthermore, the immature condyle itself has adaptive mechanisms for overload that are different from those observed in adult TMJ. However, few studies have provided evidence-based information regarding adaptive capabilities of immature condyle and impacts of TMD on development of abnormal facial profiles in juvenile patients. Furthermore, the impacts of TMD on not only mandibular growth but also on dental development and skeletal growth in juvenile patients remain to be answered.

Development of mandibular condyle begins after the 12th week of fetal development, and it contains unique structures. The prehondroblastic layer that contains undifferentiated mesenchymal cells is covered by a fibrocartilaginous layer that protects articular surface from masticatory loading. The processes of chondrogenesis and endochondral ossification progress after birth. The cortical lining begins to form around the margin of condyles during adolescence (12 to 14 years), and establishment of the cortical layer around the periphery of condyle is completed in young adulthood (21 to 22 years). Several studies have focused on timing of condylar and mandibular growth peak. A study revealed

that condylar growth spurt occurred at 12 years of age and decelerated thereafter until 15 to 16 years of age in girls. Another study reported that mandibular growth spurt occurred between CVM stages 3 and 4 and ended at least 1 year before cervical vertebral maturation (CVM) stage 5. Because a growing TMJ condylar surface lacks a true articular cartilage, load from parafunctional oral habits or mastication would be transmitted to the immature subarticular and secondary cartilages and shows different adaptation process from that shown by the adult condylar surfaces. Any process that destructs the condylar surface could interrupt normal condylar and mandibular development and finally resulting in a backward-positioned mandible and a hyperdivergent facial profile. Thus, destructive articular changes in the condylar surface could interrupt normal mandibular growth, finally resulting in abnormal facial morphology in juvenile patients during the growth period, and could lead to marked variations in direction of the abnormal mandibular growth and facial morphology.

The exact etiology of delayed dental development in TMJ OA patients cannot be derived just from the aforementioned data. However, regarding the retrognathic and steep mandibular angles in juvenile TMJ OA patients, delayed dental development may be influenced by abnormal mandibular growth and masticatory dysfunctions in growing patients with TMD, particularly in TMJ OA. Juvenile female patients showed retarded dental development, mandibular backward positioning, and hyperdivergent facial profiles in accordance with occurrence of TMD and TMJ OA.

Lei et al[336] explored degenerative TMJ changes associated with recent-onset disc displacement without reduction (DDw/oR) in adolescents and young adults. Recent TMD studies, however, suggest an increasing prevalence of TMD in children and adolescents. The frequency of TMJ osteoarthrosis/arthritis in adolescents has also risen drastically and peaks at ages 15 to 19 years. The TMJs of children and adolescents are in the process of growth and development. OA changes of the TMJ, if present, may interfere with normal condylar formation, leading to mandibular deviation, mandibular retrusion, as well as anterior open occlusal relationship (AOOR).

Disc displacement, especially DDw/oR, has been associated with OA changes of the TMJ. Displaced discs might interfere with condylar mobility and lead to increased loading of the anterior surfaces of condyles. Articular cartilage and subarticular bone destruction gradually occur over time. Early diagnosis and intervention of TMJ osteoarthrosis/arthritis associated with DDw/oR is therefore prudent, especially in adolescents, as subarticular (subchondral) cortical bone formation only commences between the ages of 12 and 14 years. This study evaluated the occurrence of degenerative TMJ changes in adolescents and young adults with recent-onset DDw/oR (less than 12 months) using high-resolution CBCT. The associations between types of condylar OA changes and clinical factors including disease duration were also examined. The age of participants ranged from 11 to 30 years, with a mean age of 20.93 ±4.77 years. Of the participants, 84.7% were female and 15.3% were male.

Bilateral CBCT images of the TMJs were obtained using a 3D multiimage micro-CT. CBCT images of condylar OA changes were classified into 6 categories: Type I, loss of continuity of the articular cortex; Type II, surface erosion or destruction; Type III, deviation in form; Type IV, sclerosis; Type V, osteophyte; and Type VI, cyst-like lesion. Types I and II were considered early-stage OA changes, whereas Types III to VI were deemed late-stage OA changes. This study evaluated the occurrence of degenerative TMJ changes in adolescents and young adults with recent-onset DDw/oR (less than 12 months) using high-resolution CBCT. The associations between types of condylar OA changes and clinical factors including disease duration were also examined.

In the present study, 59.30% of participants with recent-onset DDw/oR presented with condylar OA changes. Most of the OA changes were Type I and/or II in nature. Recent-onset DDw/oR (within 1 year) was consequently associated with early-stage condylar OA. The percentage of early-stage OA increased considerably from 24% when onset was within 1 month to approximately 60% after 1 to 12 months. The risk of developing early-stage OA changes was 5.33 times higher 1 month after the onset of TMJ closed-lock. DDw/oR and osteoarthrosis can thus interfere with facial morphology and occlusion. Interventions for DDw/oR should therefore be instituted early upon TMJ closed-lock onset to curtail possible degenerative condylar changes, especially in children and adolescents. The prevalence of TMJ osteoarthrosis/OA has been found to increase with advancing age in the latter groups.

TMJ osteoarthrosis/OA associated with recent-onset DDw/oR was not biased by age and sex in the present study. OA is age-related and generally occurs after the fourth decade of life in the weight-bearing joints, for example, knee OA. TMD OA is also found to be age-related. However, unlike the weight-bearing joints, TMD is common in the population aged 20 to 40 years, and TMD OA in adolescents and young adults has also risen drastically, which might be attributed more to pathological factors such as the overloading and joint immobility caused by DDw/oR, rather than age itself, especially in a young population. No association was also observed between sex and degenerative TMJ changes in other imaging studies. One explanation might be the age limit in this study, and the other might be that the hormonal (estrogen) effect alone does not play a significant role in the initiation of TMD.

Khojastepour et al[337] described the association between condylar bone changes revealed in CBCT and clinical dysfunction index in patients with or without TM joint disorders. TMDs, which affect the muscular soft tissue and bony components of the TMJ, present variable clinical signs and symptoms such as pain, popping, clicking, limited opening, mandibular deviation on opening and closing, muscle tenderness, headaches, earaches, and malocclusion. TMDs are frequently associated with degenerative changes in bone structures of the TMJ. Exploration of these bone changes is essential for correct diagnosis of the dysfunctions associated with TMDs and also for devising an adequate treatment plan. Radiographic examination techniques, which are essential methods for the diagnosis of degenerative bone changes in TMDs, include panoramic radiography, conventional tomography, CT, and MRI. Recently, CBCT has become the modality of choice for evaluation of TMJ osseous components. This modality, which provides greater accuracy as well as superior reliability compared with panoramic radiography and conventional tomography, allows visualization of the bony components in all dimensions in addition to providing a view of osseous changes. Furthermore, compared with CT, CBCT is less costly and involves a lower dose of radiation.

Condylar bone changes were classified into distinct types according to previous studies as follows: normal; flattening (a flat bone contour, deviating from the convex form); surface erosion (loss of continuity of articular cortex); subcortical cyst (Ely cyst), round radiolucent area just below the cortical plate or deep in trabecular bone; subcortical sclerosis, any increased thickness of the cortical plate; generalized sclerosis, increased radiopacity of the spongy bone; marginal bony overgrowth (osteophytes), local outgrowth of bone arising from the mineralized surface; and loose joint body, osteophytes that break off and lie free within the joint space. The most frequent change observed in the TMD group was flattening of the articular surface (70 joints, 83.3%), followed by surface erosion (31 joints, 36.9%). A previous investigation found that 75% of the CT-diagnosed osteoarthritic changes of the TMJ seem to escape detection on panoramic radiography, and about 40% elude detection on MRI. The results of the present study suggest that CBCT findings are associated with the variation in severity of TMD. Therefore, CBCT should be considered as an important tool for appropriate diagnosis and treatment in clinical practice.

TMJ imaging

Kellengberger et al[338] authored a TMJ atlas for detection and grading of juvenile arthritis involvement of MR imaging. MRI has become the standard for assessing the TMJ in children with juvenile idiopathic arthritis (JIA) because both joint inflammation and joint damage can be evaluated. Evaluating the level of inflammation, the degree and course of osteochondral deformity, as well as measuring the growth of the mandibular ramus in the long term is needed for assessing the effect of systemic or specific treatments targeting the TMJ.

The bilateral TMJs are ginglymoarthrodial joints at the skull base enabling the complex motion of the jaw necessary for mastication and speech. Between the upper temporal bone and the lower mandibular condyle, the joint is divided into 2 separate synovial compartments by the biconcave articular disk, which is a fibrocartilaginous extension of the joint capsule. The lower joint compartment allows for rotational motion, and the upper compartment, for anterior translation of the condyle during mouth opening. Although the joint capsule is lined by synovial membrane in the peripheral joint recesses, the fibrocartilaginous surfaces of the temporal bone and mandibular condyle as well as the articular disk are normally avascular and void of synovium.

Normally, the temporal and mandibular joint surfaces are delineated by a smooth continuous line representing subchondral bone. The temporal articular component entails the posterior glenoid or mandibular fossa and the anterior articular eminence resulting in an s-shaped configuration on sagittal oblique images. In young children, the temporal joint surface is rather flat with a shallow mandibular fossa. With further growth, the mandibular fossa deepens and the articular eminence gains height gradually with the adult shape reached around puberty. The mandibular articular component is also subject to growth-related changes in configuration. In the axial plane, the shape of the condyle changes from round to oval due to the increasing ratio between lateral and anterior-posterior dimensions. On sagittal oblique images of a young child aged 5 years, the superior contour of the condylar head is round with a straight condylar neck. With increasing age and growth, the condylar neck gains an anterior tilt, and the condylar head appears with a more angular shape, with less rounding of the anterior-superior joint surface. In the coronal plane, the convex superior joint surface becomes flatter with growth.

Bone marrow composition in the mandible changes during growth, from predominantly hematopoietic marrow initially to mostly fatty marrow later. On T1-weighted and fluid-sensitive images (T2-weighted with fat saturation or short tau inversion recovery), the signal intensity of the temporal and mandibular bones reflects the proportions of hematopoietic and fatty marrow. In an infant, bone marrow signal intensity is low on T1-weighted images (isointense to muscle) and intermediate on fluid-sensitive sequences (hyperintense to muscle and hypointense to fluid). With older age and the increasing proportion of fatty marrow, signal intensity

eventually becomes the same as that in subcutaneous fatty tissue on all sequences.

As with any other synovial joint, the TMJ contains small amounts of joint fluid derived from plasma by dialysis and secreted by the synovial membrane. Visibility of synovial fluid on MRI depends on its amount, as well as on the orientation, spatial resolution, and type of sequence used. Although a normal physiological amount of joint fluid is not apparent on T1-weighted images, it is readily detected on T2-weighted images as an area with high signal intensity similar to that of other fluids (that is, isointense signal compared with cerebrospinal fluid). Small dots or lines of high signal intensity within the joint recesses, not exceeding 1 mm width, can be considered a physiological amount of joint fluid and should not be interpreted as joint effusion.

Early inflammation of the synovial membrane is histologically characterized by synovial hypertrophy with cellular infiltrates, edema, and increased vascularity. These pathological features of TMJ arthritis are evident on MRI as joint effusion, synovial thickening, bone marrow edema, and increased joint enhancement. Prolonged inflammation may lead to disturbance of joint formation and damage of the osteochondral structures. With the main growth zones of the mandible located within the joints at the surface of the condyles, covered only by a thin layer of fibrocartilage, arthritis of the TMJ may lead to growth impairment of the mandible with shortening of the ramus resulting in micrognathia, retrognathia, or mandibular asymmetry.

Because MRI signal characteristics of bone marrow vary with the proportions of hematopoietic and fatty marrow, presence of edema in the condyle is assessed by comparing its marrow space signal intensity to that of the mandibular ramus. Bone marrow edema of the condyle is defined as hypointense signal on T1-weighted images without fat saturation and hyperintense signal on fluid-sensitive images in comparison to that of the ramus. Increased amounts of synovial fluid with high signal intensity similar to that of cerebrospinal fluid on fluid-sensitive sequences are considered a joint effusion.

A flattened appearance of both the temporal bone and mandibular condyle surfaces is characteristic of TMJ involvement in JIA. Although loss of the normal s-shape of the temporal bone is likely due to arrested development of the articular eminence, flattening of the mandibular condyle may be the result of growth disturbance, destruction, and remodeling due to inflammation. The mandibular condyle typically shows diminished craniocaudal and lateromedial dimensions, whereas the anteroposterior dimension may be increased, resulting in a flat appearance on sagittal oblique views. In an older child, resemblance of the condyle to that of an infant should also be considered a deformity.

As there is no general definition of erosions on MRI, we define erosions in the TMJ as irregularities, depressions, or breaks of the subchondral low-intensity lines that demarcate the articular surfaces. Deep breaks probably represent true erosions containing inflammatory pannus, whereas small irregularities of the articular surface more likely represent defects or disturbed mineralization of subchondral bone with preserved overlying fibrocartilage.

Abnormalities of the articular disk are well recognized in patients with JIA and can coexist with any degree of synovial or osseous abnormality. The most common findings are flat or thin disc (that is, loss of normal biconcave shape), perforation or fragmentation, and displacement.

Caruso et al[339] published a review article to summarize data on the study of TMJ through CBCT images during the period of craniofacial growth development (data derived from samples of children, adolescents, and young adults, that is, individuals aged $\leq$30 years). A great body of literature concerning the TMJ visualization in CBCT images has been acquired in recent years. Contrary to what one might consider, CBCT images are not widely used to study the pure anatomy of the joints. The findings of the studies included in this review can be divided into the following broad topics: the evaluation of the volume and surface of the mandibular condyle; the visualization of the bone changes on the cortical surface; the comparison between the 2 condyles in cases of facial asymmetry; the linear dimensions of the condyle; and the optimum position of the condyle in the glenoid fossa.

In terms of condylar volume and surface, authors report that in white young adults and adolescents (15 to 30 years old), those in skeletal class III category have a significantly higher condylar volume, with respect to class I and class II individuals, whereas class II individuals show lower condylar volume, with respect to individuals with class I and class III skeletal relationship. In white young adults and adolescents, mandibular condyle shows a significantly higher volume and surface in low-angle individuals (those with low mandibular divergence) than in high- and normal-angle groups (individuals with high and normal mandibular divergence). By the calculation of condylar volume and the index of asymmetry between the right and the left condylar volumes, CBCT 3D reconstructions allow the diagnosis of early stages of JIA in growing individuals. Condylar head volume in growing individuals with JIA is about 844 mm^3 (median value), with a statistically significant asymmetry between the right and the left condyles of about 26% in their volume. In addition, the analysis of CBCT images allows the detection of early qualitative signs of JIA which range from small erosions within the cortex to almost complete deformation of the condylar head. It has been stated that

early stages of JIA can be detected by CBCT imaging even before this disease has caused damages to the individual's facial development during growth.

In terms of detecting mandibular condylar shape, authors report that in white young adults and adolescents (data from a sample with a mean age 19.2 years (range: 15 to 29; 74 men and 76 women), CBCT 3D reconstructions allowed establishing that the shape of the condylar head is more frequently round compared with oval, followed by a flattened form and, at last, a spiked form. Degenerative changes of the mandibular condyle are undeniably more common in individuals older than 40 years because the prevalence of bone changes increases with age, but about 40% of young individuals aged 10 to 29 years seem to show bone changes in their TMJs, and these bone changes are well detectable using CBCT images. Among the bone changes, the small erosions of the surface are more common among adolescents and young adults and can be effectively detected with CBCT images using a field of view of 6 inches.

The flattening and the osteophytes are instead more frequent in adults and old individuals and well detected by CBCT images. CBCT is additionally intended to be the superior method to acquire adequate information on the extent, the nature, and precise location of TMJ fractures in growing individuals who have suffered severe maxilla-facial trauma, with the involvement of the TMJ. CBCT images are not suitable to view inflammatory reactions (such as marrow edema) or to view synovia or cartilage or changes in the deeper zones of the condylar head (such as cysts) because the segmentation of the structures, based on the thresholding, is restricted to the delineation of the cortical region in those individuals where the cortex had not yet reached its final maturity and density, as it happens in growing individuals. Therefore, in these individuals, the segmentation is restricted to delineating only the cortical region, without taking possible changes in the deeper zones into account.

In terms of evaluating linear measurements, the most recent literature states that CBCT images are reliable to evaluate the linear measurements of the condyle: the condylar length (linear distance between anterior point of mandibular condyle and posterior point of mandibular condyle), the condylar width (linear distance between the lateral point and the medial point of mandibular condyle), and the condylar height (linear distance between superior point of mandibular condyle and mandibular lingula.)

In terms of young adults with facial asymmetry, the coronal condylar angle appears significantly different between the 2 sides and remarkably larger with respect to asymptomatic individuals. In those with facial asymmetry, the angle measures 19.18 degrees. In addition, the horizontal condylar angle in young adults with facial asymmetry also is significantly larger than that in the asymptomatic individuals, no matter if it is on the nondeviation or the deviation side.

In terms of clarifying condylar positioning in young adults, the optimum mean joint spaces in the coronal view, that is, the coronal lateral space, the coronal central space, and the coronal medial space, are 1.8 ±0.4 mm, 2.6 ±0.4 mm, and 2.3 ±0.4 mm in men, respectively, and 1.8 ±0.4 mm, 2.7 ±0.6 mm, and 2.4 ±0.7 mm in women, respectively, with no significant sex differences in these measurements. The mean spaces from the axial view, that is, medial axial space and lateral axial space, are 2.1 ±0.6 mm and 2.2 ±0.7 mm, in men, respectively, and 2.2 ±0.6 mm and 2.4 ±0.6 mm, in women, respectively, with no significant sex differences in these measurements. These data clarify that in young individuals, the joint space is smaller laterally than centrally or medially in the coronal view. In the axial view, instead, data indicate that the condyle is nearly centered within the fossa, when observed axially, in a normal joint. The ratio among lateral, central, and medial spaces in the coronal view is 1 to 1.5 to 1.3, whereas the ratio between lateral and medial spaces in the axial view is 58% to 52%.

TMD refers to a collective term including clinical problems that involve the masticatory muscles, TMJ, and associated structures. TMD is frequently associated with disc displacement and degenerative changes in the TMJ. Degenerative joint disease (DJD) affects both soft and hard tissues including cartilage, subchondral bone, and synovial membrane. DJD can be diagnosed when there is either crepitus or radiographic bony changes. Osteoarthrosis is also a DJD in which joint form and structures are abnormal but without signs of arthralgia. DJD causes secondary synovial inflammation, TMJ remodeling, articular cartilage abrasion, and bone degradation characterized by development osteophytes, erosion, flattening, subchondral sclerosis, and pseudocysts. Detection and evaluation of these bony changes are fundamental for successful diagnosis of DJD. The condition of TMJ can be evaluated by a variety of imaging modalities. CBCT is a fairly new imaging modality that can produce images of high diagnostic quality with a lower radiation dose than medical CT.

The issue of the artifacts associated with the patient's accidental movements during the acquisition is not yet resolved, which can be a problem in the pediatric population, especially in case of no compliance. In addition, a further technical problem is the Hounsfield Units distortion, so CBCT cannot be used to estimate bone density (bone density is estimated using micro-CT). A further limitation is that the decrease of the radiation dose is accompanied by a proportional decrease in image quality, especially regarding the contrast resolution, so the soft tissues are not displayed well, especially if internally positioned, near to bone structures such as the TMJ articular disc. Finally, in growing individuals, CBCT

imaging has some limitations when it tries to highlight the changes in the deeper structures of the condylar head (for example, cysts) that are not well detectable with CBCT images if the cortex of condylar head has not yet reached its final maturity and density. This seems to happen because the segmentation of the CBCT images is based on the thresholding and, when the cortex is not mature, is consequently restricted to delineate the cortical region, without taking possible changes in the deeper zones into account.

Alhammadi et al[340] discussed the 3D assessment of condylar position and joint spaces after maxillary first premolar extraction in skeletal class II malocclusions. The aims of this study were to investigate the changes in the anteroposterior, vertical, and mediolateral positions of the mandibular condyle, as well as the changes in condylar orientations and TMJ spaces, following therapeutic maxillary first premolar extraction and incisor retraction. The TMJ is formed of bony structures such as the mandibular condyle and the glenoid fossa, as well as nonbony elements such as the articular disc. It is essential to determine whether there is a correlation between CBCT measurements and MRI regarding the position of the disc.

The most significant measurements that relate to disc position are the condylar position, anterior joint space, posterior joint space, and superior joint space. The anterior wall inclination and tubercular height might increase or decrease the possibility of disc displacement. The relation between joint space and subsequent condylar position with disc position was investigated in several studies based on MRI, and the results indicated that condylar retropositioning is frequently observed in joints with disc displacement and that posterior condyle position could indicate anterior disc displacement. In partial disc displacement, the condyles were displaced posteriorly in the fossae with increased anterior and decreased posterior space. In DDw/oR, the condyles are displaced posteriorly with slightly reduced superior joint space, and the displacement in the anteromedial direction is accompanied by increased medial joint space.

The possible effect of more posterior positioning of the condyle after therapeutic extraction and incisor retraction depends on the radiographic original position of the condyles as well as the presence or absence of signs and symptoms of TMD before orthodontic treatment. Furthermore, this effect may worsen the preexisting condition specifically in patients with disc displacement with reduction but also may be beneficial in the case of early DDw/oR; however, this assumption requires extensive research both clinically and radiographically. A major shortcoming of the study was the lack of MRI, resulting in the inability to assess a change in disc position.

Occlusal device therapy

Hasewaga et al[341] discussed occlusal appliances relative to whether long-term occlusal device therapy facilitates improvement of the ranges of motion of the condyle and disc. Occlusal appliance therapy has been recommended as a reversible nonsurgical option for management of many TMDs. It has been suggested that occlusal device therapy can reduce pain caused by excessive occlusal pressure in the TMJ. In this manner, the device restores blood circulation to the TMJ by maintaining a wide gap between the mandibular condyle and the mandibular fossa. Although most patients experience symptomatic relief in response to an occlusal device, approximately 30% of patients do not experience any improvement in temporomandibular arthrosis. Occlusal device therapy should not be used indiscriminately so that irreversible occlusal changes can be avoided. The objectives of this study were to clarify whether altering mandibular condyle and disc positions by occlusal device therapy reduces TMJ pain and to determine whether long-term therapy facilitates improvement of the ranges of motion of the condyle and disc.

Fifty-one women and 24 men (mean age: 38.4 years; range: 17 to 70 years) with a history of clicking, catching, or restricted mouth opening and unilateral or bilateral joint pain were enrolled. All patients were treated with a hard acrylic resin stabilization device with a flat surface that covered all the maxillary teeth. The devices were adjusted to have contact points with all the opposing teeth with the patient in the supine position. The occlusal vertical dimension between the central incisors of the maxilla and the mandible was maintained at 5 mm. Patients were instructed to wear the device only during sleep, and they visited the hospital 1 week, 1 month, 2 months, and 3 months after device insertion for evaluation; a VAS was used to evaluate TMJ pain at each visit. Patients were asked to grade pain felt, with zero indicating "no pain" and 100 indicating "the worst pain possible", during the following times: A, at rest; B, when the mouth was opened and closed; and C, while eating. On the day the devices were given to the patients, they were assessed with/without devices in the mouth open and closed positions using MRI. MRI was performed with the patient in the supine position with a 1.5-T MR scanner using TMJ surface coils. MRI was used to examine the positions of the condyle and disc, as well as the configuration of the disc.

The 150 joints evaluated in this study were classified into 5 categories, with some modifications: partial anterior disc displacement with reduction, partial anterior DDw/oR, complete anterior disc displacement with reduction (ADDwR), and complete anterior DDw/oR (ADDWOR). Diagnosis of partial or complete anterior displacement was made from the oblique sagittal MRIs of each joint (right and left) in the closed mouth position.

Disc configuration was classified into five categories, including biconcave, biplanar, hemiconvex, biconvex, and folded. Joint effusions were classified into 3 categories: none or minimal fluid, moderate fluid, and marked or extensive fluid. OA, as demonstrated by condylar osteophytes or erosion, was classified into 2 categories, negative or positive. Bone marrow abnormalities of the condyle, or osteonecrosis, were classified into 2 categories, negative or positive. Displacement of the condyle and disc achieved by placing the device was quantified using an image-analysis software program.

The results showed that older patients and patients with anterior condyle movement had less TMJ pain when wearing the device. In contrast, patients with superior-inferior condyle movement, anterior-posterior movement, and rotational disc movement did not have less joint pain when wearing the device. Age, biconvex articular disc configuration, and positive bone marrow abnormality were identified as significant variables by the simple/multiple linear regression analyses. These results suggest that the TMJ pain level was likely to increase easily in cases in which the articular disc configuration was biconvex and a bone marrow abnormality was found.

Occlusal device therapy has been frequently indicated for treating TMD. The most common conditions are masticatory myalgia, TMJ arthralgia, and TMJ dysfunction. However, there is insufficient scientific evidence showing that occlusal device therapy helps reduce myalgia or arthralgia. Namely, it has not been determined which type of TMD would most likely respond to occlusal device therapy. The therapeutic advantage of device therapy, especially stabilization appliances, lies in producing stability of occlusion and equal distribution of abnormal forces causing overload of the masticatory muscles and the TMJ. However, this theory raises the question of how occlusal device therapy reduces myalgia or arthralgia.

Assessments of efficacy of occlusal device therapies on improvement of TMJ conditions have relied on the attending doctor's judgment based on the subjective symptoms of the patient. However, objective clarification of failure with occlusal device therapy may be meaningful for clinicians if joint symptoms are not relieved. Therefore, objective evidence that occlusal device therapy is useful to lessen myalgia or arthralgia is very important.

This study showed that patients with reduction of pain were observed to show anterior movement of the condyle while wearing an occlusal device. This is probably because this led to joint space expansion, and elastic tissues in the deeper layer expanded the inner space of the plexus, increasing its blood supply. In addition, if a biconvex disc was found at the beginning of occlusal device therapy, it was difficult to decrease TMJ pain. It has been reported that disc displacement on mouth closing and opening with the biconvex discs was somewhat greater than that with biconcave or biplanar discs. Accordingly, pain in the joints with biconvex-type discs may be induced through various complicated processes, almost irrespective of disc displacement. For instance, the articular cavity was narrowed by parafunction, and synovial fluid production was reduced, leading to increased friction, limitation of condylar motion, and mechanical injury to the articular soft tissue layer. For the treatment of the joint pain induced by such a biological mechanism, the effect of occlusal device therapy is less known, although it has been advocated in patients with pain of muscular origin. Further studies are required to clarify the effects of occlusal device therapy for pain of joint origin.

It is known that condyle bone marrow abnormalities are pain-producing factors. It has been reported that the degree of pain was greater in joints with abnormal bone marrow than in joints with normal bone marrow signals on MRI scans. However, there are reports that bone marrow abnormalities do not always depend on the pathologic state of the TMJ. The present study did not find that occlusal device therapy was effective in the treatment of TMJ pain in patients with bone marrow abnormalities. Therefore, it is important in future studies to determine which types of bone marrow abnormalities tend to cause joint pain based on the characteristics of the disc and condyle dislocation in the TMJ. Surgical treatments are necessary for TMD if conservative approaches are unsuccessful. The present study may give a clue to elucidating the pathogenesis of internal derangement (ID) of the TMJ associated with lack of coordination of the articular disc and condyle, and it is very meaningful for clinicians who should take great care in the selection of surgical procedures. The conclusions of the present study were as follows. Occlusal devices causing anterior movement of the condyle had a weak relationship with TMJ pain reduction. There was a high probability that occlusal device therapy would not be successful in patients with visible abnormalities such as bone marrow abnormalities and biconvex disc configuration of the TMJ.

Takahara et al[342] explored the association of TMJ pain according to MRI finding in patients with TMDs. Once disc displacement occurs, ID almost certainly facilitates the progression of pathology, particularly the development of bony changes observed in the condyle. The pathologic changes, including those in the disc, have been well described by Wilkes and illustrate the progressive nature of the disease. Degenerative bony changes are characterized by deterioration of articular tissue with concomitant osseous changes in the condyle and articular eminence, such as osteophytes, erosion, subchondral cysts, and generalized sclerosis. The purpose of this study was to investigate the relationship between TMJ pain and disc displacement, OA, joint fluid, and

bone marrow edema, as well as to analyze MRI findings as a predisposing factor for TMJ pain.

The study included 646 TMJs of the 323 patients in the study. This study showed a significant relationship between the presence of TMJ pain and MRI diagnoses of ADDWOR. The results suggest an association of TMJ pain with ADDWOR, severe bony change, joint fluid, and bone marrow edema. Thus, the diagnostic accuracy of TMJ pain can possibly be improved by combining different MRI variables.

Chen et al[343] discussed anterior repositioning splints (ARSs) which are used primarily for the management of ADDwR. They aim to re-establish normal disc-condyle-fossa relationships with therapeutic mandibular positions that are forward to maximum intercuspation. The mandible is guided into the protrusive jaw positions by means of occlusal indentations and reverse guidance inclines integrated into the ARS. Two main theories exist pertaining to their usefulness in reducing TMJ pain, clicking, and dysfunction. The first proposed that ARS reposition condyles anteriorly to catch or recapture displaced discs, establishing normal disc-condyle relationships in the mandibular fossae. The disc-condyle complexes are subsequently walked back along the posterior slope of the articular eminence by periodic modification of the ARS. The second theory asserted that ARSs allow for the displaced discs to slip back into their normal positions in the therapeutic mandibular positions.

Maxillary complete-coverage acrylic resin ARSs with occlusal indentations and anterior reverse inclines were fabricated for the 31 participants in the study. To obtain the therapeutic protrusive jaw position, participants were instructed to open their mouths fully beyond the clicking point and to close in a protruded position with the incisors in an edge-to-edge relation. Participants wore the ARS continuously for 3 months and were only allowed to remove the splints when brushing their teeth. They were reviewed monthly to ensure splint acceptance/compliance and to monitor subjective/objective treatment progress. At the end of 3 months, the splints were worn only during sleep. Participants were first asked whether their back teeth were contacting, followed by checking with 40-μm-thick articulating paper to ascertain the re-establishment of occlusion. The original occlusal conditions were gradually re-established over 1 to 2 weeks upon stopping daytime splint wear. The participants were recalled at 6 months and clinically assessed for signs and symptoms.

Participants were assigned 2 imaging visits. During the first visit, before treatment, MRI was acquired with the participants' mouth closed in maximum intercuspation and opened fully. This was followed by an immediate postsplint insertion MRI with the mouth closed in the therapeutic protrusive jaw position. After 6 months, a second imaging visit was scheduled, where after treatment, MRI was performed again in the closed and opened mouth positions without the ARS. Disc and condyle angles/positions were assessed using 2 central and sagittal MRI images of the TMJs by a single evaluator.

Upon ARS insertion, all TMJs with ADDwR were found to achieve ideal spatial disc-condyle relationships. The latter was achieved by significant forward and downward movement of the condyles and concurrent backward movement of the discs. The stability of this relationship could not be maintained in the majority of TMJs upon ARS removal, 6 months after splint treatment. Normal disc-condyle relationships were observed in only 40.6% of joints with ADDwR. Most condyles returned to their posterior pretreatment positions, whereas the discs generally moved anteriorly again. Findings provided new insights into the short-term and longer-term effectiveness of ARS.

Orthognathic surgery

Al-Moraissi et al[344] authored a systematic review and a meta-analysis determining whether orthognathic surgery has a beneficial or deleterious effect on preexisting TMDs. A total of 5029 patients enrolled in 29 studies were included in this meta-analysis. The results showed that a preexisting TMD may improve with orthognathic correction in both class II and III patients. It is important to note, however, that not all surgical procedures resulted in improvement in TMDs. For patients treated by mandibular advancement, an isolated bilateral sagittal split osteotomy (BSSO) resulted in a significant improvement in TMDs, but the bimaxillary surgical procedure did not. Conversely, an isolated BSSO to achieve setback of the mandible resulted in no improvement in TMDs, but there was an improvement when it was combined with Le Fort I osteotomy. These different results may have much to do with sample sizes and many other individual variables such as the method of analysis, bias, presence and type of TMJ pathology, surgical technique, surgeon skill, postsurgical orthodontics and patient management, and adjunctive procedures.

Class II patients with high occlusal plane angles and articular disc displacement may have a poorer outcome than those with normal- or low-angle mandibular retrognathism and prognathism. Although there is overall statistically significant TMD improvement in this study, the results do not indicate that orthognathic surgery will predictably improve a patient's TMD problem, and careful patient assessment needs to be conducted by the clinician before planning any surgical correction. Although many patients with TMD symptoms show improvement with orthognathic surgery, a significant percentage of patients do not show improvement, some patients' symptoms may become worse, and TMD develops after surgery in some asymptomatic patients.

Because of this unpredictability, surgeons should inform patients that orthognathic surgery may or may not improve preexisting TMJ and TMD signs and symptoms.

TMJ surgery

Bianchi et al[345] submitted an interesting case study of the effect of TMJ articular disk repositioning in an AOOR malocclusion. Clinical characteristics of the anterior open malocclusion include excessive gonial, mandibular, and occlusal plane angles; small mandibular body and ramus; increased lower anterior facial height; decreased upper anterior facial height; class II tendency; and inadequate lip coverage. It has been shown that many conditions of the TMJ may be related to this type of malocclusion. The most common disorders are articular disc displacement, adolescent internal condylar resorption, reactive arthritis, condylar hyperplasia, autoimmune diseases, OA, and advanced reactive arthritis. TMJ OA is noteworthy because of its involvement with occlusal development, craniofacial growth, and long-term stability. A common complication of this disease is condylar resorption, which can lead to an anteriorly displaced disc and an AOOR.

A 20-year-old woman had a slight mandibular retrusion and a class I dental malocclusion, mainly associated with her AOOR, which extended to the posterior teeth. Her skeletal pattern was vertical, and the maxillary and mandibular incisor inclinations determined the convexity of the lips within adequate parameters for her ethnic background. Her main complaints were the dental esthetics altered by the AOOR, the deficient occlusion of the posterior teeth with interference of the maxillary molar palatal cusps over the mandibular molar buccal ones, and severe orofacial pain with episodes of migraine since her childhood.

Radiographic examination showed bilateral condylar remodeling (more pronounced on the right side), third molar impactions, narrow symphysis, and AOOR. Muscular and articular TMD became apparent during the physical examination, with the right side being the most affected. Bilateral TMJ clicking with deviation of the mandible to the right side on opening was noted. OA was also considered as a diagnosis. MRI and CBCT examinations of the TMJs were required to confirm the hypothesis. The MRI showed reduced mandibular condyles, increased cortical range, and signs of degeneration in the joint discs, with more pronounced degeneration on the right TMJ. The left disc had anterior displacement with reduction, and the right TMJ disc had anterior displacement without reduction.

An AOOR malocclusion has several etiologic possibilities, and the treatment is a challenge in orthodontics. The patient must first be correctly diagnosed so that stability can be maintained after the treatment. Interventions in skeletal AOOR differ from growing to nongrowing patients. In growing patients, the reduction of the vertical skeletal growth with intraoral or extraoral force is the main treatment objective. In nongrowing patients, the treatment objective is to correct the dentoalveolar position with camouflage or surgical intervention. Extrusion of the anterior segment with elastics, retraction and vertical repositioning of the maxillary and mandibular anterior teeth by extraction of the premolars, and intrusion of the posterior teeth are also strategies used to treat skeletal AOOR in nongrowing patients. An orthognathic surgery is indicated when the AOOR is associated with skeletal discrepancies.

AOOR, reduced horizontal occlusal relationship, and increased vertical occlusal relationship are known to be associated with ID of the TMJ and TMJ OA. When condylar resorption is bilateral, the mandible rotates posteriorly and frequently presents as a skeletal class II malocclusion with AOOR. Many treatment options have been described in the literature. In general, patients primarily undergo nonsurgical treatments, such as physiotherapy, occlusal splint therapy, and medication to relieve functional limitation and pain. After initial conservative treatment, orthodontics and surgery become options, such as intrusion of the maxillary molars with miniscrews or miniplates, maxillary or mandibular surgery for occlusal deformity correction, gradual mandibular advancement with distraction osteogenesis, and TMJ interventions followed, or not, by orthognathic surgery.

An alternative is to combine the orthodontic treatment with the use of a splint. After the initial splinting therapy, orthodontic treatment is conducted for occlusal reconstruction at the splint-induced condylar position. Both archwires (maxillary and mandibular) are used simultaneously with the splint and vertical elastics to prevent anterior intrusion. Afterward, the splint is reduced in size gradually according to the orthodontic progress. However, if a pathologic condition such as OA with TMJ disc displacement is not treated, the long-term prognosis of this condition may allow a new progression of condylar resorption, occlusal relapse, and TMJ pain.

The clinical approach in the case study consisted of surgical and orthodontic treatment that included a bilateral TMJ articular disc repositioning surgery and fixed orthodontic appliances. Initial leveling and alignment of the maxillary dental arch was achieved with 0.016-in nickel-titanium thermal archwire, using the straight-wire technique and Roth prescription 0.022-inch slot appliances. The patient had requested rheumatoid, endocrine, and gynecologic screening. The results were negative for autoimmune disease and any other pathology. After 18 days, bilateral TMJ articular disc repositioning surgery and extraction of all 4 third molars were performed. It was noticed during the TMJ surgery that there was a high adherence of the disc on the right side

with signals of DJD. Fourteen days later, alignment and leveling of the mandibular dental arch was achieved with the same protocol as used in the maxillary arch. After a 1-month period, both archwires were replaced by 0.017×0.025-inch nickel-titanium wires. The final 0.19×0.025-inch stainless-steel archwires were placed, and dental occlusal adjustments were performed during 9 months. The total active orthodontic treatment period was approximately 12 months, including the surgical time. According to the patient's report, the headaches and TMJ pain decreased significantly after the TMJ surgery. Considerable bone remodeling was observed on the right condyle. The 2-year follow-up showed occlusal stability and significant decreases in TMJ pain, headaches, and functional limitation.

Candirli et al[346] described a retrospective evaluation of 3 different joint surgeries for IDs of the TMJ. ID of the TMJ describes a wide spectrum of abnormal positional relationships between the articular disc and both the mandibular condyle and the articular eminence. The mechanical obstacle caused by anterior or anteromedial disc displacement in the joint during function commonly results in considerable pain and restricted mouth opening. Clinically, condylar hypomobility concomitant with reciprocal painful clicking or chronic closed lock can be a sign of advanced ID with perforation of the articular disc or various degenerative changes in the disc and/or the articular surfaces. The initial treatment of ID is conservative. Most patients are successfully treated with nonsurgical techniques, including physical therapy, splints, pharmacotherapy, and/or intraarticular lavage and lysis. However, some patients do not respond to conservative measures aimed at improving mandibular function and are therefore candidates for open joint surgery. Patients with pain well localized to the TMJ, who are not responsive to conservative therapy, are also candidates for surgery. There is a disagreement in the literature concerning the surgical techniques with the highest probability of success and minimal morbidity. The surgical options for patients with early intermediate to advanced stage of the disease are also controversial, with differences in opinion regarding the results obtained using the techniques described in the aforementioned studies. This retrospective study compared the outcomes of discectomy alone, discectomy with an abdominal dermis fat graft, and eminectomy in the treatment of patients with unilateral IDs of the TMJ.

The results showed better outcomes after discectomy rather than eminectomy in terms of pain reduction and improved mandibular function. Long-term studies have shown that discectomy is effective in resolving joint pain and dysfunction, with most patients able to enjoy a restriction-free diet postoperatively. However, despite the positive results of discectomy alone, this procedure accelerates the development of degenerative changes on the condylar surface, including flattening and sclerotic changes similar to those seen in later-stage ID. The main clinical finding in the postdiscectomy joint is crepitus, a functionally adaptive mechanism of the glenoid fossa and the reduced area of the condyle. The relationship between the radiographic changes and postoperative symptoms is often unclear. Dimitroulis was the first to report the use of ADFG in TMJ ankylosis in 2004, and the successful use of this approach in discectomized TMJ was then demonstrated in many subsequent studies.

Given the continued uncertainty regarding the criteria for discectomy with or without replacement, the patient population in many studies did not have a uniform clinical diagnosis, and different joint pathologies, ranging from Wilkes stage II to V, were evaluated. In addition, some studies were retrospective and nonrandomized. Another issue is the lack of uniformity in the performance of the surgical procedure. Discectomy is often recommended for patients with late-stage ID of the TMJ who present with severe disc deformity, displacement, or degeneration and degenerative osseous changes. Some studies have shown a greater likelihood of success when discectomy is performed before the development of degenerative changes, typically Wilkes stages IV and V.

It has been reported that ADFG after discectomy resulted in remodeling, as seen on the postoperative orthopantomogram, in over two-thirds of the treated joints (68.8%) along with pain relief and smooth joint function. The best surgical method for the treatment of IDs of the TMJ has yet to be determined, given the many aspects that have to be taken into account in each patient, including the surgeon's training and experience, the interpretation of the TMJ signs, and their relationship to the clinical findings. However, these results suggest that excision of the disc without, but especially with, ADFG replacement effectively reduces pain and restores smooth mandibular function.

Otologic consideration in TMD

De Toledo et al[347] wrote a systematic review that found high prevalence of otologic signs and symptoms in adult patients with TMD. The results of the meta-analysis show that ear fullness (74.8%) is the most frequent symptom associated with TMD in adult patients. The second most frequent symptom is otalgia (55.1%), followed by tinnitus (52.1%), vertigo (40.8%), and hearing loss (38.9%). The frequencies of earache (65.0%) and dizziness (21.9%) were retrieved from a single study. Further research in a well-structured, population-based prospective study is necessary to provide a more accurate prevalence of otologic signs and symptoms in a TMD population.

Craniocervical considerations in TMD

Westersund et al[348] wrote about the relationship of the craniocervical junction (CCJ) and occlusion. The CCJ

consists of the kinematically complex connection between the skull and the first 2 cervical vertebrae, also referred to as the occipital-atlanto-axial joint complex. The joints connecting these vertebrae create a functional unit that facilitates the majority of the movement of the CCJ. The TMJ is also a kinematically complex bilateral connection between the mandible and the temporal bones of the skull. If the CCJ is displaced from its normal neutral juxtaposition, and the positional neutral is no longer attainable by the head, this malposition is directly transferred to the temporal portion of the TMJ, creating a potential for a shift in occlusal contact.

This study investigated whether there is a change in occlusion that can be measured using a dental force plate after a national upper cervical chiropractic adjustment (NUCCA) adjustment to the CCJ. Overall, consistent postural trends were observed within each set of pretreatment and posttreatment measurements. The patients were not observed to always occlude consistently, and thus, it was more difficult to obtain trends; this is reflected in the size of the error for some patients. However, occlusions were observed within each series that showed representative effects. Traditional dental viewpoints saw the TMJ as the determinate force in the function of the mastication and parafunctional actions of the mandible. There is little attention given to the influence of the CCJ on the action of the mandible or the position of the TMJ within the mandibular fossa and the consequences that variations in the position of the CCJ would have on muscle and ligamentous tissue associated with the TMJ. Some dentists treating TMD are beginning to understand the interaction between the TMJ and CCJ. Traditional dental treatments such as occlusal adjustments, dental orthotics, and reconstructive treatment options often do not provide consistent results in dealing with patient complaints. The interconnection of the stomatognathic complex to the rest of the body needs to be recognized to understand the influences on the occlusal system. TMD is affected by malocclusion and posture; therefore, it is necessary to address all related physiologic issues with the patient if there is to be an effective method of treating problems with the biomechanics of the stomatognathic system.

This study shows a link between the alterations of an individual's CCJ alignment and the generation of occlusal forces into a maximum occlusion. It is possible that a change in biomechanics of the occlusion is linked to head and neck postural parameters, and this relationship should be considered during treatment by both chiropractors and dentists focusing on the CCJ and TMJ, respectively.

Interocclusal records

Braganca et al[349] discussed the influence of neuromuscular deprogramming on the effect of interocclusal records in centric relation (CR). Many prosthetic, orthodontic, and occlusal treatments require the registration of the mandibular position and the transfer of that record to the casts on an articulator. Thus, a maxillomandibular relationship is not only stable but is also required for reproducible diagnosis and satisfactory treatment planning. The position of the mandible at CR, in which the condyle is at the most anterior region of the articular fossa and properly aligned, is more accepted as a reference position, especially when the maximum intercuspal position is not stable. When evaluating the condylar position, one should consider that the influence of the dental contacts on the muscle function, which would naturally lead the mandible toward CR position, might be interrupted due to the presence of deflective contacts. The proprioception of the periodontal ligament of the teeth involved in occlusal interferences accounts for inducing the central nervous system to avoid this position, which leads the mandible toward maximum intercuspal position, regardless of the position of the condyle heads in the articular fossa. Therefore, the use of neuromuscular deprogramming tools that eliminate or reduce the influence of the dental contacts on mandibular positioning is widely reported in the literature and facilitates the proper manipulation and CR recording. Electronic position analysis (EPA) has recently been performed to evaluate the condyle position. This system is similar to electrognathography, which has the accuracy of 0.1 mm. The system is based on measurements related to the latency period of the ultrasonic pulses in real time. These are sequentially transmitted among 4 emitters on the mandibular arch and 8 emitters on the facial arch. The latency time is converted in distances, which represents the arch position. By using EPA, it is possible to register the static position of the mandibular condyle. Different from electrognathography, this system does not capture the movement, but it is similar to a photograph of the condylar position. This study aimed to analyze, by EPA, whether the muscle relaxing promoted by the ULF-TENS would change the condylar position registered with different techniques of CR manipulation and whether the ULF-TENS use would influence the intratechnical repeatability of these records.

Twenty-five participants (15 women and 10 men) were selected, with mean age of 28.80 ±7.53 years, good functional occlusion, and absence of TMDs, according to axis I of the Diagnostic Criteria for TMDs. Because of the action of muscle relaxation, the literature recommended the use of ultra low frequency transcutaneous electrical nerve stimulation (ULF-TENS) before the maxillomandibular record to find a more physiological position for the patient. However, in this study, the use of ULF-TENS did not influence the total displacement or the direction of condyle displacement. Some disturbances in the lateral pterygoid muscle activity are still

related to the condylar position and intraarticular disorders, but there is no strong scientific evidence that supports this concept or explains the exact function of this muscle in the stomatognathic system. McKee[350] performed a similar study, in which the condyle position was evaluated for the repeatability without the influence of dental contacts on the musculature. Thus, four CR records were obtained by Dawson's bimanual technique before and after the use of a muscle deprogrammer for 60 minutes, which in that case, was the device. The results showed that regardless of the muscle deprogramming, the condyle was led to the same CR position, corroborating the data found in this study. The ULF-TENS application, before the CR record, did not change the total displacement or the condylar position when using Dawson's bimanual, long strip, or harmonic centric occlusal relationship (R.O.C.A.) system techniques. For Dawson's bimanual technique, the ULF-TENS discreetly improved the repeatability, but the fact that this technique already had good repeatability before the use of ULF-TENS should be taken into consideration. For the long strip and R.O.C.A. system techniques, there was no improvement with the use of ULF-TENS. Therefore, there is no clinical relevance for using the ULF-TENS before the CR record with these studied techniques.

Whiplash

Landzberg et al[351] authored a systematic review related to whiplash injuries (WIs). A WI is the result of the sudden deceleration or acceleration of the thorax independent of the head movement. This type of injury is commonly associated with motor vehicle collisions, specifically when an automobile is impacted from the rear. Because of the acceleration/deceleration motion, it is thought that patients may sustain bony or soft tissue injuries. Symptoms resulting from the injury are grouped together as whiplash-associated disorders (WADs). WADs encompass a wide range of symptoms, including neck pain, headaches, dizziness, and sleep disturbances. Among the often-overlooked aspects of WADs are TMDs that result in jaw pain and dysfunction and may be associated with headache and regional pain. TMDs are often not diagnosed in the initial assessment after WIs. This may be attributed to a delayed onset of symptoms but may also be the result of more severe cervical spine pain masking the TMD symptoms. The delay in diagnosis can be expected to be up to 4 weeks after the accident. WAD-associated TMD blows to the mandible within the vehicle can also result in TMD and have the potential for jaw and dental trauma. Diagnosis of TMD is further complicated by the fact that many injuries are not detectable by radiographic or manual examination and may not be the focus of and be within the expertise of the health-care worker. In addition, diagnosis often relies on self-reporting of symptoms by patients. It is therefore essential that detailed initial examination, including evaluation of masticatory muscles, the TMJs, and the range of mandibular movement be completed and recorded at the first presentation after trauma. This examination should include past history of TMDs, changes in the preexisting condition after trauma, and the effect of symptoms on daily functions, such as mastication, speech, and overall quality of life. Patients should be followed up for an appropriate period and evaluated intermittently for changes in symptoms.

The challenging nature of diagnosis of chronic locoregional pain, headache, and TMDs requires the attention of health-care workers, including medical and dental professionals and physical therapists to make careful inquiries; to thoroughly examine the patient's head, neck, and jaw regions; and to make appropriate referrals for management by experienced providers. Comprehensive management of patients with WADs requires timely assessment for TMDs, appropriate follow-up examinations, and a multidisciplinary approach to management. Future high-quality studies evaluating the success of various TMD treatment modalities in patients with WADs will allow for more directed management of these complex situations.

SLEEP-RELATED BREATHING DISORDERS

Oral appliance therapy

The research related to mandibular advancement devices (MADs) is primarily short-term studies. The reviewer's opinion is that these short studies do not show the true effectiveness of the MAD. If we relate back to Dr William H. McHorris' (Memphis Tennessee, past president of the AARD) work with the treatment of TMDs, he reminds us of philosophies of any treatment of the body. Dr McHorris' statement that we "Create an environment conducive for healing" may indeed be true for the treatment of obstructive sleep apnea (OSA). Dr McHorris attributes this quote to Dr Hunter Brinker (deceased, Orlando, Florida, past president of the AARD). Dr John Hunter, the famous English physician said, "The only rationale for treatment is that which facilitates the body's recuperative powers." The body takes time to reestablish homeostasis. Treatment of OSA by the use of the MAD is a different treatment from continuous positive airway pressure (CPAP), commonly used by sleep physicians. The CPAP is mechanical, requiring little from the body, but the MAD functions with the body to allow for a more physiologic process of breathing. The author believes that this will prove to be a positive benefit and indication for the use of the MAD.

The available mandibular advancement appliances fabricated today are very different from one another with a myriad of design differences. Even within the same basic design, the appliances vary because of fabrication

variation of each individual technician. The author believes that these design differences impact outcomes and are a reason why physicians have been somewhat reluctant to accept MAD therapy. It is suggested that the reader keeps this possible factor in mind as he or she studies the literature presented in the following sections.

One trial set out to elucidate whether patients with severe OSA who were treated with MADs demonstrated improved EF after the therapy.[352] Endothelial dysfunction is a major predictor of late cardiovascular events and is linked to the severity of OSA. Patients with severe OSA and overt CVD were randomized to either effective MAD therapy or a sham device. Reactive hyperemia index is a validated measure of EF and was the primary outcome, assessed on an intention-to-treat basis. Treatment compliance was monitored with an embedded microsensor in the appliance. One hundred fifty patients (86% men, mean [SD] age: 54 [10] years; median [interquartile range] apnea-hypopnea index (AHI), 41 [35-53]; mean [SD] Epworth sleepiness scale (ESS), 9.3 [4.2]) were randomized to treatment with MAD (n=75) or sham (n=75). On intention-to-treat analysis, effective MAD therapy was not associated with improvement of EF compared with the sham group; blood pressure outcomes did not differ between the 2 groups. Effective MAD treatment led to significant improvements in AHI ($P<.001$); microarousal index ($P=.008$); and snoring, fatigue, and sleepiness ($P<.001$). Mean ±SD objective compliance was 6.6 ±1.4 hours/night with MAD versus 5.6 ±2.3 hours/night with the sham. They concluded that in moderately sleepy patients with severe OSA, MAD therapy reduced severity of disease and associated symptoms but had no effect on EF and blood pressure despite high treatment compliance. It is however noteworthy that the study duration was only 2 months; longer studies are warranted to assess whether EF does indeed improve with effective MAD over a longer time interval, promoting time for the endothelium to heal.

A network meta-analysis sought to integrate evidence from available studies on the relative efficacies of CPAP, MAD, supervised aerobic exercise training, and dietary weight loss in OSA patients.[353] Eighty RCTs studying participants with OSA were evaluated from PubMed, SCOPUS, Web of Science, and Cochrane database from inception to September 8, 2015. CPAP decreased AHI the most (by 25.27 events/hour [22.03-28.52]), followed by exercise training, MADs, and dietary weight loss. The difference between exercise and CPAP was nonsignificant (−8.04 [−17.00 to 0.92]); a significant difference between CPAP and MAD existed on AHI and oxygen desaturation index (−10.06 [−14.21 to −5.91] and −7.82 [−13.04 to −2.59], respectively). Exercise significantly improved ESS (by 3.08 [0.68-5.48]) but with a nonsignificant difference compared with MADs and CPAP. The authors concluded that CPAP is the most efficacious in complete resolution of OSA and in improving the indices of oxygen saturation during sleep. Although MADs offer a reasonable alternative to CPAP, exercise training significantly improved daytime sleepiness and could be used as an adjunct to the former 2 modalities.

Another project evaluated dentoskeletal changes associated with long-term and continuous MAD use in sleep-related breathing disorder patients.[354] Twenty individuals with snoring and OSA were treated with an MAD; cephalometric measurements and 3D model analysis were performed at baseline and after 3.5 ±1.1 years. Intragroup differences were evaluated using paired *t* test or Wilcoxon signed-rank test. Regression analysis was performed for variables that demonstrated a statistically significant difference between time points to evaluate the influence of treatment time and patient's initial characteristics on their differences ($\alpha=.05$). Cephalometric analysis illustrated that the maxilla exhibited a significant decrease in horizontal position (stella, nasion, A point [SNA]: −0.4 ±0.72 degrees, $P=.021$) and a significant retroclination of maxillary incisor position (−1.59 ±1.07 degrees, $P<.001$); the mandible exhibited a significant downward rotation (0.88 ±1.28 degrees, $P=.006$) and a proclination of the mandibular incisors (2.27 ±1.38 degrees, $P<.001$). Model analysis revealed a decrease in maxillary total space discrepancy (−0.66 ±0.72 mm, $P=.002$), vertical overlap (VO; −0.34 ±0.47 mm, $P=.011$), and horizontal overlap (−0.4 ±0.52 mm, $P=.004$). In the regression analysis, treatment time influenced the mandibular incisor inclination (Beta: −0.713; $P=.018$) and VO (Beta: −0.218; $P=.018$); patients' initial characteristics had an impact on VO (Beta: −0.195; $P=.011$). They concluded that MAD use after a mean of 3.5 years leads to statistically significant but clinically irrelevant dentoskeletal changes. Their potential occurrence should be thoroughly discussed with patients; regular follow-up appointments by a specialist experienced in dental sleep medicine are also mandatory during treatment in addition to polysomnographic studies. They noted that a larger sample size could increase the generalizability of the findings.

A prospective study sought to investigate the influence of long-term MAD therapy on the TMJs, orofacial function, and occlusion.[355] Thirty men and 13 women (median age: 54) with OSA (AHI: 7-57) participated. Their examinations included the Nordic Orofacial Test Screening; the Research Diagnostic Criteria for TMDs; and CBCT of the TMJs. Examinations were performed at baseline (T0), 3 to 6 months (T1, no CBCT), 1 year (T2), and 3 years (T3) after commencing treatment. The results were analyzed as long term (T0-T3, n=14) and short term (T0-T2, n=24) by *t* test, Fisher exact test, and ANOVA. The analyses demonstrated a reduction in AHI ($P=.002$). Significant long-term findings were increased scores in

Nordic Orofacial Test Screening (P=.045), reduced VO (P=.031), and increased jaw protrusive movement (P=.027). TMJ changes were noted as joint sounds in terms of reciprocal clicking and crepitus; short term as a decrease and subsequent recurrence (P=.053; P=.037). No significant findings on CBCT were noted. The authors concluded that MAD treatment is beneficial to some patients with OSA; however, alterations in the TMJs, orofacial function, and occlusion may occur. These changes appeared to be less harmful than the previously reported ones with careful adaptation, control, and follow-up.

Another trial assessed the ability to prospectively identify therapeutic responders to mandibular advancement therapy and establish an efficacious mandibular position.[356] Two hundred and two patients with OSA took part in a blinded, 2-part investigation. A system for identifying therapeutic responders was developed in part 1 (n=149); the predictive accuracy of the method was prospectively evaluated on a new group of participants in part 2 (n=53). Each individual underwent a 2-night, in-home feedback-controlled mandibular positioner (FCMP) test, followed by treatment with a custom oral appliance (OA) and an outcome study with the device in place. A machine learning classification system was trained to predict therapeutic outcome on information obtained from FCMP studies on part 1 participants. The accuracy of the system was then evaluated on part 2 participants by exploring the agreement between prospectively predicted outcome and observed outcome; a predicted efficacious mandibular position was arrived at from each FCMP study. Predictive accuracy was found to be 85% sensitive, 93% specific, 97% positive predictive value, and 72% negative predictive value. Of participants who are correctly predicted to respond to the therapy, the predicted mandibular protrusion was efficacious in 86% of treatments. They concluded that an unattended, in-home FCMP test prospectively identified individuals with OSA who will respond to MAD therapy and provided an efficacious mandibular position.

A different study examined the reliability of a built-in thermal sensor in an MAD to measure the use as compared with a self-reported diary of MAD usage.[357] Eighty consecutive individuals who were referred to a specialist outpatient sleep medicine clinic were enrolled. Men and women aged 25 to 70 years with a diagnosis of mild to severe OSA were included. For the purposes of this study, it was deemed sufficient to include the first 30 nights of MAD use in the reliability analysis; at the 30th night follow-up visit, the diary with duration of device use was returned, and data on the duration of MAD use with the embedded sensor were retrieved. From a total of 2400 nights, complete data from both methods were available for 2108 nights (84.6%). Missing data were largely a result of missing self-reported diaries, whereas technical failure occurred in 6 nights (0.002%). The relative reliability was very high with $ICC_{3,1}$ 0.847, and the absolute reliability for digitally recorded MAD usage was calculated to be −0.17 (95% CI, 1.47 to −1.81) hours in decimal conversion. It was concluded that objectively collected data from built-in thermal sensors in MADs were reliable as that of self-report record keeping, allowing for more accurate measurement of MAD adherence in the future.

A review was performed to update the evidence in favor of oral appliance therapy for patients with OSA.[358] A high level of evidence demonstrates that oral appliance therapy is effective in the treatment of OSA, but CPAP is more efficient. Higher adherence with oral appliances (OAs) may compensate for this difference. Daytime sleepiness is better treated with CPAP than with an OA in patients with severe sleep apnea. In those with milder disease, it is unclear whether sleepiness is significantly reduced. The long-term effectiveness of OAs is uncertain because of side effects and the risk of OSA deterioration. The author noted that oral appliances are effective, but their efficacy is more variable than that of CPAP; more research is warranted concerning OA mechanism, impact on subjective symptoms, and long-term health outcomes.

A randomized, placebo-controlled clinical trial evaluated the long-term effects of an oral appliance on clinical symptoms, respiratory sleep variables, sleep quality, and attention measures in individuals with upper airway resistance syndrome (UARS) as compared with a placebo.[359] Thirty patients with UARS were randomized into 2 groups: placebo and MAD. UARS criteria were presence of sleepiness (ESS: $\geq$10) and/or fatigue (Modified Fatigue Impact Scale: $\geq$38) in conjunction with an AHI score of $\leq$5; a respiratory disturbance index score of >5 events/hour of sleep; and/or flow limitation in more than 30% of total sleep time. All participants completed the Pittsburgh Sleep Quality Index (PSQI) questionnaire, the Functional Outcomes of Sleep Questionnaire, and the Beck Anxiety and Depression Inventories assessment and underwent full-night polysomnography (PSG), multiple sleep latency test, and psychomotor vigilance test. Evaluations were performed at baseline and after 1.5 years of treatment. Respiratory disturbance index, number of respiratory effort-related arousal, percentage of total sleep time with flow limitation, and arousal index all significantly decreased after 1.5 years of MAD therapy. The PSQI total score improved, severity of depression symptoms diminished, and mean reaction time in the PVT (based on the first measurement made at 8:00 AM) significantly decreased (P=.03) at the end of the trial. The authors concluded that MAD was effective in decreasing respiratory events in UARS patients, as well as improved

sleep quality, sustained attention and decreased depressive symptoms.

A case report in sleep medicine presented a MAD as an alternative for CPAP in a patient with lacrimal duct air regurgitation as a result of CPAP therapy.[360] A 52-year-old woman with moderate OSA was using CPAP for her OSA. She complained of air regurgitation through the right eye, morning scleral injection, and xerophthalmia with CPAP therapy; symptoms resolved after discontinuing PAP. Switching to a MAD alleviated the air regurgitation and effectively treated her OSA (pretreatment AHI: 16 events/hour; AHI with MAD: 3 events/hour, as shown via home sleep test). The investigators concluded that recognition of lacrimal duct air defects can increase compliance with treatment for OSA with MAD as an alternate therapy.

Pathophysiology and medical implications

OSA is a known risk factor for stroke, and cerebral microbleeds (CMBs) are considered a precursor to symptomatic stroke. This trial set out to clarify the relationship between OSA and CMBs.[361] Patients referred to the clinic for SDB underwent both overnight PSG and brain MRI, which included T2*-weighted gradient-recalled echo images. Multivariate logistic regression and partial correlation analysis were used to estimate the relationship between OSA and CMBs. Seventy-five patients were enlisted (45 men and 30 women), with a mean age of 60.5 years. Patients with CMBs had a significantly higher AHI score than those without CMBs. An AHI score ≥15 was a significant independent predictor of CMBs (adjusted OR, 4.51; 95% CI, 1.40 to 14.58; *P*=.012) in the multivariate regression analysis. In addition, a partial correlation analysis adjusted for age, hypertension, diabetes, and CVD revealed a positive relationship between AHI and the number of CMBs (r=0.585, *P*=.028). They concluded that moderate-to-severe OSA can be an independent predictor of CMBs, which are considered a surrogate marker of overt stroke.

A population study sought to determine the relationship between OSA and chronic kidney disease (CKD).[362] A cross-sectional analysis was performed for unselected participants of the Men Androgens Inflammation Lifestyle Environment and Stress (MAILES) study, aged >40 years. Renal data were available for 812 men without a prior OSA diagnosis who underwent full in-home PSG. CKD was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m^2 or ≥60 and albuminuria (albumin-creatinine ratio: ≥3.0 mg/mmol). CKD (10.5%, n=85 [stage 1-3, 9.7%; stage 4-5, 0.7%]) of predominantly mild severity showed significant associations with OSA (AHI: ≥10; OR=1.9; 95% CI, 1.02 to 3.5), severe OSA (AHI: ≥30/hour; OR=2.6; 95% CI, 1.1 to 6.2), and respiratory-related arousal index (≥7.6/hour; OR=2.3; 95% CI, 1.1 to 4.7), but not measures of hypoxemia after adjusting for age, hypertension, diabetes, smoking, obesity, and NSAID use. CKD was not associated with daytime sleepiness. In men with CKD, those with OSA were not significantly more likely to report sleepiness, snoring, or apneas or be identified with the STOP questionnaire compared with men without OSA. The authors concluded that predominantly mild CKD is associated with severe OSA and arousals. Further population studies exploring the longitudinal relationship between CKD and OSA are called for, and improved methods are needed to identify OSA in CKD.

A systematic review and meta-analysis was performed to examine altered craniofacial anatomy on lateral cephalograms in adults with diagnosed OSA.[363] Craniofacial disharmony is an important risk factor for OSA. Identifying the cause of OSA in a particular ethnic population/individual helps with understanding the etiological factors and effective management of OSA. Significant weighted mean difference with insignificant heterogeneity was found for the following variables: anterior lower facial height (2.48 mm); position of hyoid bone (Go-H: 5.45 mm, S-H: 6.89 mm, GoGn-H: 11.84 degree, GoGn-H: 7.22 mm, N-S-H: 2.14 degree); and pharyngeal airway space (PNS-Phw: −1.55 mm, pharyngeal space: −495.74 mm^2, and oropharyngeal area: −151.15 mm^2). Significant weighted mean difference with significant heterogeneity was found for the following parameters: cranial base (SN [plane projecting from the stella-nasion line]: −2.25 mm, S-N-Ba: −1.45 degree); position and length of mandible (SNB [stella-nasion, B point]: −1.49 degree and Go-Me: −5.66 mm, respectively); maxillary length (ANS-PNS [autonomic nervous system-peripheral nervous system]: −1.76 mm); tongue area (T: 366.51 mm^2); soft palate area (UV: 125.02 mm^2); and upper airway length (5.39 mm). This meta-analysis supports the relationship between craniofacial disharmony and OSA. Strong evidence exists for reduced pharyngeal airway space, inferiorly positioned hyoid bone, and increased anterior facial heights in adults with OSA compared with normal controls. The cephalometric analysis provides insight into the anatomical basis of the etiology of OSA that can influence therapy options.

A study using the murine model of OSA sought to examine the mechanisms between intermittent hypoxia and hypercapnia (IHC) and induction or progression of atherosclerosis.[364] Atherosclerotic formation was compared between 2 mouse models, the apolipoprotein E (ApoE) and the low-density lipoprotein receptor deficient mice, with or without IHC exposure. Ten-week-old ApoE−/− or Ldlr−/− mice were fed a high-fat diet for 4 or 8 weeks in the presence of IHC exposure 10 hours/day or room air 24 hours/day. En face lesions of the aorta, aortic arch, and pulmonary artery (PA) were examined. Also, 3,3-dimethyl-1-butanol (DMB), an inhibitor of microbial trimethylamine production, was

used to determine the contribution of oxidized microbial trimethylamine in IHC-induced atherosclerosis. Eight-week IHC exposure accelerated the formation of atherosclerosis in both PA and aortic arch of ApoE−/− mice but only in PA of Ldlr−/− mice (ApoE−/− PA, 8 weeks; IHC [35.4±19%] vs room air [8.0±2.8%], $P<.01$). The lesions evolved faster and more severely in ApoE−/− mice than those in Ldlr−/− mice (PA IHC, 8 weeks; ApoE−/− [35.4 ±1.9%] versus Ldlr−/− [8.2 ±1.5%], $P<.01$). DMB significantly attenuated though did not completely eliminate IHC-induced PA atherosclerosis. The authors concluded that their findings suggest that IHC, a hallmark of OSA, speeds the progression of atherosclerosis in aorta and especially in PA. This process is partially inhibited by DMB, showing that microbial metabolites may serve as therapeutic targets for OSA-induced atherosclerosis.

Another trial evaluated the association between OSA during rapid eye movement (REM) sleep and a composite cardiovascular endpoint in a community sample with and without prevalent CVD.[365] Full-montage home PSG was used as part of the Sleep Heart Health Study; the cohort was followed up for an average of 9.5 years during which cardiovascular events were assessed. Only participants with a non-REM AHI score of <5 events/hour were included. A composite cardiovascular endpoint was determined as the occurrence of nonfatal or fatal events including MI, coronary artery revascularization, congestive heart failure, and stroke. Proportional hazards regression was used to derive the adjusted hazards ratios for the composite cardiovascular endpoint. The sample consisted of 3265 individuals with a non-REM AHI <5.0 events/hour. Using a REM AHI <5.0 events/hour as the reference group (n=1758), the adjusted hazards ratio for the composite cardiovascular endpoint in those with severe REM OSA (≥30 events/hour; n=180) was 1.35 (95% CI, 0.98 to 1.85). Stratified analyses illustrated that the association was most notable in those with prevalent CVD and severe OSA during REM sleep with an adjusted hazards ratio of 2.56 (95% CI, 1.46 to 4.47). They concluded that severe OSA that occurs primarily during REM sleep is associated with higher incidence of a composite cardiovascular endpoint but only in those with prevalent CVD.

Sleep bruxism and TMDs

Individuals with TMD report poor sleep quality on the PSQI. However, PSG studies in these situations demonstrate meager evidence of sleep disturbance on objective measures. This study sought to evaluate self-reported sleep quality in TMD as a function of myofascial pain, PSG parameters, and depressive symptoms.[366] PSQI scores from 124 women with myofascial TMD and 46 matched control participants were hierarchically regressed onto TMD presence, scores of pain intensity and pain-related disability, in-laboratory PSG variables, and depressive symptoms using the Symptoms Checklist-90. As compared with controls, those with TMD had higher PSQI scores, meaning worse subjective sleep and more depressive symptoms ($P<.001$). Higher PSQI scores were strongly predicted by more depressive symptoms ($P<.001$, $R^2=26\%$). Out of 19 PSG variables, 2 had modest contributions to higher PSQI scores: longer REM latency in TMD patients ($P=.01$, $R^2=3\%$) and more awakenings in all individuals ($P=.03$, $R^2=2\%$). After accounting for these factors, presence of TMD and pain ratings were not significantly related to PSQI scores. These results demonstrate that reported poor sleep quality in TMD is better explained by depressive symptoms than by PSG-assessed sleep disturbance or myofascial pain. The authors note that as patients with TMD lacked typical PSG features of clinical depression, the results suggest a negative cognitive bias in TMD and caution against taking self-report sleep scores as accurate indicators of PSG sleep disturbance. They state that future research should take account of depressive symptoms when interpreting reports of poor sleep.

A systematic review was performed to assess the effects of botulinum toxin (BoNT-A) injections in the management of bruxism.[367] The databases searched were PubMed, Scopus, Web of Science, Embase, Cochrane, Scielo, and Lilacs. Three independent researchers searched for pertinent studies from 1980 to March 2016. RCTs, prospective studies, and before-after studies that applied BoNT-A at the masseter and/or temporalis muscles were included. Three RCTs and 2 uncontrolled before-after studies out of 904 identified citations were included in the review. All 5 articles involved sleep bruxism (SB) and featured small sample size; none included awake bruxism. Two RCTs were double-blinded, with a control group using saline solution. Two studies used PSG/electromyography for SB diagnosis, whereas others were based on patient history and clinical examination. All studies using subjective evaluations for pain and jaw stiffness showed positive results for the BoNT-A treatment. However, the 2 studies using objective evaluations did not show any reduction in bruxism episodes but showed a reduction in the intensity of muscle contractions. The reviewers concluded that BoNT-A seems to be a plausible management option for SB, despite the lack of study on the topic. It might minimize symptoms and decrease the intensity of muscle contraction. They note that further studies are necessary especially as far as the treatment indications for bruxism itself is concerned.

A different systematic review examined the relationship between OSA syndrome (OSAS) and SB.[368] OSAS is a clinical risk factor for SB; both are reported to be associated with sleep-related arousal reactions, but no clear causative link has been established. A literature

Table 1. Tabulation of NOAC agents with relevant clinical information and perioperative management recommendations[371,372]

Agent	Prescription Pattern	Monitoring for Drug Efficacy	Recommended Perioperative Management for Surgery With Higher Risk of Bleeding	Antidote
Dabigatran (Pradaxa)	Twice daily	Not applicable	Omit morning dose, take evening dose	Available
Rivaroxaban (Xarelto)	Once daily	Not applicable	Omit daily dose	Available
Apixaban (Eliquis)	Twice daily	Not applicable	Omit morning dose, take evening dose	Available
Edoxaban (Lixiana)	Once daily	Not applicable	Omit daily dose	Not available

NOAC, novel oral anticoagulants.

search was conducted with Medline, ScienceDirect, Wiley Online Library, SAGE Journals, and EBSCOhost databases, from January 2006 through September 2016. Sequential screenings at the title, abstract, and full-text levels were performed. The review included observational studies in English with a clearly stated aim to assess the relationship between OSAS and SB using full-night PSG. The 7-item quality assessment tool for experimental bruxism studies was used to assess the methodologies across the studies. After the comprehensive screening was performed, only 3 studies that met the predefined criteria were ultimately included in this systematic review. Two studies gave evidence that OSAS is associated with the occurrence of SB events: SB events frequently occur during micro-arousal events consequently on apnea-hypopnea (AH) events, and most SB events occur in temporal conjunction with AH event termination. However, 1 study did not report a robust association between AH and SB events. The reviewers concluded that there are not enough scientific data to define a clear causative link between OSAS and SB; they do appear to share common clinical features. Further research should examine intermediate mechanisms between respiratory and SB events.

A pilot study set out to evaluate the role of specific neurochemicals in the genesis of SB.[368] They used proton magnetic resonance spectroscopy (^{1}H-MRS) to determine whether the levels of γ-aminobutyric acid (GABA) and glutamate are different in the brainstem and bilateral cortical masticatory area (CMA) between possible SB patients and control participants and to discuss whether the brainstem or cortical networks that may affect the central masticatory pathways are under the genesis of SB. Twelve possible SB patients and 12 age- and sex-matched controls underwent ^{1}H-MRS using the "MEGA-Point Resolved Spectroscopy Sequence" (MEGA-PRESS) technique in the brainstem and bilateral CMA. ^{1}H-MRS data were processed using the LCModel. Because the signal detected by MEGA-PRESS includes contributions from GABA, macromolecules (mostly proteins), and homocarnosine, the GABA signal is designated GABA+. The glutamate complex signal contains both glutamate and glutamine, which mainly reflects the glutamatergic metabolism. Edited spectra were successfully obtained from the bilateral CMA in all individuals. There were no significant differences in neurochemical levels between the left and right CMA in possible SB patients and controls. In the brainstem, significantly lower GABA+ levels were identified in possible SB patients than in controls (P=.011), whereas there was no significant difference (P=.307) in glutamate complex levels between the 2 groups. The authors concluded that SB patients may possess abnormalities in the GABAergic system of brainstem networks.

Another systematic review sought to answer the question, "Is there an association between any specific signs and symptoms of bruxism and the presence of tori?"[369] Observational studies evaluating the association between signs and symptoms of bruxism and the presence of tori were selected. Teeth grinding, jaw clenching, abnormal tooth wear, facial muscle hypertrophy, pain, or fatigue had to be determined by questionnaire or anamnesis and tori within a clinical assessment. Search strategies were developed for 5 databases, in addition to 3 gray literature's databases. Bias risk was evaluated using the "Meta-Analysis of Statistics Assessment and Review Instrument." A summary of overall strength of evidence was estimated using GRADE's (grading of recommendations, assessment, development and evaluation) Summary of Findings table. Five studies were included out of a possible 575. Two studies were categorized as moderate risk of bias and 3 as high risk of bias. Self-reporting of teeth grinding and/or clenching presented contradictory results. Presence of an abnormal tooth wear increased the odds of having tori, mainly for torus mandibularis. The overall quality of evidence ranged from low to very low. The reviewers concluded that based on available evidence, abnormal tooth wear might be associated with tori, mainly mandibular tori. The evidence is not sufficient to credit or discredit the association of tori and other signs and/or symptoms of bruxism.

ORAL MEDICINE AND ORAL SURGERY

Comprehensive dentistry not only involves restorative and operative dentistry but also oral medicine and oral surgery. Both fields are integral parts of periodontology, implant dentistry, and prosthodontics. Therefore, selected new developments in oral medicine and oral surgery may have direct implications on the daily practice of many dental specialists. The literature review of 2017

has identified 3 topics in the field of oral medicine and oral surgery that are of special interest for dentists: management of patients taking (novel/direct) anticoagulants; antibiotic prophylaxis in the dental practice; and the discussion of innovations in the application of local anesthesia.

There are many indications for the prescription of anticoagulation drugs, such as the prevention and treatment of deep vein thrombosis, atrial fibrillation, stroke, and embolism after heart valve replacement.[370] In recent years, the novel oral anticoagulants (NOACs)/direct oral anticoagulants dabigatran, rivaroxaban, apixaban, and edoxaban (Table 1)[371,372] joined the vitamin K antagonists (warfarin, phenprocoumon) and heparin in the group of widely prescribed anticoagulants.[370,372,373] Not only the nomenclature but also the drug administration pattern and the absence of monitoring tools for drug efficacy of the NOACs may be confusing for dentists.[373] The perioperative management of the patients taking any of those drugs remains a challenge. However, new findings have simplified the care of patients taking anticoagulants.[370,374,375]

There is strong evidence that the cessation of anticoagulation drug treatment for surgical procedures increases the patients' risk for potentially lethal cardiovascular events,[375,376] whereas postoperative bleeding complications—if they occur at all—can mostly be controlled with rather limited local measures (occluding on gauze, hemostyptics, sutures, antifibrionlytic agents). Therefore, it is recommended that oral surgical procedures with no or limited risk of postoperative bleeding should be carried out under continued anticoagulant therapy[370,373-375] if all local measures of hemostasis are applied. The latest literature states that this approach is advised regardless of the prescribed anticoagulative agent (either vitamin K antagonists or NOACs).[370,374] A low risk of postoperative bleeding is assumed for straightforward tooth extractions, periodontal treatment, and crown preparations involving subgingival margins.[371]

If an increased bleeding risk can be inferred from a surgical procedure (surgery involving flaps, complicated extractions, implantology involving flaps), interruption of the anticoagulant treatment can be considered.[371,372,376] Patients taking NOACs should not be taken off the drug for more than 24 to 48 hours (omission of 1 or 2 application doses depending on the prescription pattern and the patients' renal function; Table 1).[372,377] There is no need for the so-called bridging therapy with low-molecular heparin (subcutaneously injected heparin) in patients taking NOACs.[372,375,376]

In summary, there are only few indications for the cessation of NOAC treatment when performing oral surgery procedures. Only surgical procedures that carry an elevated risk for postoperative hemorrhage warrant discontinuance of NOACs that should be limited to 1 or 2 doses depending on the prescription pattern and the patient's general health status. Communication with the prescribing physician is recommended to ensure optimized patient care. An appropriate perioperative setting (surgery early in the week, morning surgery, correct surgical wound care and intraoperative hemostasis, provision of an emergency contact to the patient) should be implemented when treating patients taking conventional or novel anticoagulants.[371,372]

In 2015, the American Dental Association published a practice guideline about the administration of perioperative antibiotics in patients with orthopedic implants undergoing dental treatment and oral surgery.[378] After thorough review of the then-available scientific evidence, the authors correctly concluded that there was no rationale to prescribe prophylactic antibiotics for patients with joint replacement to prevent prosthetic infections. This recommendation was confirmed in reviews that have been published since,[379,380] and new RCTs examining this matter have not been reported. Interestingly, despite the unchanged level of evidence, the American Academy of Orthopedic Surgeons (AAOS) published a new statement in 2017—approved by the American Dental Association—that advises a renunciation from this very defensive approach.[381] The statement suggests individualized decisions about the necessity of prescribing prophylactic antibiotics for patients with orthopedic implants with respect to various factors (extent of procedure, patient immune status, general patient condition, history of periprosthetic infection, and elapsed time since orthopedic implant placement).[382] In contrast with the previously advocated clinical practice to omit antibiotic prophylaxis in patients with joint replacement,[378] the expert panel of the AAOS statement identified indications for the administration of preventive antibiotics in about 40% of the conceivable patient scenarios.[381,382] The AAOS has launched a Web-based application that can be accessed at www.orthoguidelines.org/go/auc/ under the category "Management of Patients with Orthopedic Implants Undergoing Dental Procedures" to facilitate the decision whether or not preventive antibiotics may be indicated.

In general, there is sparseness of well-designed studies examining the benefit of any indication for the use of prophylactic antibiotics in dentistry.[383,384] Although the recommendations for the administration of antibiotics to prevent infective endocarditis remain unchanged,[383] there is accumulating evidence that antibiotics cannot prevent infectious complications after dental extractions effectively and should not be used.[384-386] In every patient, clinicians should carefully weigh the risks (adverse events, antibiotic resistance) and benefits of the application of prophylactic antibiotics, considering the obvious lack of evidence supporting this practice in many situations.

The application of local anesthesia for pain relief is among the most frequently executed procedures in dentistry. In most patients, the administration of local anesthesia is well tolerated. However, both infiltration and nerve block techniques can be painful, and the failure rate especially in the mandible can be high.[387] To reduce the patients' discomfort, less and even minimally invasive local anesthesia techniques have been suggested.[387-392]

The buccal and palatal infiltration of a local anesthetic has been taught to be the technique of choice to obtain appropriate numbness when performing dental extractions in the maxilla.[393] Especially, the palatal injection site causes significant pain. Therefore, several studies have been conducted in the last decade to examine the efficacy of maxillary anesthesia without palatal infiltration.[393] Those studies vary significantly in sample size and methodology. In 2017, conflicting data were published in the same journal.[390,392,393] The study of Bataineh and Al-Sabri[390] found that the omission of palatal infiltration will result in satisfactory pain suppression during tooth extractions in the maxilla, whereas the work of Majid and Ahmed[393] found the exact opposite. Owing to the difference in the applied methods and sample size, these studies may not be entirely comparable. However, the publication of conflicting evidence in this matter highlights the potentially subjective interpretation of reported pain scores. It is interesting to note that a survey performed by the Canadian Association of Oral and Maxillofacial Surgeons revealed that most of the respondents performed palatal infiltration in most patients requiring maxillary exodontia.[391] This shows that some academic discussions about the benefit or burden of different procedures might be of limited clinical importance for clinicians.

Two minimally invasive anesthesia techniques, namely intraligamentary anesthesia (ILA) and infiltration anesthesia via pressure syringe (IA–P), were further investigated.[387,389,392] A study by Kämmerer et al[387] showed equal results of pain control rates when comparing inferior alveolar nerve block (IANB) and ILA in mandibular exodontia. The normally distributed sample consisted of 266 patients (301 tooth extractions), and 2 groups were formed. In the first group, the patients received either IANB (140 tooth extractions) or ILA (105 tooth extractions). In the second group, a split-mouth design was implemented for bilateral extractions (56 tooth extractions). There were no significant differences in anesthetic efficacy and duration of numbness in either of the groups. The latency until the onset of the anesthetic effects and the overall treatment time were significantly shorter in the ILA group. The authors concluded that ILA is a viable alternative to IANB when performing mandibular extractions (including molars). Aggarwal et al[392] showed that the efficacy of ILA can be augmented when the injected volume is increased from 0.2 mL per root to 0.6 mL per root.

The effectiveness of IA–P in comparison to IANB was researched in a study by Thiem et al.[389] The authors used the Biofeedject system. The entire sample was composed of 101 patients, of whom 48 received IA–P and 53 received IANB for local anesthesia during mandibular molar extraction procedures. An adequate anesthetic effect could only be achieved in 35% of the patients by using IA–P, whereas this rate was 100% in the IANB group. The authors did not suggest IA–P as a surrogate for IANB in this indication.

DENTAL CARIES AND CARIOLOGY

In 2017, a significant number of RCTs and systematic reviews were published. Although not all of them were of strong scientific value, this can be considered a promising trend for the advancement of knowledge on dental caries. Therefore, this year's review, with some exceptions, will focus primarily on RCTs and systematic reviews.

Sealing and infiltration of caries

Minimally invasive dentistry is based on the principle of avoiding or delaying the restorative treatment as much as possible because the sacrifice of sound dental tissues is always a side effect of any restorative treatment. With this goal, dental sealants have been used successfully not only in preventing but also in arresting noncavitated lesions. While sealants remain on the surface, the idea of caries infiltration is to infiltrate a low-viscosity resin into the enamel subsurface, filling the tiny pores created by the initial caries. The consequence is that the pathways used for the diffusion of acids and minerals through the lesion are occluded, and caries progression is arrested.

In 1 RCT, 54 teeth, with similar caries, not invading more than the middle one-third of the dentin substrate, were treated in 49 patients by supervised dental students. Sealants were applied in 1 group of teeth and conventional restorative treatment in the other half.[305] The sealing of occlusal carious lesions in permanent teeth succeeded in controlling caries over a 3- to 4-year period, and the failure rate of restored teeth was 6%, wheras for the sealed teeth, it was 26%. The significant difference in the durability of the treatment was due to failure of the sealants that frequently debond from the surface and not to the progression of caries itself. Therefore, the authors concluded that "sealed carious lesions require patient compliance in attending regular follow-ups to control the occurrence of clinical failures of the sealants," but the procedure functions efficiently if the sealant stays in place. Caries infiltration can be considered a good alternative to the use of dental sealants.

A well-designed RCT, more powerful because of a split-mouth design, evaluated the efficacy of caries infiltration in controlling progression of noncavitated proximal lesions in primary molars.[394] Fifty pairs of primary molars were compared in a 12 months period. One tooth in each participant randomly received the control treatment consisting of flossing twice daily plus the use of fluoridated toothpaste, whereas the test tooth was treated with resin infiltration by a single operator after a standardized procedure. After 12 months, a radiographic assessment of the 2 groups of teeth was performed, and although 8 participants, out of the 50 initially recruited children, were lost from the study, the caries infiltration of proximal caries lesions in primary molars was significantly more efficacious than the standard therapy alone. The studied population was subdivided into 3 groups according to their caries risk (low, medium, and high). The result of the study may be influenced by the fact that out of the 8 patients who interrupted their participation to the study, 5 were in the medium-risk group and 3 in the high-risk group, whereas none in low-risk group were lost for evaluation. Nevertheless, clinicians are encouraged to consider this efficacious clinical procedure when facing proximal lesions in primary teeth because this treatment is a less invasive and well-accepted clinical procedure.

An additional study by Anaute-Netto et al[395] investigated the effect of resin infiltration over a longer period of 3 years. The infiltrant was effective in preventing caries progression in noncavitated pit and fissures after 3 years of clinical evaluation compared with the conventional sealants. The infiltrant also presented better results in terms of caries progression at the 3-year evaluation time using a radiographic analysis.

Stepwise excavation has been considered for years the treatment of choice for deep caries with the risk of pulp involvement. The protocol is based on the complete removal of carious dentin from the surrounding cavity walls, followed by the removal of the more necrotic and infected dentin at the pulpal wall. Calcium hydroxide is placed in the deepest portion close to the pulp. Sealing for 6 to 9 months is accomplished with an interim restorative material, and then the cavity is reopened for the definitive excavation of caries and the tooth is restored. However, because it has been widely demonstrated that the presence of carious tissue does not interfere with the mechanism of caries arrest, the essential need for definitive reopening has been questioned, and an alternative treatment approach was proposed. This alternative treatment consists of leaving the deepest portion of carious tissue close to pulp and obtaining a perfect seal with a definitive restoration in a single visit. In a controlled randomized multicenter study by Maltz et al,[394] the 2 treatment approaches were compared over a 5-year period. Although, with a high drop-out rate, 299 teeth were followed up for up to 5 years divided in 2 groups: first, used as control, received the stepwise treatment, and the second one was treated with a single visit with partial excavation approach. The success rate of the experimental 1-step procedure was significantly higher (80%) than the 2-step treatment (56%). However, when analyzing the data, it can be observed that the high failure rate of the 2-step approach is due to the high dropout rate and the fact that the second treatment step was not performed. When the second visit, 6 to 9 months later, was completed, the success rate was similar. If similar success percentages among the 2 groups can be reached, therefore, the partial caries removal performed in 1 appointment must be considered the treatment of choice, being a less time-consuming and less costly procedure.

The efficacy of selective caries removal appears comparable to that of nonselective caries removal in children, with similar pulpal symptoms and failure, but selective caries removal may result in a low incidence of pulpal exposure. However, larger-scale RCTs with long-term follow-up are required to confirm this conclusion.[395] If carious tissue can be left untouched and sealed with a restorative material, it means that a great change in the understanding of the disease has occurred in these past few years. An elegant review by Professor Schwendicke[396] summarizes all these changes to provide clinical recommendations for the readers. Readers are encouraged to read the complete article for full comprehension, but the key points can be summarized as follows. Removing all carious dentin from a cavity is no longer required; instead, the carious tissue should be treated to arrest its activity while conserving sound tooth structure and pulp vitality. If the teeth are vital, several removal strategies have been proposed. First is the nonselective (complete) removal, which is not recommended any longer. Second is the selective removal to firm dentin, where firm dentin is left centrally and hard dentin is left peripherally, allowing the placement of a long-lasting restoration while avoiding the removal of remineralizable tissue; this is recommended for shallow or moderately deep lesions. Third is the selective removal to soft dentin, where soft dentin is left close to the pulp and sealed under a restoration; this is particularly recommended for deep lesions. The final one is the stepwise removal that combines different strategies and is also suitable for deep lesions, at least in adult patients. Alternatives involve not eliminating but sealing carious tissue with resins (for shallow, noncavitated lesions) or stainless-steel crowns (the Hall Technique, for cavitated lesions in primary molars) or opening up the lesion and regularly cleaning it (nonrestorative cavity control, currently not supported by sufficient evidence). Growing evidence indicates that 1-step incomplete excavation seems suitable to treat deep caries lesions and might have

advantages compared with 2-step incomplete or complete caries removal. However, it is too early to recommend certain clinical strategies, and clinicians should adopt their carious tissue removal strategy according to tooth type and, more importantly, the depth of the lesion.[397]

Silver diamine fluoride

Fluoride has demonstrated anticaries effects in primary dentition in many in vivo and in vitro studies, and its cariostatic potential carried in various media such as fluoride varnishes,[296,398,399] tap water,[400,401] gels, dentifrices,[402-404] and mouthrinses[405] has been proven for decades. However, fluoride has a dose-response relationship, and improper delivery of fluoride agents may lead to adverse effects such as fluorosis, which may adversely affect quality of life, even when delivered through fluoridated water.[406,407] A relatively new way of using fluoride is in SDF compounds, an effective treatment strategy for primary teeth and also permanent teeth in very specific situations.

Several studies related to SDF have been discussed in the Dental Materials Section of this review, and interested readers should refer to that section to have a complete understanding of new studies on this topic published on 2017. To avoid unnecessary duplication, only additional studies not covered in the Dental Materials section are covered here.

A systematic review analyzing 7 clinical studies concluded that SDF is an alternative treatment for controlling dental caries when other approaches are not available.[408] It is a minimally invasive, inexpensive, and easy-to-use method that can decrease anxiety in young children. The studies reviewed in this article used a wide diversity of SDF concentrations, application frequencies, follow-up intervals, and outcomes. Concentrations of 30% and 38% of SDF resulted more effective for arresting caries than all the other lower concentrations. The main adverse events related with the application of SDF are irritation of the dental pulp, staining, and oral soft tissue irritation. From this SR, pulpal irritation did not seem to be a clinically relevant issue similar to documented soft tissue irritation. All the articles analyzed reported staining as a side effect, although an in vitro study demonstrated that tooth discoloration could be reduced, but not eliminated, by the incorporation of potassium iodide (KI) to SDF during application. Appropriate timing between applications could not be determined with the available data, and application every 6 months remains a reasonable clinical guideline although not based on solid scientific evidence.

From the previous data, we can conclude that sodium diamine fluoride can be considered an effective treatment against caries particularly for younger population and therefore an important alternative to most common treatments available such as fluoride varnishes and sealants. This is particularly relevant if we consider that fluoride varnishes, although found to be as effective as sealants in 1 study[296] and reported to be able to reduce *Streptococcus mutans* count in another study,[409] were found to not be effective in Germany[410] and in Chile, a low socio-economical rural environment, where caries rate is high.[411] In the latter study, a triple blind randomized control trial, 131 participants were included in the intervention group and 144 were included in the placebo group. Of these children, 89 (67.9%) in the intervention group and 100 (69.4%) in the control group completed the protocol. The participants were randomly assigned to receive varnish or placebo every 6 months, and the comparative analysis of caries incidence after 24 months of follow-up showed that the caries incidence was 45.0% for the experimental group and 55.6% for the control group (P=.081). From a statistical point of view, it could be concluded that biannual fluoride varnish application is not effective in preschool children from rural nonfluoridated communities who are at a high risk of caries.

Xylitol and other preventive agents

Xylitol has been used as an alternative sugar to sucrose, glucose, fructose, or maltose in the food industry because of its unique property of being preferred by bacteria, such as *S mutans*. Although chosen by *S mutans* as a primary source of energy, even if in the presence of other sugars, xylitol cannot be fermented completely. It is initially phosphorylated to xylitol-5-phosphate (X5P) via phosphoenolpyruvate-dependent phosphotransferase system, but X5P cannot be further metabolized. As X5P accumulates in the cells of *S mutans*, it acts as an inhibitor of glycolytic enzymes of *S mutans*, such as glucose-6-phosphate isomerase and phosphofructokinase. X5P is then excreted out of the cells in the form of xylitol by dephosphorylation. Three interesting studies were published on xylitol.

A randomized placebo-controlled clinical trial, in a high-risk caries population, was performed in Italy, following up the participants for up to 24 months. Adults (N=179) were divided into 2 groups: the experimental group used xylitol containing chewing-gum on a regular basis, and the control group used a sugar-free chewing gum (polyol).[412] Both the groups used the assigned chewing-gum for 12 months then stopped using them for the following 12 months. Therefore, data comparison between the study groups was performed both after a year of chewing-gum consumption and after 12 months, without any special community-based caries-prevention strategy, except for personal oral hygiene habits.

Analysis of caries status, *S mutans* count and pH were compared at baseline and at 12 and 24 months. The 1-year use of chewing gums provides an effective means for

the prevention of caries disease. Although xylitol was found to be effective in preventive caries in this Italian study, a systematic review performed at the University of Maryland examining the effectiveness of xylitol on caries incidence in children showed a small effect size in RCTs and a very low quality of evidence that makes preventive action of xylitol uncertain.[413] Similarly, a second systematic review by Wang et al,[414] with a rigorous scientific approach, looking at several nonfluoride-containing products and their effect on teeth for caries prevention, reported both low doses of xylitol-containing (0.5 to 1.0 g) tablets and xylitol gummy bears (7.8 g/day) to be not effective in increasing the preventive effect of regular oral hygiene. However, the authors did find that "daily use of xylitol wipes is a useful adjunct for caries control in young children." This assumption should be read with caution though because the study had a very small sample size (20/17).

RCTs are the most powerful type of clinical studies and are, unquestionably, the most needed type of study in medicine to draw definitive conclusions. However, there are, unfortunately, multiple ways to perform even rigorous studies such as RCTs. Systematic reviews are a great tool if performed correctly, such as in this case, to help understand this problem. If the articles included in this review were read, readers could be misled by the fact that they are looking at RTCs and take for granted the conclusion of the authors. When an unbiased external eye looks at the same data with a standardized approach, the real scientific weight of the research will be balanced against the risk of bias and the true value of the research will be determined. Wang et al, in their final discussion, remarked that a limitation of their review is, first, that the general quality of the currently available RCTs was not high and second, of the 14 studies included for final analysis, only 1 had a low risk of bias. Therefore, future trials should adopt a more rigorous approach in the study design, and strict universal guidelines should be followed.

Although xylitol can reduce cell growth and lactic acid production of *S mutans*, its inhibitory effect is definitely inferior to fluoride. In addition, *S mutans* can become resistant to xylitol if often exposed to it. Therefore, the development of alternative anticariogenic substances is highly desirable. Yun et al[415] evaluated the anticariogenic effect of 3,6-anhydro-L-galactose (AHG), a rare sugar from red macroalgae, on *S mutans*, in comparison with xylitol. They found that in the presence of 5 g/of AHG, the growth of *S mutans* was retarded, whereas at the concentration of 10 g/L, the growth and acid production by *S mutans* were completely inhibited. These outcomes imply that AHG can be used as a novel anticariogenic sugar substitute for preventing dental caries.

New treatment approaches that destroy virulent species within a pathogenic biofilm could be successful alternatives to conventional antimicrobials that indiscriminately kill commensal bacteria. Promoting the formation of a biofilm with substrates that encourage alkali production may prevent tooth demineralization and positively regulate the microbial metabolism and composition within dental plaque, in accordance with the modern ecological theory on dental caries. For this reason, ingestion of probiotics that strengthen the immune system to combat allergies, stress, exposure to toxic substances, and other diseases,[416] may be a promising method for preventing caries without destroying indiscriminately all the microbiota of the biofilm. In a high caries risk population, 4 types of *Lactobacilli* were tested for their efficacy against *S mutans* and were found to be efficacious while maintaining the integrity of the good microbiota.[417] Metabolism of urea and arginine offer 2 important sources of alkali in a biofilm. Arginine in the mouth is catabolized mainly by the microbial arginine deiminase system, which can be found in some streptococcal species, particularly *Streptococcus sanguinis* and *Streptococcus gordonii*. A correlation between elevated salivary arginine concentration and caries resistance has been established. Furthermore, several articles found that caries-active individuals or participants who were affected by caries in the past exhibited significantly lower arginine deiminase system activity than caries-free individuals, thus supporting the theory that alkali-generation by oral bacteria may stop the growth of dental caries.[418] For these reasons, arginine has been incorporated into oral hygiene products for years, mainly in toothpastes. Zheng et al,[419] in a cohort of 21 caries-free patients and 21 patients with active caries, reported that the use of arginine-containing toothpaste changed the oral microbiota of caries-active individuals in terms of microbial structure, abundance of typical species, enzymatic activities of glycolysis and alkali-generation related enzymes, and their corresponding transcripts, similarly to that of caries-free individuals. Furthermore, arginine associated with fluoride could better enrich alkali-generating *Streptococcus sanguinis* and suppress acidogenic/aciduric *Streptococcus mutans* and thus significantly delay the demineralization induced by oral biofilm.

In another Chinese study, 12 volunteers who wore a "self-developed in situ dental plaque acquisition device" were divided into 2 groups: the first one with patients with NC, and the second one with patients with a very high caries risk (HC).[420] Within the 2 groups, participants were randomly assigned to use either arginine-free toothpaste or arginine-containing toothpaste. After the usage of arginine-containing toothpaste, biofilms in both the groups considerably reduced lactic acid production compared with the use of arginine-free toothpaste. Biofilms in the HC group produced more lactic acid than the biofilms in the NC group, and there were significant differences in lactic acid production between the NC and

HC groups using the 2 treatment methods. Furthermore, the decrease in lactic acid production in the HC group was more noticeable (about 50%) than that in the NC group (about 30%). No significant changes in the metabolic activity within the biofilms were observed, and the use of arginine-containing toothpaste did not significantly decrease the total biofilm biomass or the live/dead bacteria ratio in any groups.

Similar conclusions were reported in another study by Ledder et al[421] assessing the effects of the long-term dosing of laboratory dental plaques with arginine toothpaste. Data indicate that the addition of arginine dentifrice during sucrose challenge significantly increased plaque pH, thus theoretically moderating caries risk. Counts of some functional groups of bacteria related to dental caries were drastically reduced in the laboratory plaques during exposure to the arginine dentifrice. Although often these types of studies are sponsored by dental companies producing the products to be tested and therefore the power of the research may not be considered as strong as that of totally independent studies, the efficacy of arginine is well established today as anticariogenic agent and it represents a promising research field for future further development.

Mouth rinses are a popular method for prevention and plaque control in the management of both gingivitis and dental caries. An RCT was conducted in India among a 12- to 15-year-old population of students divided into 3 groups.[422] Group 1 received a fluoride mouth rinse, group 2 received an herbal based mouth rinse, and group 3 received a placebo. The participants used the mouth rinse for 1 minute/day for 1 year, and they were randomly assigned to each group. Saliva samples were collected and compared for *S mutans* count and glucan concentration, to assess the level of sugar transformation made by *S mutans*. Caries assessment of study participants was performed using the International Caries Detection and Assessment System (ICDAS) criteria for detection of caries on coronal tooth surfaces. Follow-ups were performed at 6 months and 1 year, when the final analysis was performed. A post hoc analysis revealed that the difference among the group receiving herbal mouth rinse and the one assigned to placebo mouth rinse was statistically significant. However, there was no statistical difference between groups using fluoride and herbal mouth rinses. The results indicated that herbal mouth rinse was effective in reducing the *Streptococcus mutans* count and glucan synthesis by *Streptococcus mutans*. Therefore, herbal mouth rinses can be considered an efficient alternative to fluoride-based mouth rinses in controlling plaque formation for caries prevention. However, herbal mouth rinses are so different from each other and in their efficacy against pathogens that no general conclusion can be drawn for all mouth rinses but only for the specific product used in this study.

One of the abovementioned systematic reviews,[414] beside xylitol, looked at other nonfluoride agents in the prevention of dental caries and more specifically at chlorhexidine and casein phosphopeptide–amorphous calcium phosphate and 0.3% triclosan varnish and arginine. Readers were encouraged to read the full article and particularly the final discussion. The conclusion of the systematic review is that chlorhexidine and casein phosphopeptide–amorphous calcium phosphate may be more effective than a placebo in managing caries in the primary dentition, but their efficacy relative to fluoride is still unclear. Arginine-containing mint confection and 0.3% triclosan varnish were found to reduce caries development in primary teeth, but the evidence was at high risk of bias. High-quality RCTs are needed to make definitive recommendations.

A study from Turkey looked at the efficacy of a tooth-friendly candy in a new sugar-free, orange-flavored lollipop containing an extract of licorice root that has shown promise in targeting and killing *S mutans*.[423] The main purpose of introducing herbal lollipops was to provide a straightforward and successful way of fighting caries for young children who are at high caries risk. The study was a randomized, double-blind, controlled study with parallel groups, and the study population was divided into 3 groups: high caries risk population, low caries risk, and caries free. Each of the 3 groups was subdivided into 2 parts according to the use of the test lollipop or a placebo. Saliva samples were collected for analysis and *S mutans* counts. The authors used *S mutans* counts as a measure of the anticaries potential of the lollipop but did not find any difference before and after its consumption. However, after 3 months in the high-caries group, there was a statistically significant difference in *S mutans* counts between the placebo and herbal lollipop group. Although the authors did not comment on this finding in their final discussion, the delayed effect of the herbal lollipop may suggest, in accordance with the ecological theory of dental caries, a slow effect of the herbs toward a healthier biofilm. It could be interesting to repeat the same study looking not only at the *S mutans* counts but also at the other pathogens such as lactobacilli that tend to influence the dental biofilm toward its more aggressive status.

Finally, a study from India looked at the potential of ozonated water as a mouth rinse and reported a considerable decrease of MS counts. Owing to the easy availability of economical table-top ozone generators, ozonated water, which has shown to also have remineralizing potential in the past,[424] can be recommended as an alternative daily mouth rinse.[425]

Genetic/biomolecular studies

A goal of modern restorative dentistry is to be as minimally invasive as possible, and having both dental enamel and dentin remineralizing capabilities, in the proper conditions, it is crucial to preserve sound dental structure and to diagnose dental caries at the earliest stage possible. Therefore, diagnostic aids have been proposed as an alternative to tactile detection that, by applying the pressure on the explorer tip, may result in cavitation. One of the most recent methods, which is very promising but not yet ready for commercial use, is based on fluorescent nanoparticles functionalized so as to specifically target the inside of dental caries lesions.[426] The nanoparticles are made from food-grade corn starch, and they are tagged with a safe fluorescent dye so that the caries will illuminate and be easily seen using a standard dental polymerization light. This would allow dentists first to detect early lesions, second to differentiate whether a carious lesion is active or inactive, and therefore it could be used both to decide appropriate treatment strategies and to monitor treatment results.

The oral microbiota plays a crucial role in health by counteracting colonization of the oral cavity by pathogens. Metagenomic studies have identified a high degree of bacterial diversity with more than 700 taxa in the human oral cavity. Bacteria mature in complex multispecies biofilms on the hard and soft oral tissue surfaces with saliva or gingival exudate as the major nutrient sources. Dental biofilms are dominated by sacharolytic bacteria, which produce energy by breakdown of carbohydrates from salivary glycoproteins as well as ingested food through the glycolytic pathway. The conversion of sugars then results in acidic end products, which can rapidly lower the pH. If the pH remains lower than 5.5 for a prolonged period, demineralization of the enamel will occur. In a study by Sennerby et al,[427] the acid challenge method was used to investigate biofilm acid tolerance at different tooth sites in the same individual, as well as the variation between individuals. Furthermore, short- and long-term changes in acid tolerance were studied. This research, according to the authors, represents the first step in the evaluation process of biofilm acid tolerance in vivo as a possible biomarker in caries prediction.

Forty adolescents aged 12 or 13 years in Sweden were enrolled in the study. Plaque biofilm samples were collected by a dental hygienist, who was trained in the procedure. For half of the adolescents, biofilms were sampled from all supragingival approximal surfaces between second premolars and first molars (four sites) at baseline and after 6 and 12 months. In the second group, biofilms were collected in the same manner from all proximal surfaces between second premolars and first molars (four sites), between canines and first premolars (four sites), and between the central incisors in both the jaws (2 sites). This sampling took place at baseline, after 3 days, and after 1 month. Samples were transferred to sterile microfuge tubes and sent to the laboratory for analysis. In this research, the percentage of acid-tolerant bacteria in biofilms collected ranged from low to high, confirming that the method can discriminate between individuals with different levels of biofilm acid-tolerance. The majority (92%) of the participants presented low levels of acid tolerance, suggesting that they do not have the prerequisite conditions essential for development of caries and would be expected to have a low risk for disease development. On the contrary, 8% had a high level of acid-tolerant bacteria, suggesting that these individuals may have an increased risk of developing caries. Biofilm acid tolerance presented short-term stability and minimal variation between different sites in the same participants. The acid tolerance test is an indicator of the acid-producing potential of a biofilm and is therefore closely related to the demineralization process. For this reason, it can be considered a promising biological biomarker candidate for caries prediction, although its diagnostic accuracy has not been totally proven.

In the same research field, Valdez et al,[428] while looking at genotypic diversity and phenotypic traits of *S mutans* isolates and their relation to severity of early childhood caries, concluded that "although genotypic diversity was similar in children, regardless of caries status, *S mutans* genotypes from caries-active children were more acid-tolerant and presented higher ability to form biofilm than those isolated from caries-free children. Acid tolerance seems to be the most important *S mutans* trait related to the pathogenesis of severe early childhood caries."

Conventional approaches for controlling or reducing plaque biofilm result in the total eradication of the microbiome. Unluckily, this tends to favor the imbalance by removing the beneficial colonizers and allowing for pathogenic micro-organisms to recolonize. Therefore, clinical treatment should aim to reestablish the equilibrium by targeting key pathogens. Various selective targeted antimicrobial peptides (STAMPs) have been developed and tested and proven to be successful, at least at the in vitro stage and initial clinical trial evaluation against *S mutans*, with the aim of selectively eradicating the initiator of the carious lesion. STAMPs are short peptides with a target portion that selectively binds to a specific portion of a specific microorganism and a killing portion that is able to destroy the cell after binding to it. A new STAMP (GH12) was developed in China by Wang et al,[429] and its ability against 8 types of cariogenic bacteria was tested. *Streptococcus mutans, gordonii, and*

sanguinis; *Lactobacillus acidophilus, casei, and fermentium*; and *Actinomices viscosus* and *naeslundii* were the tested pathogens. Three different types of STAMPs with slight differences among them were compared and tested against chlorhexidine. GH12 was the more efficacious among the available STAMPs and therefore was selected for comparison with chlorhexidine. It showed proper hydrophobic-cationic balance and amphipathicity, strong capacity to form an alpha-helix, meaning high antibacterial potential, low cytotoxicity, excellent bactericidal efficiency, and good antibiofilm activity in vitro. Now the clinical study can be initiated to evaluate its efficacy in real clinical condition and demonstrate its true potential.

An excellent review article was written by Stone and Xu[430] on the topic of selective antimicrobial therapy, and readers who want to deepen their knowledge on this subject are encouraged to fully review this article to truly appreciate the state of the art in research and what the possible future developments are. Similarly the review by Wong et al[431] is a must read for interested clinicians and a very comprehensive summary on dental caries.

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Corresponding author:
Dr Terence E. Donovan
Department of Operative Dentistry
School of Dentistry
University of North Carolina
437 Brauer Hall
Chapel Hill, NC 27599
Email: terry_donovan@dentistry.unc.edu

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