OPERATIVE DENTISTRY

AMERICAN ACADEMY OF GOLD FOIL OPERATORS

ACADEMY OF OPERATIVE DENTISTRY

Management Alternatives for the Carious Lesion

SUPPLEMENT NO. 6

OPERATIVE DENTISTRY

Supplement 6

August 2001

Aim and Scope

Operative Dentistry publishes articles that advance the practice of operative dentistry. The scope of the journal includes conservation and restoration of teeth; the scientific foundation of operative dental therapy; dental materials; dental education; and the social, political, and economic aspects of dental practice. Review papers, book reviews, letters, and classified ads for faculty positions are also published.

Operative Dentistry (ISSN 0361-7734) is published bimonthly for $60.00 per year in the USA (all other countries $70.00 per year) by *Operative Dentistry*, Indiana University School of Dentistry, Room S411, 1121 West Michigan Street, Indianapolis, IN 46202-5186. Periodicals postage paid at Indianapolis, IN, and additional mailing offices. **Postmaster:** Send address changes to: *Operative Dentistry*, Indiana University School of Dentistry, Room S411, 1121 West Michigan Street, Indianapolis, IN 46202-5186.

Subscriptions: Fax (317) 852-3162

Yearly subscription in USA is $60.00; all other countries, $70.00 (sent by air where appropriate); dental students (send verification of student status), $25.00 in USA; other countries, $34.00; single copy in USA, $14.00; other countries, $17.00. For back issue prices, write the journal office for quotations. Make remittances payable (in US dollars only) to *Operative Dentistry* and send to the above address. Credit card payment (Visa, MasterCard, or JCB—Japanese equivalent) is also accepted by providing card type, card number, expiration date, and name as it appears on the card.

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Charleston, South Carolina
September 15-17, 2000

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Management Alternatives for the Carious Lesion

Supplement No. 6

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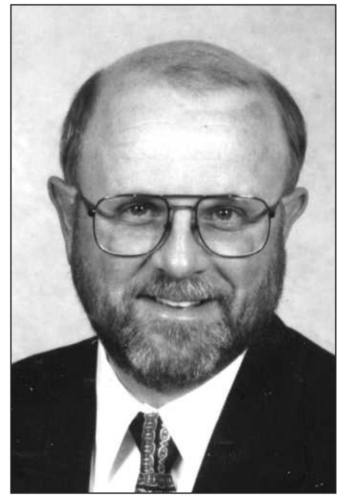
Carious Lesions: Management Alternatives

W Dan Sneed



W Dan Sneed

During an editorial board meeting of the Journal of Operative Dentistry *in 1997, Dr Richard McCoy, then editor, mentioned that there was some interest in an international symposium on alternatives to dental amalgam. No one at the meeting volunteered for the job. Upon returning home from Chicago, I called Richard and said that the Medical University of South Carolina would be interested in organizing and hosting such a symposium. From that phone call, an executive organizing committee was formed. It consisted of Dr Fred Eichmiller, Dr Ivan Stangel, Dr Richard McCoy and myself. We decided to ask some of the most influential and respected people to serve on a larger planning committee.*

From that discussion, the following individuals agreed to serve: Dr Erik Asmussen, University of Copenhagen, Department of Dental Materials, School of Dentistry, Copenhagen, Denmark; Dr Tom Berry, University of Texas HSC, School of Dentistry, Department of Restorative Dentistry, San Antonio, TX; Dr Frank Caughman, Department of Oral Rehabilitation, Medical College of Georgia, School of Dentistry, Augusta, GA; Dr Michael Cochran, Indiana University, School of Dentistry Indianapolis, IN; Dr Frederick Eichmiller, ADAHF-Paffenbarger Research Center, National Institute of Standards & Technology, Gaithersburg, MD; Dr Paul Lambrechts, Dental Materials, Department of Operative Dentistry, Leuven, Belgium; Dr Mark A Latta, Assistant Dean for Research and Continuing Education, School of Dentistry, Omaha, NE; Dr Dorothy McComb, University of Toronto, Toronto, ON, Canada; Dr Richard McCoy, University of Washington Dental School, Department of Restorative Dentistry, Seattle, WA; Dr Ivar Mjör, University of Florida, College of Dentistry, Department of Operative Dentistry, Gainesville, FL; Dr Toru Nikaido, Department of Operative Dentistry, Tokyo, Japan; Dr Dan Sneed, Medical University of South Carolina, College of Dental Medicine, Department of General Dentistry; Dr Ivan Stangel, Bethesda, MD; Dr Henry St Germain, Adult Restorative Dentistry, University of Nebraska Medical Ctr, College of Dentistry, Lincoln, NE; Dr Ed Swift, University of North Carolina, School of Dentistry, Department of Operative Dentistry, Chapel Hill, NC; Dr Van Thompson, Department of Prosthodontics and Biomaterials, UMDNJ, Newark, NJ; Dr Nairn Wilson, University Dental Hospital, Restorative Dentistry, Manchester, England; and Dr Henry Young, Meharry Medical College, School of Dentistry.

"It is my sincere hope that the recommendations contained in these pages will be implemented so that our patients may benefit from the tireless work of these consummate professionals."

I want to express my sincere appreciation to each member of this committee for the time and effort expended to make this conference a reality.

Through the use of e-mail, the committee began suggesting topics that should be included in an agenda. It quickly became apparent that there was much more to this subject than just materials to replace dental amalgam. The broader concept of managing decay emerged, and the Committee slowly realized that a unique opportunity might be at hand to literally change the direction of dentistry.

A number of respected dental manufacturing companies were contacted for financial support. Four companies agreed to become co-sponsors (ESPE, Procter & Gamble, Heraeus Kulzer and Dentsply International, Inc) and seven became corporate patrons (3M, GC, Ivoclar, Kerr, Shofu, Ultradent and BISCO). Without their help, the conference would not have been possible. In addition, grants were received from the National Institute of Dental and Craniofacial Research and the Centers for Disease Control. Also, this publication was partially underwritten by the Founder's Fund of the Academy of Operative Dentistry. The Committee thanks these agencies and corporations for their crucial financial support.

For thousands of years dental decay has plagued the human race causing immeasurable pain and suffering. Our profession has understood for at least 70 years that dental decay is caused by a bacterial infection. Yet, we have continued to treat this disease primarily with a surgical model. We excise the diseased hard tissue and place a prosthesis. When the disease returns, we excise the lesion, along with the restoration, and place a new one. This cycle continues uninterrupted in many cases until the tooth is ultimately lost. Most of us would agree that this model has failed. However, thankfully, the use of fluoride and oral hygiene measures have attenuated our failure and dental decay worldwide is less today than at any time in modern history. Still, our approach to the prevention of dental decay and the treatment of its effects have not progressed to a satisfactory end point.

Recently, alternative models have been proposed. Caries is now more clearly than ever viewed as an infectious disease process; a medical model of treatment has been advocated and non-restorative approaches such as remineralization, prevention, gene replacement therapy and tissue engineering are being explored. However, these are poorly understood by many in the dental profession. This conference was conducted to convene leading authorities on restorative as well as non-restorative alternatives for the management of carious lesions. These authorities were to consider our current knowledge of dental caries, the alternatives to amalgam presently available and research into new ways of viewing the carious process, its prevention and control and the restoration of its effects.

I believe that after reading this publication you will agree—the group of scientists, clinicians and educators assembled at this conference achieved that purpose. It is my sincere hope that the recommendations contained in these pages will be implemented so that our patients may benefit from the tireless work of these consummate professionals.

Finally, I want to thank all members of the faculty and staff at the Medical University of South Carolina who worked so hard to make this program possible. Ms Donna Platt, departmental administrative assistant, deserves special thanks for her careful attention to this project. I greatly appreciate her skill and dedication.

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Non-Restorative
Approaches

Non-Restorative Approaches

THEME 1

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Current Concepts of Dental Caries and Its Prevention

MH Anderson

Maxwell H Anderson

Diseases in general can be modeled using a non-exclusive contributory model (Figure 1). This model suggests that all diseases may be viewed within its context and that one or a combination of two or three of the elements may interact in any specific disease. For instance, autoimmune diseases such as juvenile onset diabetes require the single constituent known as "genetic." A disease such as West Nile fever has all three of the component parts required to become active. It takes a susceptible person (genetic), an infectious agent (the virus) and environmental factors to breed the *Culex pipiens* mosquitoes that acquire and transmit the infectious agent.

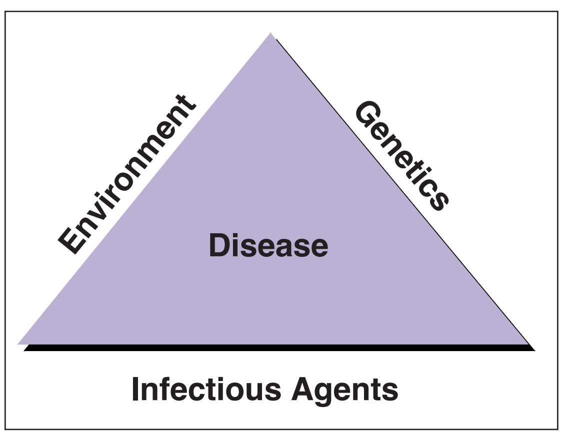

Figure 1. The contributory mode of disease. One or more of these elements cause virtually all disease, either alone or in combination.

The two primary diseases of dentistry, caries and periodontal diseases, seemingly require all three elements of the model to be in play. The classic Keyes diagram for dental caries (Figure 2) is an adaptation of the non-exclusive contributory model. Each element must be present for the diseasse to manifest itself. Each element featured in Figure 2 provides strategies for preventing or intercepting the disease process.

The infectious agent(s) associated with dental caries are generally classified into three bacterial groups: the *mutans streptococci, lactobacilli* and the *actinomyces* species. Table 1 lists the suspect organisms in each of these species.

The organisms most often associated with dental caries are *mutans streptococci*. They have long been the focus of studies related to dental caries (Clarke, 1924). This group of organisms has consistently grown in greater proportions in the bacterial flora of saliva from caries-active people (Splieth & Bernhardt, 1999). However, there has been a problem with the application of this information to assessing risk in individual patients. While predictive of *population* disease patterns, predicting the risk for *individual* patients has been too low to be clinically useful (Alaluusua, Kleemola-Kujala & others, 1990; Vehkalahti, Nikula-Sarakorpi & Paunio, 1996; Tanzer, 1997). The tests traditionally used in these clinical studies are selective media cultures. They use a media designed to grow streptococci, while adding one or more ingredients that select against all streptococci except *S mutans*. The selective ingredient is bacitracin. *S mutans* grow in the presence of specific amounts of bacitracin, while other streptococci find the same amount of bacitracin lethal. In practice, these cultures are not precisely selective. They kill some *S mutans*, but a few non-*S mutans* organisms, including some streptococci, survive. These issues make selective media cultures of limited value in assessing the risk of *individual* patients.

Table 1

Species	Subspecies
Streptococcus	Mutans
	Sobrinus
Lactobacillus	Casei
	Fermentum
	Plantarum
	Oris
Actinomyces	Isralies
	Naslundii

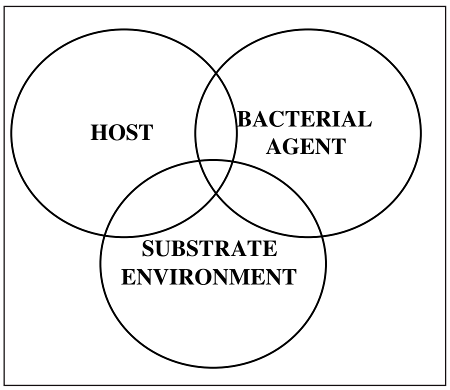

Figure 2. Keyes diagram. A modification of the contributory model where all three elements must be present for pathology to occur.

Recently, new technology has been developed that uses monoclonal antibodies that identify only specific sterotypes of *S mutans* and the other major putative pathogens for dental caries (Shi, Jewett & Hume, 1998). This new kind of highly accurate testing offers hope that salivary testing can predict individual patients' risk for cavities. Figures 3, 4 and 5 identify *S mutans*, *Lactobacillus oris* and *Actinomyces naslundii*, respectively, in human plaque. The monoclonal antibody has had a fluorescent marker attached, and the glowing areas are monoclonal-labeled bacteria. In preliminary studies, a combination of *S mutans* and *L oris* provide a reasonably accurate prediction of caries-active children (Figure 6). If these or other accurate microbial tests can provide reliable risk prediction, our long-held hope of targeting individual patients for added interceptive services that preclude cavitation can be realized.

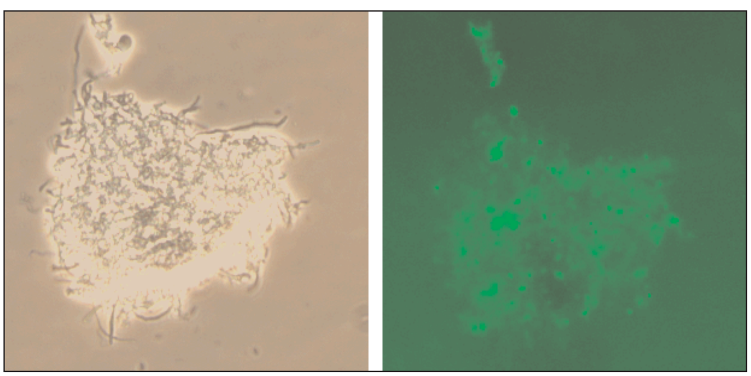

Figure 3. Human plaque as seen with a light microscope on the left and viewed under florescent microscopy on the right (40x).

(Figures 3, 4 and 5 provided by Dr. Wenyuan Shi, UCLA, School of Dentistry.)

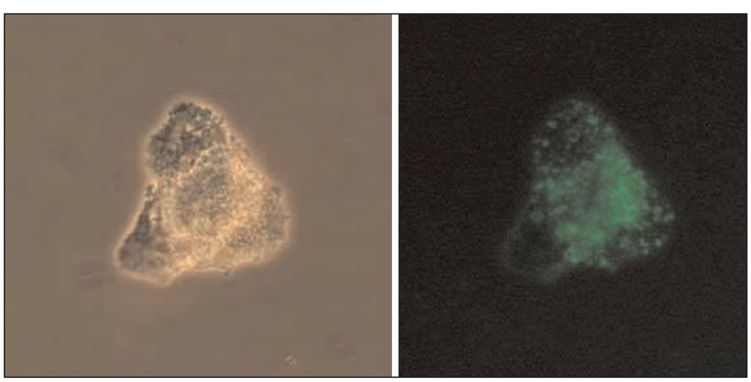

Figure 4. Lactobacillus oris-light microscopy (L) and florescent microscopy (r) (x40).

One of the features of human bacterial plaque that has recently been elucidated is that plaque is a biofilm, not unlike the biofilms that concern us in our waterlines (Marsh & Bradshaw, 1995). Biofilms have some unique properties. Dr Bill Costerton and his colleagues at Montana State University have provided much of our knowledge on bacterial biofilms (Marsh & Bradshaw, 1995). They have demonstrated that biofilms are complex ecological systems with a rudimentary circulatory

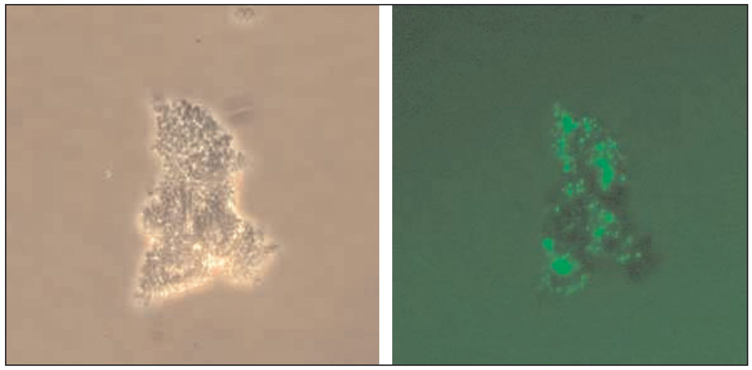

Figure 5. Antinomyces naeslundii light microscopy (L) and florescent microscopy (r) (x40).

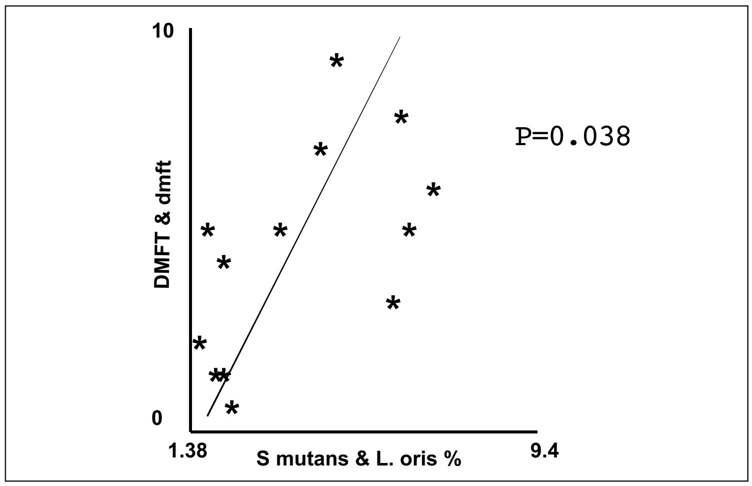

Figure 6. When combined, the salivary bacterial counts of monoclonal labeled S mutans and L oris appear in preliminary studies to give a relatively high predication of dental caries.

(Courtesy of Dr Wenyuan Shi, UCLA, School of Dentistry.)

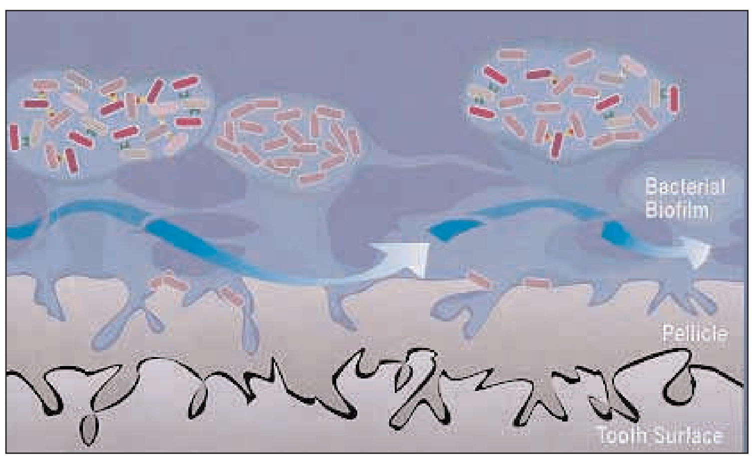

Figure 7. A drawing of bacterial biofilm with its nutrient water channels and specific and sequestered microenviroments.

system that manifests as water channels (Figure 7). Within the biofilm are numerous microenvironments, including strictly anaerobic areas that reside next to areas with high oxygen tensions and support only aerobic organisms. Biofilms are able to achieve metabolic cooperation between different components through the use of the circulating water channels. A colony of organisms upstream of another colony may produce metabolic byproducts that are useful nutrients to downstream colonies. These complex biological systems can be disrupted through chemomechanical interventions. While we often do not think about it in these terms, a toothbrush with a fluoridated dentifrice applied to the teeth is a wonderful chemomechanical delivery device. Other strategies to affect biofilms are being developed. For instance, it is known that low-level electric currents effect biofilm stability (Costerton, Ellis & others, 1994). Perhaps toothbrushes can be adapted to give small electrical signals not dissimilar to the strategies used in pulp testing devices. This would further destabilize the biofilm, making it vulnerable to more therapeutics.

Moving away from the infectious agents, we will look at the patient or, in the Keyes model, the susceptible host containing the *genetic* components. We can further divide the genetic component into two aspects based on their genotype and phenotype. Genotypical expression is realized in the immune system. We appear to inherit our immune system, including the kinds and robustness of immunoglobulins that we produce and the chemotactic aggressiveness of our lymphocytes. For dental caries, the primary immunoglobulin that affects the causative organisms is secretory immunoglobulin A (sIgA). Depending on a patient's expression, sIgA may be eluted in saliva in sufficient levels to impact specific *S mutans* species. The principal effect of sIgA is to tie up specific sites on *S mutans* that allow it to bind to the tooth-pellicle complex. Complexing these sights lowers the opportunity for *S mutans* to establish itself in the plaque ecosystem, thereby reducing its opportunity to produce the acid challenge that demineralizes tooth structure. The other major immunoglobulins, IgM and IgG, are serum antibodies expressed in crevicular fluid but are generally not present in sufficient quantities in the supergingival environment.

The phenotypic expression of the host is also of interest. Two important elements of this subset are tooth morphology (the shape of the pits and fissures) and salivary flow and composition. As with the genotypic expression, today's technology does not allow great opportunities to effect the salivary components. The exception to this is in the area of monitoring the medications our patients receive. By working proactively with physicians, we can help ensure that patients' medications are chosen with concern for optimization of their salivary flow.

Tooth morphology, on the other hand, offers us greater opportunities. Through the judicious use of dental sealants, we can effectively alter the morphology of a tooth and remove one of the favorite ecological niches of *S mutans*. The cost efficacy of this action in specific populations has been recently questioned (Dennison, Straffon & Smith, 2000). Two considerations must be made before deciding whether sealants are cost-effective in specific populations. First, risk assessment is prudent prior to any intervention. Where a child, their parents and siblings have not been caries active, there is questionable value for sealants unless the clinician has other signs or symptoms of pending disease activity. Second, the calculations of cost-efficiency need to disclose the time frames under consideration. If the time frame for the episode of care is considered to be the lifetime of the patient, then cost calculations return far different results than at the five-year mark (Simonsen, 1985). Simonsen calculated the cost of surgical intervention in a molar using the average published values for longevity and cost of specific restoration types. An adaptation of this model is seen in Figure 8. Simonsen noted that once the first surgical intervention has occurred, there is a progression of restoration and re-restoration that may eventually lead to a full-coverage restoration. The lifetime costs are significantly lower if the first cutting of the tooth can be avoided or significantly delayed. Today's adhesive restorative systems may mitigate some of this risk as will tomorrow's new restorative materials, but surgery always contains risks, and if it can be avoided, it is generally a good practice to do so.

Bravo & others showed that sealants protect not only the fissure system but also exert a significant influence on smooth surface caries (Bravo & others, 1997). In analyzing our treatment data for this effect on approximately one million patients in our insured population, we found that children who receive sealants are 72% less likely to experience any restorative services over the next five years compared to those who receive no sealants. Clearly, there is selection bias in selecting an insured population, but the results are impressive even given this bias. After all, both those with and without sealants are part of the insured population. This finding also argues that cost-effectiveness studies of sealants should assess the total caries/restorative experience versus just occlusal surfaces.

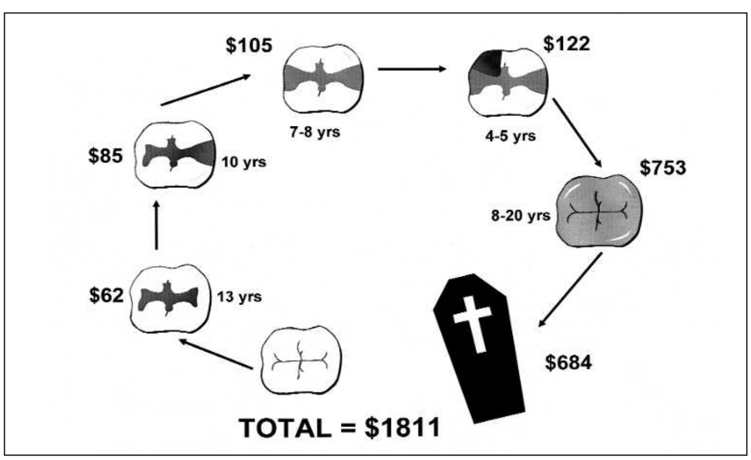

Figure 8. The molar life-cycle after surgical intervention. Avoidance or delay in cutting the tooth's surface minimizes the impact.

(After Simonsen, JADA, 1992).

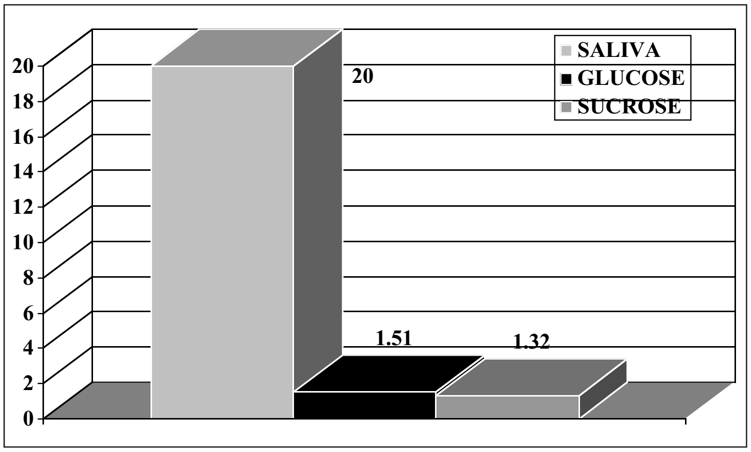

Figure 9. The time for S mutans to double its population when fed by saliva only, glucose or sucrose.

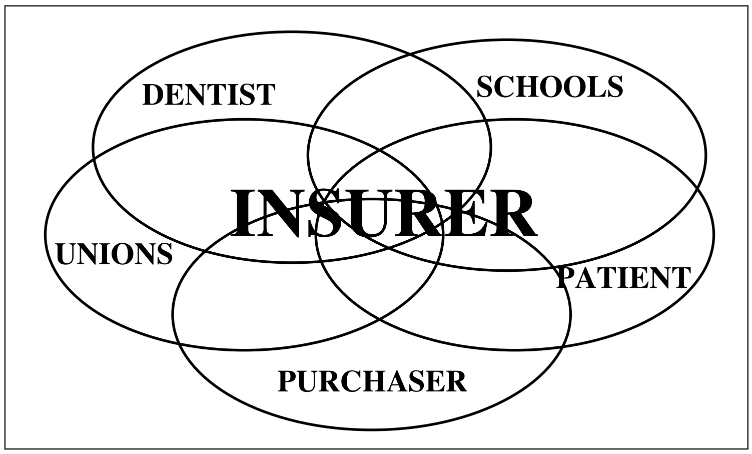

Figure 10. A conceptual diagram representing the "system" of dentistry with an insurance entity acting as a mediator for the competing interests of the system's players.

The third component of the Keyes diagram is the nutrient substrate or environmental component. This is an important component in that unless the bacteria that are able to elute acids are given the appropriate foodstuffs, they do not raise their relative numbers in their ecosystem and concomitantly do not produce significant quantities of acids. As a profession, we have achieved limited success in getting our patients to alter their dietary patterns, so as to achieve reductions in caries incidence (Kay, 1998; Sprod, 1998). The significant issues for the cariogenicity of foods are related to their physical form, chemical composition and the frequency of ingestion. These components primarily effect the bacterial biomass. Figure 9 shows the time it takes for *S mutans* to double its numbers in three different environments. It takes >20 hours for *S mutans* to double its bacterial members in saliva alone. When glucose is added to saliva, the doubling time drops to 1.51 hours. For sucrose addition, the time again drops to 1.32 hours. This ability to reproduce and increase the potential acid production in the plaque biofilm is the primary reason we have attempted to gain compliance from our patients in not eating sticky or retentive foods (physical form), high sugar foods (chemical composition) and limit between meals snacks (frequency of intake).

Preventive strategies can be targeted at intercepting one or more of the necessary disease components of the Keyes diagram. In reality, we have focused most of our strategies on the causative bacteria and the local environment (substrate). Fluorides and chlorhexidine chemotherapeutics are aimed at bacteria. Fluoride, under specific conditions of pH, is highly bactericidal (Loesche, 1982). Fluoride's other roles in remineralization and the formation of fluoridated and acid-resistant carbonated appetites arguably play a significant but smaller role than its antimicrobial activity (Featherstone, 2000). Strategies involving competitive inhibition and passive administration of monoclonal antibodies are not addressed here but covered elsewhere in this publication.

Finally, this paper addresses the role of third-party payment systems in the provision of services related to dental caries and its conservative management. Figure 10 shows a series of interlocking rings that constitute a diagram of the component parts of the delivery "system" in the United States. These parts are separate but interdependent entities within a Coesian economic model. Each component adds value to the delivery "system." In today's economic system, the third-party payer operates as a mediator between the parties in a series of business transactions. Purchasers of dental services

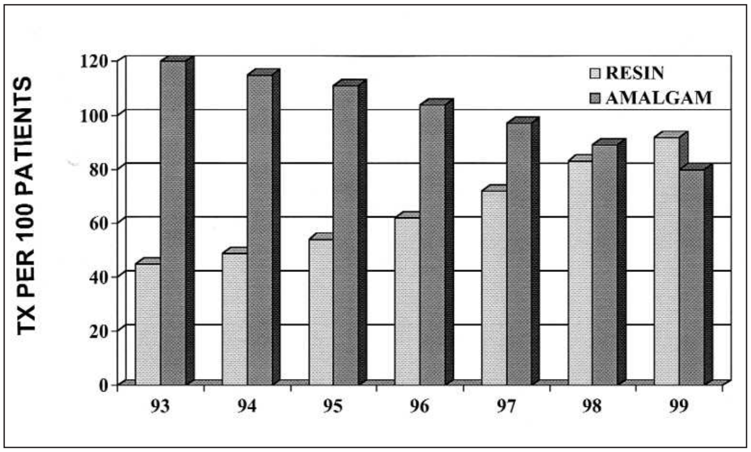

Figure 11. Frequency of placement of resin based restorations and amalgam restorations from 1993 through 1999 in an insured population of approximately one million. (Delta Dental Plan of Washington data).

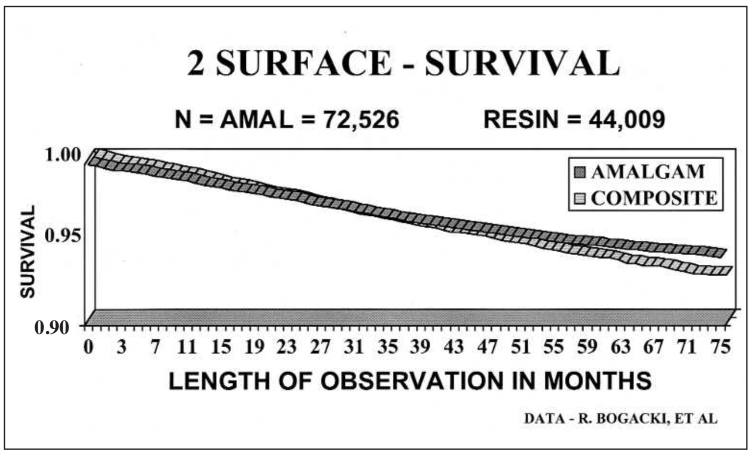

Figure 12. Survival of resin based and amalgam restorations in posterior teeth for 100 months. (Courtesy of R Bogacki & others, Virginia Commonwealth University using Delta Dental Plan Washington data).

want less costly programs to decrease their business overhead, thereby increasing profits for their shareholders. Patients want lower out-of-pocket expenses and access to appropriate and desired services. Unions want the best services for their members. Dentists want fair compensation for the application of their knowledge and skills. Dental schools, in turn, are charged with training the next generation of dentists to work in a world that encompasses rapid changes in science, consumerism and demographics. Third-party payers sit at the crossroads of these interactions and act as mediators in this process. From the financial perspective, they strive for balance between the players' competing goals. There is a natural and appropriate tension between the dentist and the third-party payer. As dentists, we are charged with the health of the individuals we treat. Third-party payers, however, are charged with the public health mission of obtaining the most health-effective and cost-effective treatment coverage for an insured population. These separate goals sometimes conflict, particularly when a patient's needs are outside the "norm" of the population. Plans are designed for average disease and do not contemplate non-standard needs, nor do they contemplate many elective procedures. This tension between the dentist and the insurer is productive in that emerging patterns of care can be identified, evaluated and programmatic designs changed to meet those emerging needs.

Also, third parties have an opportunity to contribute to the knowledge base of dentistry. Treatment data on large numbers of patients show treatment trends and can provide important data to all players in the "system." For instance, Figure 11 shows the comparative use of dental amalgam and composite resins in posterior teeth in approximately one million patients in the state of Washington. These data show that amalgam was supplanted by resin restoratives as the most frequently provided posterior restoration between 1998 and 1999. With further investigation, our preliminary data shows that the longevity of these two types of restorations are essentially equal (Figure 12). That is, the survival of either type of restoration in posterior teeth is clinically equivalent for the time measured. This reflects a change in the published data relative to survival of these materials. Previous studies have concluded that dental amalgam significantly out-performs posterior composites. These data reflect measurement over a period of time that is different from previous studies, and there has been an incremental improvement in resin materials over time. These and other kinds of data can help all the individuals involved in the transaction "system" above. They allow schools to understand the emerging needs and desires of our population. More information is being acquired about the baby-boomers as they move through our society. This group is different from any before it, as will be the subsequent generations born in the 1970s and 1980s. Our training needs must reflect the needs and desires of the populations we service, and to that end, third parties can meaningfully contribute to the "system" by collecting and publishing treatment information and their outcomes through academic centers.

In conclusion, dental caries is a potentially treatable bacterial infection primarily transmitted within family units. The fundamental bacteria involved are *S mutans*, *Lactobacillus species* and perhaps *Actinomyces species*. Both the genotype and phenotype of a person with a cariogenic infection influence disease severity. Foods, their physical form, chemical composition and the frequency of ingestion also bias the infecting organisms' ability to influence the bacterial biofilm in which they reside. Our primary efforts at defeating this disease are focused on the infecting organisms and limiting their reproduction and acid production. New and innovative strategies that leverage one or more of the component elements necessary for this chronic bacterial infection to thrive are emerging. These will surely advantage our patients and our practice of dentistry.

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©Operative Dentistry Supplement 6, 2001, 19-26

Caries Risk Assessment

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Rationale for Risk Assessment

Risk assessment of individual patients is necessary to select optimal therapeutic regimens for the prevention, diagnosis and management of caries as an infectious disease. Because of a marked decline in caries prevalence over the past three decades, the proportion of patients at high risk for caries has declined. We estimate that 25% of adolescents suffer from 75% of the disease consequences. Thus, it is important that this population be targeted with specific therapies to reduce the risk for the disease and to enhance the probability for remineralization of early lesions. Although fluoride is available in many forms, including drinking water, fluoride rinses, gels, varnishes and components of restorative materials, these products are not totally successful in arresting the disease in certain patients. Treatment of extremely high-risk patients may also require an antibacterial agent in combination with fluoride. However, the precise schedule for treatment depends on the initial risk of each patient and his or her compliance with prescribed treatments and home care.

Why should caries risk be assessed? There are two major reasons for assessing caries risk in the current era of reduced caries prevalence: (1) to direct individually-based preventive measures to the highest risk persons who benefit most from prevention and (2) to identify low-risk patients in order to delay restorations and prevent unnecessary surgical intervention. There is a strong likelihood that private practice strategies for caries prevention are based in great measure on concepts learned in dental school during a time of high caries prevalence. Thus, most patients with carious lesions are treated in a similar way, that is, by restoring most teeth with lesions, whether or not the tooth surfaces are cavitated, and recalling all patients at six-month intervals, whether they are at high, moderate or low risk.

By targeting high-risk patients with chemotherapeutic treatment (fluoride and chlorhexidine), plaque control and diet management, several benefits may be realized. This minimally invasive treatment will increase the resistance of teeth to caries attack, delay or prevent surgical intervention, avoid the placement of fillings that will fail by secondary caries, reduce discomfort and trauma and reduce long-term treatment costs.

Disease-Controlling Factors

We know that *S mutans* is the major organism responsible for primary and secondary coronal caries. It is also the main micro-organism associated with root caries. The impact of *S mutans* on caries severity is strongly affected by the frequency and duration of sucrose consumption. Caries is a site-specific disease that occurs on particular areas of teeth. These sites are associated with their potential to harbor cariogenic organisms, including *S mutans* and lactobacilli. Caries develops at sites where *S mutans* is highly localized and initial white spots appear at these sites. Not only are there risk factors for supporting initiation and development of caries, there are also tooth sites that have greater or lesser risk for caries progression. According to the tooth site, the risk for caries progression generally decreases from highest to lowest risk as follows: (1) white spots; (2) pits and fissures; (3) areas below the approximal contact area; (4) sites below buccal and lingual convexities; (5) cusp tips and (6) surfaces above the height of contour.

Because caries is a site-specific disease, whole mouth measurement of *S mutans* levels is not an accurate predictor of future caries activity (caries increment). Thus, oral examination for risk factors must include careful inspection of the most likely sites for bacterial accumulation, and site-specific *S mutans* data should be considered together with other risk factors such as dmfs or DMFS score, intake frequency of fermentable carbohydrates, fluoride availability, plaque removal effectiveness and frequency, fissure morphology and saliva flow characteristics. Obviously, there are numerous other factors, but the simplest risk assessment method is probably the best for private clinical practices until a computer-based decision support system is available. In this regard, the recent history of carious lesions and caries activity most consistently are the best predictors of caries increment. Exceptions to this are cases where conditions that promote or prevent carious lesion initiation or progression have suddenly changed. Examples of these situations include a reduction in saliva flow and a marked shift from high to low risk by increased compliance or through bacterial reduction measures.

Recent Changes in Caries Prevalence

During the past several decades, caries prevalence in industrialized countries has declined by 50% in five-year-olds, 40% in 12-year-olds and 33% in 15-year-olds. A small percentage of the world population suffers the majority of caries. For example, 10% of 14-year-olds have 75% of approximal lesions. Dental caries in the pediatric and adolescent population has continued to decline significantly over the past two decades, with approximately 50% of US school children considered to be caries-free. However, this is an overstatement since disease in primary teeth has been ignored. By age 17, only 15% of young adults have not experienced caries. In spite of the availability of sealants, more than 85% of the lesions in permanent teeth involve pits and fissures. Approximately 17% of children and adolescents account for 67% of disease. This skewed distribution of dental caries experience suggests an urgent need for a reliable risk classification system to determine individuals at high risk for caries initiation and progression. Identification of these caries-susceptible children and adolescents, and the development of matched, caries-preventive protocols are essential to creating a disease-free population.

There has also been an increase in non-cavitated approximal surfaces for D2 lesions, that is, those in the middle-third of dentin. The percent of non-cavitated surfaces when radiolucency is in the outer half of dentin has decreased over time from 13% in 1970 (Marthaler & Germann, 1970) and 48% in 1982 (Bille & Thylstrup, 1982), to 60% in 1986 (Pitts & Rimmer, 1992). Bohannan & others (1985) suggest that caries progression rates are slower when fluoride availability is adequate. As shown in Table 1, the mean

Table 1: Mean Progression Time of Carious Lesions Through Enamel (Schwartz & others, 1984)

	Time (months)		
Population	Outer Half of Enamel	Inner Half of Enamel	Total Enamel Thickness
Swedish Adolescents	38	47	85
US Adolescents	16	27	43

time for approximal radiolucencies in US adolescents to reach the DEJ from the outer enamel surface is 43 months. In contrast, the time for these lesions in Swedish adolescents to reach the DEJ is 85 months. This difference is surprising considering that Sweden does not have fluoridated municipal water systems. One of the explanations is that the Swedish health system provides free dental care and patient/parent education on caries management to all residents through age 18. In addition, there is continuity and consistency of care in the country through county dental clinics, so that even if residents move, there is minimal interruption of dental services.

Classification of Lesion Severity

To classify the caries risk of individual patients, a measure of lesion progression or arrest is needed. It is unlikely that a lesion classification system is used in most practices since these systems have not been used in dental school curricula until recently. These systems permit the monitoring of lesion severity (depth) over time and allow the clinician to determine whether the caries risk is high, moderate or low. One useful classification system is as follows: E0, no lesion; E1, lesion confined to outer half of enamel; E2, lesion that extends into the inner half of enamel; D1, lesion that extends into the outer third of dentin; D2 lesion in the middle third of dentin and D3, lesion in the inner third of dentin. However, the validity of methods used in the majority of scientific studies for the detection of carious lesions has been limited.

Table 2: Sensitivity and Specificity of Caries Detection Methods

Detection Method	Sensitivity	Specificity
Fiberoptic exam (approximal cavitated lesion)+	0.00-0.08	0.99
Visual inspection (approximal cavitated lesion)+	0.12-0.50	>0.90-0.97
Visual inspection (occlusal lesion; 1x magnification)++	0.32	0.97
Visual inspection (occlusal lesion; 3.25x magnification)++	0.42	0.94
Visual inspection (noncavitated occlusal lesion)*	0.12	0.93
Visual inspection (cavitated occlusal lesion)*	0.62	0.93
Visual & explorer probing (noncavitated occlusal lesion in dentin)*	0.14	0.93
Visual & explorer probing (cavitated occlusal lesion in dentin)*	0.82	0.93
Bitewing radiograph (noncavitated occlusal lesion in dentin)*	0.45	0.83
Bitewing radiograph (cavitated occlusal lesion in dentin)*	0.79	0.83
Visual and bitewing radiograph (noncavitated occlusal lesion in D1/D2)*	0.49	0.87
Visual and bitewing radiograph (cavitated occlusal lesion in D1/D2)*	0.90	0.87
Bitewing radiograph (noncavitated occlusal lesion in D1/D2)*	0.45	0.83
Bitewing radiograph (cavitated occlusal lesion in D1/D2)*	0.79	0.83
Stained fissure#	0.74	0.45
Secondary caries (amalgam and composite restorations examined in practices in Brazil, Venzuela, and the US)**	0.68	0.98
Laser fluorescence (Diagnodent) (noncavitated occlusal lesion in E2)*	0.87	0.78
Laser fluorescence (Diagnodent) (noncavitated occlusal lesion in D1/D2)*	0.76	0.87
Electrical conductivity (ECM) (noncavitated occlusal lesion in E2)*	0.87	0.64
Electrical conductivity (ECM) (noncavitated occlusal lesion in D1/D2)*	0.92	0.78

+ Hintze & others(1998)
++ Forgie, Pine and Pitts(2000)
* Lussi & Hibst (2000)
# Verdonschot & others(1992)
** Gonzalez-Cabezas & others (2000)

As shown in Table 2, the sensitivity of the most commonly used methods for detection of non-cavitated lesions range from 0.12 (visual inspection) to 0.74 (stained fissure). However, the recent introduction of electrical conductivity and laser fluorescence methods has increased the sensitivity for occlusal lesions in E2 to 0.87. Thus, the existing literature is flawed by the inability of diagnostic devices and methods to detect the presence of carious lesions when they are indeed present. Because of this deficiency, assessment of true caries risk may be underestimated because of the relatively high fraction of false negative diagnoses. To increase the sensitivity of lesion detection, one should monitor early or suspected lesions until sufficient validation can be ensured. This level of sensitivity can be achieved for occlusal and approximal lesions by delaying surgical intervention until the lesions are clearly visible in the outer third of dentin, that is, the D1 level of severity. Use of laser fluorescence or electrical conductance methods may also improve the sensitivity of detection although the specificity is reduced. If used in combination with radiographs and visual inspection, a reasonably valid caries detection approach is possible. Accurate detection of virtually all carious lesions would then lead to the most reliable assessment of caries risk since the previous caries history (dmfs or DMFS score) is one of the most powerful predictors of future caries events.

Caries Risk Assessment

Caries risk may be defined as the probability that a specific number of new lesions will develop and/or a specific number of existing lesions will progress over a specified period of time. One may classify the origin of caries risk factors as protective or destructive. Protective factors include (1) saliva flow rate and buffering capacity, (2) fluoride exposure and (3) chlorhexidine exposure. Destructive factors include (1) plaque, (2) microorganism types and concentrations, (3) frequency and amount of fermentable carbohydrate consumption and (4) tooth position and anatomy (overlap, fissure morphology) and (5) restoration defects (overhangs, tight or rough appproximal contacts). Since the caries process is multifactorial in nature, weighting factors must be assigned to each protective and destructive factor to assign a risk level to each patient. Such an analysis would be best performed using a computer-based decision support system. However, as demonstrated in the review below, certain risk predictors far outweigh most of the other factors and a simplified risk analysis is possible to differentiate high-risk from low-risk patients.

Twetman & Petersson (1996) found that the overall fluoride exposure of four-and five-year-old children was a significant factor in caries risk assessment. The authors studied 1022 children, dividing them into three groups: (1) a low fluoride group (n=374) with low fluorine levels in tap water and no topical fluoride applications; (2) a low fluoride group (n=442) with low fluorine levels in tap water, who received semi-annual applications of fluoride varnish and (3) an optimal fluoride group (n=206) with exposure to optimally fluoridated tap water, who received semi-annual applications of fluoride varnish. Compared with Group 1, Groups 2 and 3 exhibited lower caries incidence levels of 30% and 60%, respectively. The caries prediction ability decreased with increasing fluoride exposure; for example, sensitivity plus specificity decreased from 151% (65% + 86%) for Group 1 to 131% (40% +91%) for Group 3, and the positive predictive value was greatest (62%) for Group 1.

In a study of first and fifth grade children in two different US cities, Disney & others (1992) developed a caries risk assessment model to predict mean three-year caries increments. The model was based on data from clinical examinations, salivary microbiological tests, sociodemographic and dental behavior. The major contributors to the model were prior DMFS, pit and fissure morphology and clinicians'-predicted caries risk. This model yielded a sensitivity of 0.60 and a specificity of 0.83. The predictive power of these indicators was greater than 90%, indicating a high probability of predicting two or more new carious surfaces within the next three years.

Mattiasson-Robertson & Twetman (1993) reported that fluoride exposure had a limited influence on caries predictive ability for 12-year-old school children. A statistically significant positive relationship was found between caries increment and salivary mutans streptococci level and/or past caries experience score at baseline. The sum of sensitivity and specificity was higher for the low fluoride group (138%) compared with that (123%) for the group living in the high fluoride area.

van Houte (1993) suggested that caries prediction based on caries risk factors is most reliable when based on multivariate analyses rather than through the use of single parameters. Based on an analysis of DMFS, dental fluorosis, plaque, mutans streptococci, lactobacilli, total viable flora, demographic data, prior fluoride exposure, dietary habits, oral hygiene practices and concentrations of fluorine, calcium and phosphate, Leverett & others (1993) predicted which caries-free six-year-olds would develop carious lesions within a period of six to 12 months. Through linear discriminant analysis, they were able to predict which children would develop lesions in 82.8% of the cases (sensitivity) and those who would not develop new lesions in 82.4% of the cases (specificity).

Alaluusua (1993) found that baseline DFS values were a more powerful predictor of caries increment for teenagers rather than salivary test levels of mutans streptococci and lactobacilli. Axelsson & others (1993) reported excellent caries prevention outcomes over a 12-year period for three- to 19-year-olds based on caries risk assessment and monitoring by a computerized epidemiological system. During this period they decreased caries prevalence and caries incidence by a minimum of 75%. The percentage of caries-free three-year-olds increased from 51% to 94%. The mean DFS score (caries prevalence) for 12-year-olds decreased from 6.5 to 1.0 during this period, the lowest in Sweden. In 1990, the mean annual treatment time per child associated with this system was the lowest in Sweden.

Ravald, Birkhed & Hamp (1992) reported that smokers had significantly more root caries over a 12-year period than non-smokers. Based on three fluoride regimens used as an adjunct to professional plaque control in periodontally-treated 33- to 76-year-old patients every three-to-four months during a two-year period, (1) professional application three to four times/year of Duraphat varnish (n=34); or (2) a 0.4% stannous fluoride gel (n=33) or (3) daily mouthrinsing with a 0.05% NaF solution (n=33), Ravald & Birkhed (1992) found no difference among the three treatments relative to caries prevention. However, in spite of the fluoride and plaque control therapy, 246 new decayed or filled surfaces (DFS) were detected, 29.3% of which were diagnosed as active, 50.4% as inactive and 20.3% as filled. Baseline root caries prevalence and root plaque scores showed the highest correlations (r=0.43 and 0.36, respectively) with the DFS root caries scores.

Powell & others (1998) found that the most significant factors associated with a high risk for coronal caries in older adults (age 60+) were high baseline root DMFS (p=0.001), high levels of mutans streptococci and lactobacilli (p=0.036), male gender (p=0.007) and Asian ethnicity (p=0.002). These relative risk ratios for these factors ranged from 1.2 to 2.0 and were considered small to moderate. For predicting the risk for root caries, significant factors included baseline coronal DMFS (p=0.078), high bacterial counts (p=0.002) and Asian ethnicity (p=0.002). The low caries predictive power of these factors for both coronal caries and root caries was attributed to a higher than usual caries incidence, which reduced the ability to discriminate among caries-active individuals. However, this study did confirm the importance of baseline DMFS and bacterial concentrations for caries risk assessment and introduced ethnicity as a useful variable for predicting caries susceptibility in older adults.

Bjarnason & Kohler (1997) studied detailed caries records and salivary microbiological data to predict caries development in a group of 15- to 16-year-old Swedish adolescents. Both caries experience and salivary micro-organisms correlated well with a subsequent three-year increment of DFS. The strongest associations were recorded between the prevalence of baseline incipient lesions and the development of obvious carious lesions (r=0.51). All predictors analyzed individually showed insufficient sensitivity for identifying true caries active individuals. However, the combined sensitivity and specificity for incipient lesions and comprehensive caries record (incipient + obvious lesions) attained values sufficient to predict caries development in the majority of individuals. Using noncavitated (precavity) lesions as a sole predictor, 79-81% of the individuals were correctly classified with regard to their future caries levels. The addition of obvious carious lesions increased the accuracy of classification to 86-89% depending on the stringency of screening and validation criteria.

Hausen (1997) evaluated the scientific literature to determine whether the current caries risk parameters can identify with sufficient accuracy the high-risk individuals who could benefit from individual protection to avoid an unacceptably high percentage of new cavities. Three prerequisites were proposed for successful application of a high-risk treatment plan for controlling dental caries: (1) the occurrence of caries in the treated population must be low enough to justify the effort and expense of identifying patients at risk; (2) accurate, acceptable and feasible measurement methods must be available to identify individuals with an unacceptably high risk and (3) the preventive treatment options to reduce risk are based on measures that are effective and feasible. The accuracy of predicting individuals at risk for developing new carious lesions was compared with the accuracy of predicting the onset of acute myocardial infarction. Six caries risk factors were considered to predict a two-year approximal caries increment for a group of 350 13-year-old children in Finland: (1) baseline DMFS score; (2) stimulated salivary flow rate; (3) mutans streptococci score; (4) sucrose intake frequency; (5) tooth brushing frequency and (6) social group (based on occupational status of the father). A graph of the percentage of subjects vs baseline DMFS scores revealed no natural threshold in the curve that could clearly differentiate individuals at high risk from those at moderate or low risk. Based on a comparative plot of the Receiver Operating Characteristic data (true positive rate at different threshold levels vs a false positive rate at these levels) and a linear logistic model consisting of all six risk variables, the power of the risk function was similar to that for the DMFS score alone. Virtually all the predictive power was derived from the DMFS score. The other five variables did not significantly increase the accuracy of risk prediction.

A concern expressed by Hausen in the above analysis was that even if a threshold DMFS score >13 was selected to separate high risk from lower risk children (DMFS scores from 0 to 13), a small number of individuals with a DMFS score of up to 11 (false negatives) would have initially been considered as low risk and would not have received appropriate therapy. However, one might argue that the vast majority of high-risk children would have been treated appropriately. Furthermore, in developing countries where governmental support for dental treatment is minimal, it may still be beneficial to spend a significant share of the limited resources on high-risk children. As Hausen stated, "A certain proportion of errors must be accepted. However, there are no generally accepted rules as to what the acceptable error rate might be."

Kidd & Beighton (1996) studied the relationship between stained and ditched margins adjacent to tooth-colored restorations and secondary caries and found that there was more bacteria in plaque over frankly carious cavities, and the dentin was soft and heavily infected. Only 22.8% of sites without frankly carious cavities had soft dentin at the EDJ. Both plaque and dentin in these sites harbored more micro-organisms, but none of the clinical criteria chosen would reliably predict the presence of this soft dentin. They concluded that only a frankly carious lesion at the margin of the filling constituted a reliable diagnosis of secondary caries.

Özer (1997) reported that the presence of secondary caries adjacent to amalgam restorations was most often related to the presence of stagnant plaque deposits. Marginal gap width was not related to the risk of secondary caries.

In summary, the multi-factorial nature of caries as an infectious disease process makes it unlikely that a very accurate risk prediction model can be developed. Nevertheless, a focus on treatment of the disease rather than on teeth damaged by the disease should be much more cost effective in the long run.

Dentists exhibit significant variability in diagnosing carious lesions and lesion activity. The principles of modern caries management indicate that lesions in low risk patients should not be restored until the radiolucency extends into the outer third of approximal dentin and that teeth with stained fissures should not be restored in the absence of occlusal dentin radiolucency (D1). Benn & Meltzer (1996) created a model to estimate the reduction in the percentage of restorations placed by adopting modern caries management strategies. In their model, two identical groups of 1,000 adult teeth with a normal distribution of 1,000 radiographic lesions in each group were assumed. For Group I, all teeth with lesions were restored at baseline, but for Group II, only teeth with lesions in dentin were restored. The model forecasted each year for 10 years the number of replacement restorations for both groups, plus initial restorations for Group II. Furthermore, a sensitivity analysis was performed, assuming slow progression rates (Group IIa) and fast progression rates (Group IIb). After 10 years, individual Group IIa patients received 49% fewer restorations and Group IIb patients received 32% fewer restorations than those receiving traditional treatment (Group I). Of equal importance is the finding that those patients in Group IIa would have smaller restorations and approximately 30% of teeth with initial lesions would still be unrestored after 10 years.

It is clear from the above review that the use of DMFS score represents the most powerful predictor of all for caries increment associated with high-risk patients. When used together with bacteria assays, fluoride levels, saliva flow and dietary factors, risk may be assessed at a reasonably high level of confidence.

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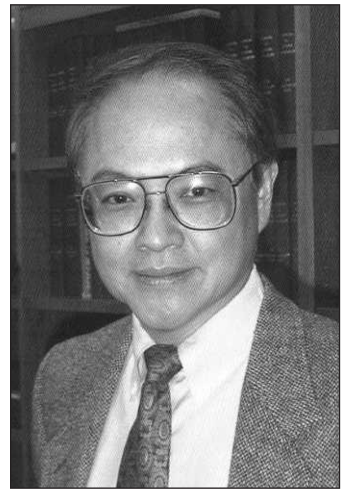
Enhancing Remineralization

LC Chow • GL Vogel



Laurence C Chow

Introduction

Reports of remineralization of enamel and dentin *in vivo* can be found in early literature in the form of clinical observations of naturally occurring arrestment of carious lesions. One of the first systematic clinical studies on caries reversal was reported in 1966 (Backer-Dirks, 1966) in which about half of the 72 white spot lesions observed in the buccal surfaces of first molars in children at age eight were found to have remineralized at age 15. *In vitro* studies on "rehardening" of softened enamel were reported as early as 1912 (Head, 1912) and for dentin in 1944 (Souder & Schoonover, 1944). In the 1960s, *in vitro* studies have shown that artificially formed lesions in enamel can be partially remineralized as evidenced by increasing hardness (Koulourides, Cueto & Pigman, 1961) or mineral content (von der Fehr, 1965). In the last two decades, a number of improved clinical diagnostic tools for detecting enamel and dentin lesions *in vivo* and reliable methods for quantitative measurements of lesion mineral contents *in vitro* were developed. This facilitated studies that have led to a significantly greater understanding of both the demineralization and remineralization processes. There is little doubt that significant remineralization of enamel and dentin lesions can occur under both *in vitro* and *in vivo* conditions, and consequently, remineralization is increasingly accepted as a viable non-invasive approach for restoring carious teeth, at least during the earlier stages of the caries process. Because several recent articles (Kashket, 1999; Zero, 1999; Featherstone, 2000) provided comprehensive reviews of research in remineralization and caries prevention, this paper focuses primarily on thermodynamic and mechanistic analyses of this process. However, because remineralization and demineralization processes are intricately linked, it is important to comprehend the different mechanisms that drive the two processes. For this reason, mechanisms of both demineralization and remineralization are discussed.

Thermodynamic and Mechanistic Analyses of Demineralization

Tooth mineral is an impure hydroxyapatite (OHAp), $Ca_{10}(PO_4)_6(OH)_2$, that also contains significant amounts of carbonate (4%), sodium (0.6%), magnesium (0.2%) and chloride (0.2%) and a very small amount of fluoride (0.01%) (Driessens & Verbeeck, 1981). For the purpose of discussing the chemistry of demineralization and remineralization, OHAp is often used as an approximate formula for the tooth mineral (Patel & Brown, 1975). In terms of mass balance, demineralization can be seen as a reaction of protons, derived from the disassociation of plaque acids (primarily lactic acid) produced by bacterial carbohydrate metabolism, with tooth mineral. The reaction leads to the release of mineral ions into the solution (equation 1)

$$\underset{\text{mineral}}{Ca_{10}(PO_4)_6(OH)_2} + 14\,H^+ \rightarrow \underset{\text{solution}}{10\,Ca^{2+} + 6\,H_2PO_4^- + H_2O} \qquad (1)$$

Phosphate in tooth mineral is in the basic form of PO_4^{3-}, while under mildly acidic conditions (pH of 5-6) where cariogenic attack occurs, dissolved phosphate ions are predominantly in a more acidic form, $H_2PO_4^-$. The extent to which tooth mineral can dissolve in a given solution is governed by the thermodynamic ion activity product or IAp (equation 2)

$$IAP\,(OHAp) = (Ca^{2+})^{10}(PO_4^{3-})^6(OH^-)^2, \qquad (2)$$

where the quantities in parentheses are the activities of dissolved mineral ions in the solution. When the IAP equals a constant called the solubility product constant, or Ksp, the solution is in equilibrium with the solid and is said to be saturated with respect to the solid (equation 3)

$$IAP\,(\text{in saturated solution}) = Ksp \qquad (3)$$

Ksp is approximately 10^{-117} for OHAp (McDowell, Gregory & Brown, 1977) and $10^{-106}$for tooth mineral (Patel & Brown, 1975). When tooth mineral is exposed to an acidic solution, as during a cariogenic attack, dissolution can continue until the condition of equation 3 is reached. Thus, the only requirement for demineralization to occur is that the IAP in the demineralizing solution is less than the Ksp (equation 4).

$$(Ca^{2+})^{10}(PO_4^{3-})^6(OH^-)^2 < Ksp\,(\text{tooth mineral}) \qquad (4)$$

Because both PO_4^{3-} and OH^- are basic ions, their activities decrease rapidly with decreasing pH. For example, for a solution containing a fixed amount of phosphate, the PO_4^{3-} ion activity would decrease nearly 4500-fold when the solution pH is reduced from 7 to 5. The OH^- ion activity would decrease about 100-fold under the same condition. These decreases would lead to 25 orders of magnitude reduction in the IAP of tooth enamel (left hand side of equation 4). Consequently, a significantly greater amount of mineral needs to dissolve in pH 5 solution than in pH 7 solution before equation 3 is satisfied. The extraordinary dependence of OHAp solubility on pH is illustrated in Figure 1. It is important to note that although the source of H^+ ions in cariogenic plaque are organic acids, acid anions are not consumed in the dissolution reaction (equation 1) nor involved in solubility equilibrium (equation 2). H^+ ions are the only solution species consumed in the demineralization reaction.

The mechanistic process of demineralization is schematically depicted in Figure 2 along with the anatomical features of the lesion. During caries progression, active mineral dissolution occurs at the advancing front situated at several hundred microns below the tooth surface. In accordance with equation 1, demineralization reaction can be seen as a process consisting of transport of H^+ ions from plaque to the advancing front and transporting dissolved mineral ions from the advancing front to plaque. Following the above example, an acidic pH of about 5 will be assumed for cariogenic plaque. Since sound enamel just beyond the advancing front is unaffected by the demineralization process, the pH of fluids in the pores of sound enamel must be near the normal physiological pH of about 7. In contrast, fluids in the pores of enamel near tooth surface would have a pH

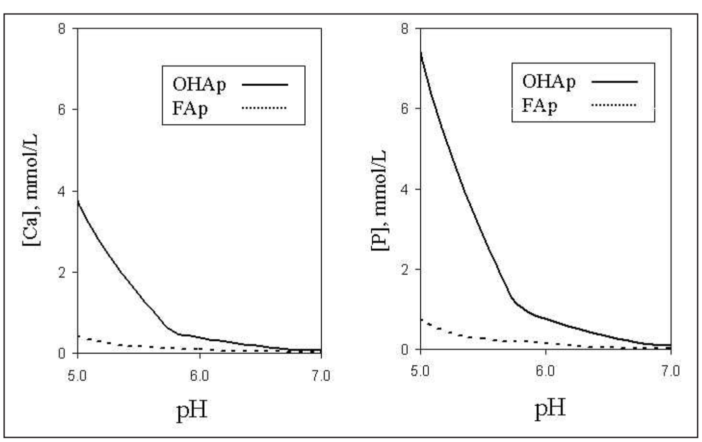


Figure 1. Solubility curves for hydroxyapatite and fluorapatite showing the calcium (A) or phosphate (B) concentrations of saturated solutions as a function of pH from 5 to 7. All solutions also contain 1x10-5 mol/L of fluoride (0.19 ppm F) as sodium fluoride.

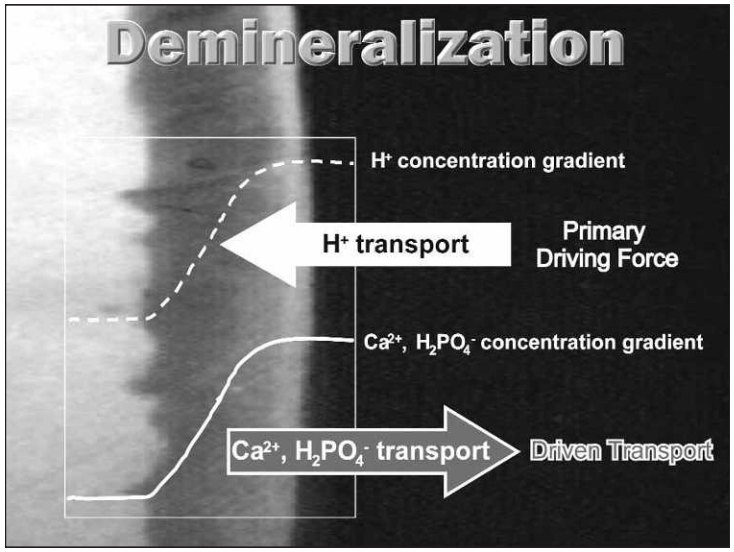


Figure 2. Schematic representation of the mechanistic aspects of the demineralization process showing that the inward diffusion of H+ being the primarily driving force, which drives the outward transport of Ca2+ and H2PO4- ions against their concentration gradients.

similar to that of adjacent plaque, that is, about 5. It has been demonstrated in *in vitro* studies (Brown, 1974, Vogel & others, 1988), and it is logical given the long and constricted diffusion of ions in a lesion, that fluids in the pores of enamel throughout the lesion are approximately saturated with respect to tooth mineral during the demineralization process. This implies (Figure 1) that calcium (or phosphate) concentration in the neutral pH fluids at the advancing front must be much lower (that is, 0.1 mmol/L) than in pH 5 fluids at the surface of enamel (calcium concentration of challenged is 5 to 8 mmol/L (Margolis & Moreno 1992). Thus, as illustrated in Figure 2, both Ca^{+2} and $H_2PO_4^-$ are being transported against their concentration gradients, a process requiring an input of energy. By examining Figure 2, it becomes clear that the energy for this process is hydrogen ion diffusion, which is driven by a 100-fold concentration gradient in this example. Such a phenomenon (one that has not been fully appreciated in caries research), known as active transport, can be found in many *in vitro* and *in vivo* membrane transport processes (Rosen & McClees, 1974). It should be noted that since salivary calcium and phosphate concentrations are lower than corresponding values in cariogenic plaque (Margolis & Moreno, 1994), salivary calcium and phosphate ions do not play a significant role in decreasing the cariogenicity of plaque. On the other hand, saliva can reduce the severity of the challenge by washing away acids and fermentable carbohydrates (Nikiforuk, 1985, Mandel, 1974), or by consuming H^+ ion with salivary buffers (Nikiforuk, 1985).

Effects of Fluoride on Demineralization

The cariostatic effects of F are well known, and F remains the single most effective agent in caries inhibition. The various mechanisms through which F manifests its effects have been extensively reviewed (see for example, *Proceedings of a Joint IADR/ORCA International Symposium of Fluorides*), and the discussion given below will focus on the physicochemical effects of F on demineralization and remineralization.

Tooth-Bound Fluoride Tooth

When F is incorporated into tooth mineral, its replaces the OH^- in the OHAp lattice, resulting in the conversion of OHAp to fluorapatite (FAp) with the formula of $Ca_{10}(PO_4)_6F_2$ and the corresponding solubility expression,

$$IAP\ (FAp) = (Ca^{2+})^{10}(PO_4^{3-})^6(F^-)^2 \qquad (5)$$

Substitution of OH^- by F^- leads to a reduction in solubility because the Ksp for FAp is 10^{-121} (Moreno, Kresak & Zahradnik, 1977), which is about four orders of magnitude lower than the Ksp for OHAp. Even when partially fluoridated, in which only some OH^- ions are replaced by F ions, the mineral appears to also have a lower Ksp than that of OHAp (Driessens, 1982). However, a more important reason for the lower solubility of FAp (and a reason that is seldom fully appreciated) is the substitution of (F^-) for (OH^-) in the formula that governs the solubility of FAp (equation 5). OH^- ion activity is 10^{-9} mol/L in a typical cariogenic plaque fluid with a pH of 5, while F^- ion activity is 4000 times higher (about 4×10^{-5} mol/L) in the same plaque fluid (Birkland & Charlton, 1976). As a result, IAP(FAp) is about seven orders of magnitude larger than IAP(OHAp) in cariogenic plaque. This, together with the lower Ksp for FAp, makes the cariogenic plaque about six orders of magnitude supersaturated with respect to FAp, while it is slightly supersaturated with respect to OHAp and vastly undersaturated with respect to tooth enamel. This implies that tooth mineral rich in F would be less soluble in cariogenic plaque than mineral that has a low F content. Indeed, several studies have shown (LeGeros & others, 1983; Ogaard, Rolla & Helgeland, 1983; Tanaka, Moreno & Margolis, 1993; Takagi, Liao & Chow 2000) that enamel containing higher amounts of apatitically bond, or tooth-bound, F was much more resistant to demineralization.

Interactions Between Solution F and Tooth Bound F

An understanding of the effects of F on tooth solubility is complicated by observations that a small amount of F present in the demineralizing solution (ambient F) appears to be highly effective in reducing demineralization whether or not the mineral contained a high level of tooth-bound F (Arends & others, 1983; Borsboom, van der Mei & Arends, 1985; Margolis, Moreno & Murphy, 1986). Under clinical condition, ambient F (in the form of salivary and plaque fluid F) can be elevated by F dentifrices, rinses and other topical F treatments that deposit "labile F" in the oral cavity. This labile F then dissolves in the mouth, thus serving as a source for ambient F. Although some of this labile F deposition may be bacterially bound (Rose, Shellis & Lee, 1996), most studies suggest it is primarily in the form of calcium fluoride or a calcium fluoride-like material (Øgaard, Rolla & Helgeland 1983; Rølla & Saxegaard, 1990). However, being soluble, labile F deposition stays in the mouth for only a short time, for example, less than two hours after a 2500 ppm F rinse (Vogel & others, 1992). The effect of ambient F on enamel solubility may be attributed to the formation of FAp or partially fluoridated OHAp at the active sites of mineral destruction (Arends & Christoffersen, 1990). This would make the mineral behave like FAp rather than OHAp in terms of its solubility behavior (Wier, Chien & Black, 1972). It should be noted, however, that non-specific adsorption of F (without reaction) has also been postulated to be important in this regard (White, Nelson & Faller, 1994). In any case, for ambient F to exert these effects, it must penetrate the area of the lesion where mineral destruction is occurring, that is, the advancing front (Figure 2). Unfortunately, tooth mineral is an efficient scavenger of solution F^-, and studies have shown that as F diffuses into enamel it is partially consumed by reaction with mineral (Duckworth & Braden, 1967; Tarbet & Fosdick, 1971). The fact that active demineralization occurs at the advancing front rather than at the tooth surface would suggest that ambient F level is low in this region. Thus, it would appear that FAp formation in enamel, by systemic incorporation during tooth formation, topical F treatments or by previous cariogenic attacks, would make the mineral less reactive to solution F, thereby facilitating penetration of F^- ion to the advancing front region where it is most needed. It follows that tooth-bound F, being effective in reducing tooth solubility as discussed above, also could promote the effects of ambient F. It may be concluded that both ambient F and tooth-bound F play important roles in reducing tooth demineralization, and formation of both types of F should be considered as important goals in designing effective F treatments.

Summary of the Mechanism of Demineralization and Strategy for Prevention

The minimum thermodynamic requirement for demineralization is that the ion activity product (which decreases very rapidly with pH) becomes smaller than the Ksp for tooth mineral. Since H^+ ion concentration gradient is the only driving force for the overall demineralization process, an increase in pH of the demineralizing medium will reduce the driving force for H^+ transport into the lesion, hence, diminishing the rate of demineralization. Similarly, an increase in calcium and phosphate concentrations of the demineralizing medium would increase the concentration gradients against which these ions are transported and should also reduce the rate of demineralization. Because low levels of solution F greatly decrease the rate of dissolution of enamel mineral, increasing the concentration of F in oral fluids is extremely effective in inhibiting demineralization. However, tooth-bound F can exert a synergistic effect.

Thermodynamic and Mechanistic Analyses of Remineralization

In terms of mass balance considerations, remineralization is the exact reverse of demineralization (equation 6)

$$10\,Ca^{2+} + 6\,H_2PO_4^- + H_2O \rightarrow \underset{\text{mineral}}{Ca_{10}(PO_4)_6(OH)_2} + 14\,H^+ \quad (6)$$

solution   mineral

Hence, the thermodynamic requirement for remineralization is also the reverse of that for demineralization, that is, the ion activity product should exceed Ksp.

$$(Ca^{2+})^{10}(PO_4^{3-})^6(OH^-)^2 > Ksp\ (\text{tooth mineral}) \quad (7)$$

However, in spite of the thermodynamic requirements for de- and remineralization being governed by the same equations, the processes are fundamentally different in several important respects.

Figure 3 illustrates the mechanistic process of remineralization. Because remineralization would mostly occur under neutral pH oral conditions, H^+ ion diffusion (in either direction) could not be a driving force for the process. Instead, passive transport of Ca^{2+} and $H_2PO_4^-$ ions down the concentration gradients from saliva and plaque into the body of the lesion are the main driving forces. Thus, it is the increase in oral fluid calcium and phosphate that drives the remineralization process. It should be noted that solubility constraints limit the level of mineral supersaturation, and therefore, limit mineral ion concentrations in the remineralizing solution to a relatively low level. The use of higher concentrations would merely cause precipitation to form in the solution. More importantly, such solutions may induce mineral deposition on tooth surface, leading to occlusion of ion diffusion pathways in the mineral dense surface layer of the lesion, inhibiting further remineralization of the body of the lesion (Larsen & Fejerskov, 1989). Thus, an additional critical requirement for effective remineralization is the ability to transport mineral ions from the exterior solution into the lesion so that precipitation occurs in the mineral-depleted body of the lesion where it is most needed.

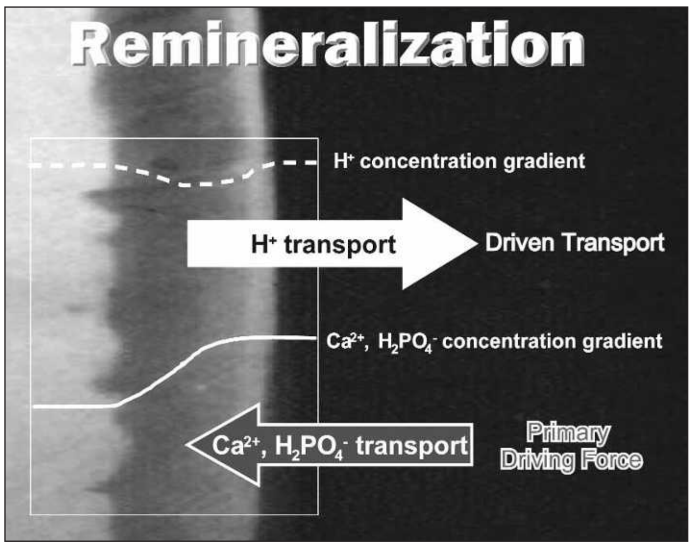


Figure 3. Schematic representation of the mechanistic aspects of the remineralization process showing that the inward diffusion being the primary driving force.

Data in the literature suggest that the maximum calcium and phosphate concentrations are about 1 to 2 mmol/L for remineralization to occur (Silverstone, 1972). Given the maximum calcium concentration permitted in remineralizing solution and the concentration of about 0.1 mmol/L for these ions at the advancing front postulated in the previous section, the driving force for remineralization is approximately 30-fold concentration gradient of calcium or phosphate compared to the 100-fold gradient of H^+ ion concentration (that is, pH 7 to pH 5) found in the demineralization process.

From the calcium content of enamel, it can be shown that the amount of calcium present in a liter of enamel is about 30 moles. Calcium concentration in saliva is about 1 mmol/L (Vogel & others, 1998, 2000a) and in a typical remineralizing solution it is less than 2 mmol/L. Since only a fraction, for example 1/3, of calcium in the solution could be precipitated during the remineralization process, it will take about 10,000 volumes of saliva remineralizing solution to obtain enough calcium to form one volume of enamel. A similar situation also exits with respect to phosphate. It appears that a large volume of remineralizing solution is required to supply the needed mineral ions, suggesting that remineralization *in vivo* is a relatively slow process and requires frequent applications.

Effects of F on Remineralization

When incorporated into mineral crystal structure as tooth-bound F, F is in a highly stable form and is not released into the solution except under extremely acidic conditions. Thus, tooth-bound F is not expected to play a significant role in the remineralization process. In contrast, ambient F is a very important parameter in remineralization. Numerous *in situ* remineralization studies have shown that topical F applications significantly promote remineralization of enamel lesions in the mouth (Faller, 1995) and remineralization is certainly a major mechanism for the clinical anticaries effect of F.

As described earlier, a small amount of F in solution will cause the IAP(FAp) to be significantly greater than IAP(OHAp). For example, even for resting plaque that has not been exposed to an F dentifrice or rinse application for 48 hours, the baseline F level in plaque fluid is about 5 $x10^{-6}$ to 12 $x10^{-6}$ mol/L (Vogel & others, 1992; 2000b). Even at the lowest concentration of F, an IAP(FAp) value of $10^{-95.6}$ would be obtained, while the IAP(OHAp) is $10^{-99.4}$, or about four orders of magnitude larger. The difference becomes even greater when plaque F level is increased by F application. Thus, solution F results in significantly greater oral supersaturation levels with respect to FAp compared to OHAp, which provides a greater thermodynamic driving force for the rapid precipitation of F-containing tooth mineral.

Ambient F plays an even more important role in the remineralization process as a catalyst for OHAp precipitation. Specifically, F has been shown to increase the rate of OHAp precipitation, the effect being highly significant even at low F concentration, for example, 0.2 ppm, (Vandenhoek, Feenstra & Debruyn, 1980), under conditions in which the resulting precipitated mineral contained only a very small amount of F. With regard to remineralization, *in vitro* studies have shown that low levels of solution F dramatically increased the rate of remineralization (Koulourides & others, 1961; Featherstone & others 1990, ten Cate, 1990). However, like calcium and phosphates, it has been suggested that an excessive level of ambient F may induce obturation of the surface layer of the lesion, thereby inhibiting the remineralization process (Ten Cate, 1990).

Summary of the Mechanism of Remineralization and Strategy for Promotion

The minimum thermodynamic requirement for remineralization to occur is simply that the ion activity product is greater than the Ksp for OHAp or partially fluoridate OHAp. The process, unlike demineralization, is driven by the passive transport of calcium and phosphate. Also unlike in demineralization, effective remineralization requires a relatively low concentration of these ions to be successful. For this reason and because very large amounts of such solutions are required to deposit a significant amount of tooth mineral, a long exposure to remineralizing conditions is required. Low concentrations of F greatly accelerate this process due to lower solubility of fluoridated apatites and the ability of solution F to accelerate the remineralization process through catalysis of OHAp appreciation. Maintenance of a low concentration of F in oral fluids is essential to achieving significant remineralization.

Clinical Considerations

The above discussion suggests that elevation of the levels of “cariostatic” ions (calcium, phosphate and F) in the oral environment (that is, in saliva and plaque) can decrease the severity of the demineralization phase of the cariogenic process and increase remineralization of the lesion after the attack has ended. Some new approaches for achieving this are featured below; however, as discussed previously, a careful choice of conditions is need to achieve these objectives.

Approaches to Increase Oral F Levels

Dentifrices that contain 250 and 1000 ppm of F as sodium fluoride (NaF) are considered “gold standards” because of their well documented, clinically observed dose response with regard to anticaries effects (Proskin, Chilton & Kingman, 1992). On theoretical grounds, one may expect that the greater anticaries effects of 1000 ppm F products are derived from their ability to produce a greater labile F deposition in the mouth. Oral F clearance data in the literature (Vogel & others, 1992; Duckworth & Stewart, 1994) suggest that after a one minute rinse with 10 mL of a 12 or 13 mol/L NaF (228 or 247 ppm F) solution, an elevated salivary F level was present for a relatively short time, for example, 30 minutes, and the level returned to baseline value in about two hours. Oral F levels increased by F dentifrice applications diminished even more rapidly when the subjects rinsed with water after the dentifrice application (Duckworth, Knorr & Stephen, 1991). Since an elevated level of F in oral fluids is important in reducing the severity of demineralization during a cariogenic challenge and enhancing the potential for remineralization during the resting condition, it would be highly desirable to prolong the time for which the F levels are elevated.

Recent studies have shown that a two-component rinse ($Na_2SiF_6/CaCl_2$) that precipitates calcium fluoride (CaF_2) as a store for labile F during oral application, deposited significantly larger amounts of F on teeth (Chow & Takagi, 1991) and in plaque and saliva (Vogel & others, 1992) can be produced compared with a conventional sodium F (NaF) rinse of the same concentration of 228 ppm F. As a result of forming a greater F store from the two-component rinse, both salivary and plaque fluid F levels were elevated for a longer time (Vogel & others, 1992) and more ambient F was released when plaque was acidified (Vogel & others, 2000b) compared to the NaF rinse. An *in vivo* remineralization study also showed that two-component rinse produced a greater remineralization effect than NaF rinse (Chow & others, 2000). Finally, studies have shown that two-component rinse with a lower F content (114 ppm F) was more effective than 228 ppm F NaF rinse in depositing F on teeth *in vitro* (Takagi, Liao & Chow, in press), remineralizing enamel lesions *in vivo* (Chow & others, 2001) and in raising plaque fluid F concentrations (Vogel & others, in press). These results suggest that F deposition and the anticaries effects of an F rinse (dentifrice) are not a function of the F dose but are dependent on the ability of the rinse to deposit F in oral substrates in a readily available form. It follows that with the use of a two-component or "active" (in which a reaction occurs during application to precipitate calcium fluoride) delivery system, the F content of dentifrices can be lowered from the current 1100 ppm without sacrificing the amount of F deposited that may later be available for maintaining oral fluid F concentration, and conversely, F deposition by dentifrices may be significantly enhanced without increasing the F content.

Approaches to Increase Oral Calcium and Phosphate Levels

There have been many studies on the use of remineralizing rinses and dentifrice in an effort to increase oral calcium and phosphate concentrations needed to effect remineralization. Some formulations have produced significant remineralization (Pearce & Nelson, 1988; Reynolds, 1997; Grant, Thompson & Tanzer, 1999). Chewing gums and candies are other potential delivery vehicles for calcium and phosphate. Early studies of calcium phosphate fortified gums and candies have not demonstrated their efficacy (Pickel & Bilotti, 1965; Richardson & others, 1972; Ashley & Wilson, 1977; Rankine & others, 1989), probably due to low solubility of the substances chosen to deliver the ions. Recent studies showed that by using additives with appropriate solubilities, chewing gums can produce significant increases in salivary and plaque calcium and phosphate levels over a 15-minute period (Chow & others, 1994). These results suggest that chewing gums and possibly candies can be effective vehicles for the delivery of calcium and phosphate because they can produce an elevated mineral saturation level for a longer period than can be produced by a rinse or dentifrice application. Furthermore, as a consequence of increased salivary flow, gums and candies can induce a desirable increase in plaque and salivary pH (Jensen & Wefel, 1989; Manning & Edgar, 1993), thereby reducing the severity of the challenge as well as helping to clear bacterial acids from plaque. Gums and candies can also be utilized several times a day at selected times when maximum anticaries effect may be realized as discussed below.

Knowing when to apply a calcium and phosphate-releasing device may be an important factor on anticaries effectiveness. In a study (Vogel & others, 1998) in which a control gum and calcium and phosphate-releasing (α-tricalcium phosphate fortified) gums were used immediately after a sucrose intake, both the control and the fortified gums produced an increase in plaque fluid pH, thereby reducing the severity of the challenge. However, the fortified gum also produced a large increase in plaque fluid calcium and phosphate levels, which, together with the pH increase, completely eliminated the challenge, that is, the IAP(OHAp) was maintained at the same level as in the resting plaque. It may be concluded that while chewing an ordinary gum immediately after a sucrose intake raised plaque pH, the use of a calcium and phosphate-releasing gum completely neutralized the acid challenge. However, in a second study (Vogel & others, 2000a) in which these same gums were used without a challenge, the calcium and phosphate-releasing gum produced only a small increase in plaque fluid free of calcium and phosphate although a large increase in whole plaque calcium and phosphate content was noted. This suggests that the deposited mineral was not "labile" under neutral conditions, and thus no significant remineralization effects may be expected. However, in this same study when a sucrose rinsing was given subsequent to chewing the fortified gum, a large increase in calcium and phosphate concentrations was seen in plaque fluid (as in the first study), no doubt due to the pH-mediated release of ions from plaque mineral stores and IAP(OHAp) calculations (eq 2) confirmed a substantial post-sucrose decrease in the driving force for demineralization. No beneficial effects were obtained from the use of an ordinary gum prior to a sucrose challenge. It may be concluded that the main beneficial effect of calcium and phosphate-releasing gum was its ability to decrease the demineralization challenge and not by increasing remineralization potential.

Synergy or Antagonism Between Calcium and Phosphate Additives and F

Although one might expect that the anticaries effects from calcium and phosphate ions deposited in plaque by chewing gums and other devices may be further enhanced by the addition of F, the analyses given below would suggest the contrary. As noted above, F incorporated in tooth mineral as FAp or F-enriched OHap is beneficial because it decreases the solubility of tooth mineral. In contrast, F deposits formed in plaque and other oral substrates must be in a labile form in order to serve as a source for ambient F. Similarly, the calcium and phosphate stores formed in plaque by dentifrices, gums or candies needs to be in a labile form, at least during the acidic challenge, such that it readily dissolves and consumes acids that would otherwise dissolve tooth mineral. When labile sources of F and calcium phosphate are both present, the likely outcome is that both would be made non-labile by the formation of FAp or partially-fluoridated OHAp in plaque. Hence, neither F nor mineral ions would be available during the subsequent acidic challenge. Also as noted above, two-component F rinse produced a significantly greater labile F deposition than NaF rinse. However, the majority of the total amount of F deposited in plaque by the two-component rinse was in non-labile form (Vogel & others, 2001). It was postulated that the high phosphate level innate to plaque, together with the calcium and F provided by the rinse, allowed the formation of a more stable form of F deposition in plaque. Additional studies should be conducted to gain a better understanding of the factors that control the formation of labile and non-labile F deposits in plaque by F applications. Care must be taken in designing treatments that promote the presence of cariostatic ions in the mouth and avoid inappropriate combinations of ingredients that can be antagonistic rather than synergistic.

Summary of Approaches to Increase Cariostatic Ions in the Mouth

Remineralization is greatly enhanced by maintaining an elevated F in oral fluids through the formation of labile F reservoirs. New types of rinses and dentifrices may enhance these deposits and permit the development of highly effective low F formulations. Remineralization from calcium phosphate rinses, fortified gums or candies appears confined to time of application. It is possible, however, to induce labile calcium phosphate deposits in plaque that would readily dissolve during a subsequent challenge, thereby reducing the severity of damages. But, interactions between the calcium, phosphate and F additives in the dentifrice, gum and other delivery vehicles remain to be examined.

Acknowledgement

This investigation was partially supported by USPHS Research Grant DE105354 of the American Dental Association Health Foundation from the National Institutes of Health—National Institute of Dental and Craniofacial Research and in part by the dental research program conducted by the National Institute of Standards and Technology in cooperation with the American Dental Association Health Foundation.

Note

Certain commercial materials and equipment are identified in this paper to specify experimental procedure. In no instance does such identification imply recommendation or endorsement by the National Institutes of Health, the American Dental Association Health Foundation, the National Institute of Standards and Technology or that the material or equipment identified is necessarily the best available for the purpose.

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Replacement Therapy of Dental Caries

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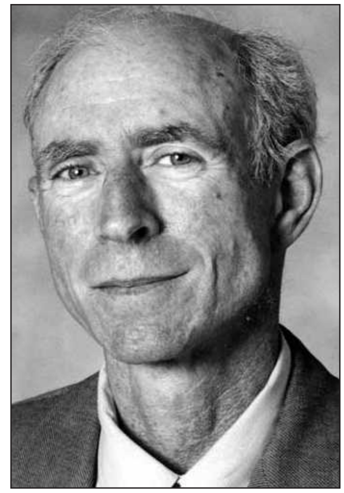

Jeffrey D Hillman

Abstract

There are many examples of positive and negative interactions between different species of bacteria inhabiting the same ecosystem. This observation provides the basis for a novel approach to preventing microbial diseases called replacement therapy. In this approach, a harmless effector strain is permanently implanted in the host's microflora. Once established, the presence of the effector strain prevents the colonization or outgrowth of a particular pathogen. In the case of dental caries, replacement therapy has involved construction of an effector strain called BCS3-L1, which was derived from a clinical *Streptococcus mutans* isolate. Recombinant DNA technology was used to delete the gene encoding lactate dehydrogenase in BCS3-L1, making it entirely deficient in lactic acid production. This effector strain was also designed to produce elevated amounts of a novel peptide antibiotic called mutacin 1140, which gives it a strong selective advantage over most other strains of *S mutans*. In laboratory and rodent model studies, BCS3-L1 was genetically stable and produced no apparent deleterious side effects during prolonged colonization. BCS3-L1 was significantly less cariogenic than wild-type *S mutans* in gnotobiotic rats, and it did not contribute whatsoever to the cariogenic potential of the indigenous flora of conventional Sprague-Dawley rats. Also, its strong colonization properties indicated that a single application of the BCS3-L1 effector strain to human subjects should result in its permanent implantation and displacement over time of indigenous, disease-causing *S mutans* strains. Thus, BCS3-L1 replacement therapy for the prevention of dental caries is an example of biofilm engineering that offers the potential for a highly efficient, cost effective augmentation of conventional prevention strategies. It is hoped that the eventual success of replacement therapy for the prevention of dental caries will stimulate using this approach in preventing other bacterial diseases.

The Theory of Replacement Therapy

The normal human oral flora is composed of more than 300 species of bacteria that collectively number in the billions. It is remarkable that the challenge presented by this very large variety and number of micro-organisms does not lead to frequent manifestations of oral disease, but, in fact, the predominant human condition is one of health. This observation accords with the Gene-for-Gene Hypothesis (Person, 1967), which states in specific regard to indigenous micro-organisms that host-parasite interactions are inherently unstable. Over eons of time, natural selection will favor mutations in the parasite that reduce its virulence and mutations in the host that promote its resistance. Ultimately, a climax state is reached wherein the parasite becomes a stable and innocuous member of the host's indigenous flora.

Empirically, most members of human dental plaque are climax organisms. However, certain species have not completed this evolutionary process and retain some pathogenic potential. Also, in other instances certain organisms may have been forced out of their climax state by the influences of civilization, as seen when modern sanitation methods resulted in polio epidemics or when increased reliance on dietary carbohydrates resulted in increased dental caries.

In the case of dental caries, we can confidently assume that evolution will continue to act on the principle etiologic agent, *Streptococcus mutans*, to bring it into a new climax state wherein it no longer expresses a pathogenic potential. However, for natural selection to act on spontaneous mutations to eliminate this organism's residual virulence may require many thousands of years to complete.

The intention of modern day replacement therapy, as it applies to diseases caused by indigenous micro-organisms, is to greatly speed this natural evolutionary process. By careful study of the pathogen, it may be possible to identify and modify certain of its genes to create, in a relatively short span of time, an effector strain that presages the climax organism that evolution would eventually select. The effector strain is used to intentionally colonize the niche in susceptible host tissues that is normally colonized by the pathogen. By being better adapted, a properly constructed effector strain will prevent colonization of the pathogen by blocking attachment sites, competing for essential nutrients or other mechanisms. In this fashion, the host is protected for as long as the effector strain persists as a member of the indigenous flora which, ideally, is for the lifetime of the host.

An Historical Summary

As reviewed by Florey (1946), the use of bacteria to fight bacteria began more than a century ago when Cantani attempted to treat tuberculosis by insufflation of a presumed harmless organism referred to as "Bacto Termo." Since then, there have been dozens of reports describing positive and negative bacterial interactions in which the presence of a particular indigenous micro-organism promotes or deters the presence of a pathogen. For the most part, these interactions were detected during *in vitro* cultivation, and their occurrence *in vivo* was inferred from correlations provided by cultivation studies. For example, the predominant micro-organism in the pharynx of healthy neonates is one or more species of alpha-hemolytic streptococci, and the absence of these species was shown to correlate with a significantly increased risk of infections including sepsis, meningitis, pneumonia and cystitis (Sprunt & Leidy, 1988). Strain 215 is a naturally occurring alpha-hemolytic streptococcus that was chosen to serve as an effector strain based largely on its ability to inhibit a variety of common pathogens that initially colonize the pharynx. A nasopharyngeal dose of 10^6 cells was given to a group of infants lacking an indigenous alpha-hemolytic streptococcus in their throat flora. In most instances, strain 215 rapidly became the predominant micro-organism in pharyngeal cultures, the numbers of potential pathogens declined to low or undetectable levels and the infants suffered a significantly lower incidence of infections than uninoculated controls (Sprunt, Leidy & Redman, 1980). Also, in older individuals, natural or antibiotic-induced low levels of alpha-hemolytic streptococci in the pharynx have been shown to correlate with increased susceptibility to *S pyogenes* infections (Crowe, Sanders & Longley, 1973; Fujimori & others, 1997; Sanders, 1969; Sanders, Sanders & Harrowe, 1976). This suggests the potential for replacement therapy in the prevention of streptococcal pharyngitis in susceptible subjects.

Application of replacement therapy to diseases caused by *Staphylococcus aureus* has also been very instructive. In recent years, *S aureus* is the most commonly isolated pathogen causing nosocomial infections. It is also the etiologic agent of chronic furunculosis. Considerable work has been done to prevent these infections (Shinefield, Ribble

& Boris, 1971; Perl & Golub, 1998), including replacement therapy using strain 502A, a naturally occurring *S aureus* strain of low virulence. Implantation of strain 502A on the nasal mucosa and umbilical stumps of newborn infants has been very successful in curtailing epidemics of staphylococcal disease in the nursery. Persistent nasal carriage of pathogenic staphylococci has also been interrupted in adults by implantation of strain 502A after antibiotic suppression of the indigenous strain. After gaining relatively widespread acceptance in the 1960s and 1970s, 502A has been little used partly because of lack of need and partly because of infections that have been reported following its use (Drutz & others, 1966; Blair & Tull, 1969; Houck, Nelson & Kay, 1972). Although the benefits of using strain 502A far outweigh the hazards (Light & others, 1967; Houck & others, 1972), this work emphasized the potential difficulty of using naturally occurring effector strains that may have residual pathogenic potential.

The molecular basis for bacterial interference has rarely been proven, even in the best studied models. Organisms that occupy the same or similar niche would be expected to compete for essential nutrients, which accounts at least in part, for the ability of alpha-hemolytic streptococci to interfere with colonization by *S pyogenes* (Sanders, 1969). The same or overlapping habitats would make competition for attachment sites a logical basis for interference. This is probably the basis for the ability of 502A to sterically interfere with the colonization of disease-causing *S aureus* strains (Bibel & others, 1983). Recently, it was postulated that cross-inhibition by auto-inducing molecules could serve as a basis for bacterial interference in quorum sensing species such as *S aureus* (Ji, Beavis & Novick, 1997). If shown to occur *in vivo*, this mechanism would be similar to other instances where the production of a metabolic end-product or antibiotic-like substance by one microorganism has been proven to prevent colonization by another sharing the same habitat. Mutant analysis was used to prove that hydrogen peroxide production by *S oralis* (previously *S sanguis* type II) inhibited the growth of *Actinobacillus actinomycetemcomitans in vitro* and in an animal model (Hillman & Shivers, 1988). However, inability to obtain persistent colonization by *S oralis* has hindered its use as an effector strain in the prevention or treatment of localized juvenile periodontitis (JD Hillman, unpublished result). As detailed below in the case of mutacin production by *S mutans*, persistent colonization by an effector strain is usually an important feature of replacement therapy that is difficult to satisfy.

Application of Replacement Therapy to Dental Caries

An effector strain for replacement therapy of dental caries called BCS3-L1 has been constructed (Hillman & others, 2000) that took into account the following logical prerequisites:

1. it must have a significantly reduced pathogenic potential;
2. it must persistently and preemptively colonize the *S mutans* niche, thereby preventing colonization by wild-type strains whenever the host comes in contact with them;
3. ideally, it should aggressively displace indigenous strains of *S mutans*, thereby allowing even previously infected subjects to be treated with replacement therapy; and
4. it must be generally safe and not predispose the host to other disease conditions.

Pathogenicity

Several different approaches to satisfy the first of these prerequisites for effector strain construction have been examined. In accord with the acidogenic theory of dental caries, lactic acid production by *S mutans* has long been considered the main pathogenic mechanism for production of caries lesions. Consequently, mutants of *S mutans* with reduced acidogenicity were tested for their cariogenic potential. Lactate dehydrogenase (LDH; Johnson, Gross & Hillman, 1980; Fitzgerald & others, 1989) and intracellular polysaccharide mutants (Tanzer & Freedman, 1978) proved to have significantly reduced cariogenicity both *in vitro* and in various animal models. Rather than directly reducing acid production by *S mutans*, several groups have exploited another oral viridans streptococcus, *S salivarius*, for its ability to serve as an effector strain. This organism is naturally less cariogenic than *S mutans*, but normally occupies its own distinct niche. Tanzer and coworkers (1985) isolated a naturally occurring *S salivarius* variant that competed effectively for the *S mutans* niche. The basis for this strain's altered colonization properties was not determined. More recently, the urease gene has been cloned from *S salivarius* with the idea of constructing a urease-producing effector strain (Chen, Clancy & Burne, 1996). It is imagined that such an effector strain could metabolize environmental or exogenously supplied urea to neutralize acids in plaque produced by *S mutans* and other acidogenic bacteria. To test this hypothesis, an *S gordonii* strain harboring a plasmid containing the cloned urease gene produced significantly less environmental acidification *in vitro* when as little as 2 mM urea was added to the cell suspension along with glucose. A ureolytic strain o*f S mutans* has been constructed and shown to have a significantly decreased cariogenic potential in a rat model (R Burne, personal communication).

For construction of BCS3-L1, which is an *S mutans* strain, LDH deficiency was chosen as the approach for reducing acidogenicity. Earlier work with a closely related *S rattus* strain had provided convincing evidence for the effectiveness of this approach. LDH-deficient mutants were virtually non-cariogenic in gnotobiotic rats and did not contribute significantly to the cariogenic potential of the indigenous flora in conventional pathogen-free rats (Johnson & others, 1980). Although the mutants used in these studies were either induced by ethylmethane sulfonate treatment or spontaneous, reversion studies strongly suggested that cryptic mutations were not responsible for the observed decrease in pathogenicity. In fact, these data provided the most direct proof of the acidogenic theory of dental caries.

Attempts to transfer these findings directly to *S mutans* proved to be difficult. LDH-deficient mutants of various strains of *S mutans* were not found using the same screening methods used to isolate mutants of *S rattus*. Abhyankar and coworkers (1985) identified two strains that were exceptions to this rule. Both strains appeared to possess one or more pre-existing mutations that affected pyruvate metabolism as evidenced by their unusually high production of ethanol, acetate and acetoin when grown in the presence of limiting glucose. These strains were mutable to LDH-deficiency using N-methyl-N'-nitro-N-nitrosoguanidine, although it was not demonstrated that they harbored single gene mutations. Cloning the structural gene encoding the *S mutans* LDH (Hillman, Duncan & Stashenko, 1990) provided the basis for solving this puzzle. Standard insertional mutagenesis methods failed to yield LDH-deficient clones, suggesting that LDH-deficiency was a lethal mutation in most *S mutans* strains (Duncan & Hillman, 1991). This hypothesis was definitively proven by creation of a temperature sensitive LDH mutant (Chen, Hillman & Duncan, 1994). This isolate grew well at 30ºC but did not grow at 42ºC under a variety of cultivation conditions. Chemostat studies indicated that some aspect of glucose metabolism was toxic during growth under the non-permissive condition (Hillman, Chen & Snoep, 1996). The toxic effect could be overcome by limiting the amount of environmental glucose. This and other data accorded with studies of *S mutans* central intermediary metabolism indicating that this organism has enzymatic activities, including pyruvate formate-lyase (Abbe, Takahashi & Yamada, 1982; Takahashi, Abbe & Yamada, 1982) and pyruvate dehydrogenase (Carlsson, Kujala & Edlund, 1985; Hillman, Andrews & Dzuback, 1987a) for pyruvate dissimilation. However, at high sugar concentrations, the levels of activity of these enzymes are apparently insufficient to compensate for the absence of LDH. It was found (Hillman & others, 1996) that a supplemental alcohol dehydrogenase (ADH) activity, when expressed in the temperature sensitive LDH mutant, could complement LDH deficiency.

With this background of information, BCS3-L1 construction started with the *ldh* gene cloned into an appropriate suicide vector for *S mutans*. Essentially, the entire gene except for transcription and translation signal sequences was deleted, and it was replaced with the *Zymomonas mobilis* open reading frame (ORF) for alcohol dehydrogenase (ADH) II. Transformation of the recombinant molecule into the *S mutans* starting strain, JH1140 and allelic exchange resulted in the isogenic mutant, BCS3-L1. This effector strain has no measurable LDH activity and ca 10-fold elevated levels of ADH activity relative to its parent. Fermentation end-product analysis showed that BCS3-L1 makes no detectable lactic acid. As predicted, much of the metabolized carbon is converted to the neutral end-products ethanol and acetoin. Under various cultivation conditions, including growth on a variety of sugars and polyols, such as sucrose, fructose, lactose, mannitol and sorbitol, BCS3-L1 yielded final pH values that were 0.4 to 1.2 pH units higher than those of its parent, JH1140.

The reduced acidogenic potential of BCS3-L1 was reflected in its decreased cariogenic potential. Gnotobiotic Fisher rats and conventional, pathogen-free Sprague Dawley rats infected with BCS3-L1 and fed a sucrose-containing diet had less than half the incidence and severity of caries lesions compared to animals infected with the parent strain, JH1140 (Hillman & others, 2000). Caries scores of conventional animals infected with BCS3-L1 did not differ from the scores of control animals that remained *S mutans*-free throughout the experiment, indicating that it did not contribute to the cariogenic potential of the indigenous flora. The results of these studies provide strong evidence that an LDH-deficient *S mutans* strain has significantly reduced pathogenic potential, and thus satisfies the first prerequisite for use as an effector strain in replacement of dental caries.

Colonization

Transmission of mutans streptococci within the human population has been extensively studied. Most studies support the idea that this organism is usually transmitted from mother (primary caretaker) to child within a several year period following the onset of tooth eruption (Alaluusua, 1991; Berkowitz & Jones, 1985; Caufield & Walker, 1989; Davey & Rogers, 1984; Genco & Loos, 1991). However, there is some recent conflicting evidence that a significant proportion of children may acquire mutans streptococci from sources outside their immediate family (de Soet & others, 1998; Emanuelsson, Li & Bratthall, 1998). These studies were fairly evenly divided on whether individual subjects harbored one or more than one strain of mutans streptococci. According to a recent report (Alaluusua & others, 1996), the acquisition of multiple strains may depend on the frequency of sugar consumption. No longitudinal studies have been conducted to determine if two or more strains can persistently colonize a subject or if one strain eventually displaces the other(s). Numerous studies (Krasse & others, 1967; Jordan & others, 1972; Ruangsri & Orstavik, 1977; Svanberg & Krasse, 1981; Tanzer, Krasse & Svanberg, 1982) have documented the difficulty of persistently introducing laboratory strains of mutans streptococci into the mouths of humans, particularly if they already harbored an indigenous strain of this organism.

From the standpoint of replacement therapy of caries, these results suggest that implantation of an effector strain would best be accomplished in children immediately after the onset of tooth eruption and before their acquisition of a wild-type strain. In order to prevent super-colonization by wild-type strains when the host comes in contact with them, an effector strain should have some significant selective advantage to colonization. This would also enable subjects who have already been infected with wild-type *S mutans* to be treated by replacement therapy. The ability of an effector strain to preemptively colonize the human oral cavity and aggressively displace indigenous wild-type strains was initially thought to be a complex phenomenon dependent on a large number of phenotypic properties. However, it was discovered that a single phenotypic property could provide the necessary selective advantage. A naturally occurring strain (JH1000) of *S mutans* that produces a bacteriocin called mutacin 1140 capable of killing virtually all other strains of mutans streptococci against which it was tested (Hillman, Johnson & Yaphe, 1984) was isolated. Mutants were isolated that produced no detectable mutacin 1140 or that produced approximately three-fold elevated amounts. The mutants were used to correlate mutacin production to preemptive colonization and aggressive displacement in a rat model. Although a number of studies (Huis Veld, Drost & Havenaarr, 1982; Kelstrup & Gibbons, 1969; Rogers, van der Hoeven & Mikx, 1978; Smith & Huggins, 1974; Takazoe, Nakamura & Okuda, 1984) performed over the years suggested a role for bacteriocins in the natural history of infection by various bacteria, this experiment provided the first strong evidence that at least certain ones are important in colonization.

A correlation was also made between mutacin 1140 production and the ability of *S mutans* to persistently colonize the oral cavities of human subjects and aggressively displace indigenous mutans streptococci (Hillman, Yaphe & Johnson, 1985; Hillman, Dzuback & Andrews, 1987b). Three years following a single, three minute infection regimen involving brushing and flossing of a concentrated cell suspension onto and between the teeth, all of the subjects remained colonized by the mutacin up-producing mutant of JH1000 (Hillman & others, 1989). No other strains of mutans streptococci were observed in saliva and plaque samples. The same results were recently found 14 years after colonization for at least two of three subjects who are still available for testing. These results indicate that this strain of *S mutans* succeeded in satisfying the second and third prerequisites for use as an effector strain in replacement therapy: it persistently and preemptively colonized the *S mutans* niche in the human oral cavity and aggressively displaced indigenous strains of this organism. Consequently, strain JH1140, which has a spontaneous mutation resulting in a three-fold elevated production of mutacin 1140, served as the starting strain for construction of BCS3-L1 described above.

The effect of LDH deficiency on colonization potential was tested in several ways (Hillman & others, 2000). First, it was found that BCS3-L1 produced as much mutacin 1140 as did its parent, JH1140, indicating that LDH deficiency did not affect this important phenotypic property. BCS3-L1 actually formed significantly more plaque than JH1140 when grown in the presence of sucrose. This phenomenon was previously reported for LDH-deficient mutants of *S rattus* (Hillman, 1978) and is likely to be a reflection of pH dependence of glucosyl transferase activities. Using previously described methods (Hillman & others, 1984), BCS3-L1 and JH1140 were shown to be nearly identical in their ability to preemptively colonize the teeth of conventional rats and aggressively displace an indigenous strain of *S mutans*. These results lend strong support to the idea that BCS3-L1 retains its parent's selective advantage for colonization and will serve as a useful effector strain in replacement therapy of dental caries.

Safety

To serve as an effector strain in replacement therapy of dental caries, BCS3-L1 must be safe in several important regards. First, it must be genetically stable. Reacquisition of an acidogenic phenotype by spontaneous reversion is extremely unlikely because construction of BCS3-L1 involved deletion of essentially all of the *ldh* ORF. No acidogenic revertants were observed among 10^5 independent colonies screened on glucose tetrazolium medium (Hillman & others, 2000). Horizontal transmission of an *ldh* gene is possible. Repeated attempts have failed to demonstrate transduction of *S mutans* by bacteriophage (A Delisle, personal communication). Transformability is known to be very strain-dependent (Perry & Kuramitsu, 1981; Westergren & Emilson, 1983) and BCS3-L1, like its parent, is very poorly transformable (Chen & others, 1994; Hillman & others, 2000). This feature made BCS3-L1 construction difficult but helps to assure its long-term stability. Certain *S mutans* strains have been shown to serve as recipients for conjugation by *S faecalis* and possibly other species (LeBlanc & others, 1978). BCS3-L1 has not been studied in this regard, but acidogenic mutants of BCS3-L1 were not recovered from conventional Sprague-Dawley rats harboring a complex indigenous flora after six months of colonization. Plaque from subjects infected for 14 years with the mutacin up-producing strain will serve as a good source of material to further study the occurrence and potential problems posed by horizontal transmission of DNA.

Mutacin 1140 has been shown (Hillman & others, 1998) to be a member of a small class of antibiotics called lantibiotics. It is a small (2,263 Da), very stable peptide containing modified amino acids, lanthionine, methyllanthione, didehydroalanine and didehydrobutyrine, characteristic of lantibiotics. Sufficient mutacin 1140 has not been purified to directly test its toxicity. However, the prototype lantibiotic, nisin, is known to have extremely low toxicity (Hurst, 1981) and has been developed as a food preservative that is "generally recognized as safe" by the FDA. Mutacin 1140 is very poorly immunogenic in rabbits (JD Hillman, unpublished result). A long-term toxicity study (Hillman & others, 2000) found that after colonization for six months, the mean weights of conventional Sprague-Dawley rats colonized with BCS3-L1 did not significantly differ from animals colonized with JH1140 or *S mutans*-free control animals. Histopathological examination revealed no treatment-related lesions in any of the major organs examined, including liver, spleen kidney, bladder, adrenal gland, pituitary, salivary glands, mandibular and mesenteric lymph nodes, thyroid, parathyroid, trachea, esophagus, heart, thymus, lungs, stomach, pancreas, intestines, testes, prostate, skin, mammary gland, tongue, palate, brain, bone and eyes.

Mutacin production by BCS3-L1 and the change in fermentation products resulting from LDH deficiency could conceivably upset plaque ecology and lead to the bloom of another microorganism with pathogenic potential. Recent studies (Costerton, 1995) have provided an appreciation for the complicated structural architecture of biofilms, presumably including dental plaque. Following specific initial attachment to a surface, the growth of cells leads to the formation of a thick layer of differentiated mushroom- and pillar-like structures consisting of cells embedded in their extracellular polysaccharide matrix. Between these cellular structures are water-filled spaces that serve as channels for the introduction of nutrients and the elimination of waste products. In biofilms consisting of two or more species of bacteria, each cellular structure may be pure or mixtures of cells depending on the pressures imposed by positive and negative bacterial interactions. These interactions may also extend over a finite area to affect the general composition of plaque in a particular habitat. Clearly, however, there is a physical limit to this sphere of influence. The mutacin 1140 up-producing strain of *S mutans* eliminated mutacin-sensitive indigenous strains of this species but had no effect on indigenous *S oralis* strains, which were equally sensitive to mutacin killing *in vitro* (Hillman & others, 1987b). These results indicate that *S mutans* has a physically distinct habitat that is separated from the *S oralis* habitat by a distance sufficient for dilution to reduce the concentration of mutacin below its minimal inhibitory concentration. A similar explanation could account for the failure to observe a change in plaque composition associated with the change in fermentation end products following colonization of conventional rats by an LDH-deficient mutant (Stashenko & Hillman, 1989).

A final aspect of replacement therapy safety is the requirement for controlled spread of the effector strain within the population. Mutacin 1140 up-production clearly provides a selective advantage to BCS3-L1 colonization, but the minimal infectious dose has not been determined for this strain or any *S mutans* strain in humans. As described above, horizontal transmission of natural strains appears to be a rare event, but mutacin up-production may promote its occurrence. It has been reported that mutacin production appears to promote mother to child transmission (Gronroos & others, 1998). Wives and children of the two subjects colonized with the mutacin up-producing *S mutans* strain were not colonized when tested 14 years after the initial infection regimen (JD Hillman, unpublished result). Clearly, additional studies with larger populations will have to be performed to properly measure the potential for horizontal transmission. It is expected that, like wild-type strains of *S mutans*, vertical transmission of BCS3-L1 from mother to child will occur at a high frequency. Control of this phenomenon and unregulated transmission in general, could be achieved by introducing a mutation into BCS3-L1 that would make it dependent on a nutritional supplement not normally part of the human host diet. As an example, persistent survival of a strain harboring a mutation in the gene encoding alanine racemase would probably require daily D-alanine supplements, perhaps in the form of a mouthwash or chewing gum.

Conclusions

In general, replacement therapy using a properly constructed effector strain provides a number of advantages over conventional prevention strategies. In the case of dental caries, a single colonization regimen that leads to persistent colonization by the effector strain should provide lifelong protection. In the event that the effector strain does not persist in some subjects indefinitely, reapplication could be performed as needed without added concern for safety or effectiveness.

One of the greatest advantages of replacement therapy is that there is no need for patient compliance. Conscientious use of conventional prevention methods, (brushing, flossing, topical fluoride, controlled sugar consumption, etc) is sufficient in most cases to maintain the *S mutans* level below its minimal pathogenic dose. The fact that dental caries remains one of the most common infectious diseases afflicting humans is a clear indication that the effectiveness of a prevention strategy is inversely related to its need for patient compliance.

In previous studies, subjects have received a pumice and rubber cup prophylaxis prior to implantation to reduce the number of indigenous *S mutans* on teeth. The need for this step has not been experimentally determined and may possibly be eliminated in the future. Research-based application of BCS3-L1 has used the cells from 100 ml cultures concentrated 20-fold in fresh medium. Ultimately, the cells could be provided to the practitioner frozen in glycerol or lyophilized and reconstituted chairside by the addition of water. In either case, a blunt, curved tip syringe would be used to deliver the cell suspension onto and between the subject's teeth. After five minutes, unattached cells would be removed by several rinses with water. The price of both labor and materials to accomplish this process is expected to make replacement therapy quite cost effective compared to other prevention strategies and is particularly suitable for use in developing countries.

Most of the pertinent safety issues regarding BCS3-L1 stability and mutacin 1140 toxicity have already been addressed. Two others can be briefly mentioned. First, it should be noted that spontaneous resistance to mutacin 1140 does not readily occur in sensitive species. In one experiment, plating of over 10^{12} cells of several different streptococcal species on medium containing mutacin 1140 failed to give rise to a single, genetically stable resistant clone (JD Hillman, unpublished result). Thus, outgrowth of resistant variants does not seem to be a likely problem. And second, although dental treatments in general do not seem to be a risk factor for infective endocarditis (Strom & others, 1998), the possibility of bacteremia during implantation will be minimized by directing the stream of cells away from the gingival sulcus and any observable mucosal lesions. Antibiotic prophylaxis will be performed in subjects with conditions deemed to be high or medium risk as defined by the American Heart Association (Dajani & others, 1997).

Finally, although experimental data obtained to date indicates that horizontal transmission of BCS3-L1 is not likely to occur, vertical transmission from mother to child is expected. Thus, treatment of one generation would lead to protection of future generations. In this regard, replacement therapy with BCS3-L1 will mimic the climax organism that evolution would eventually select.

It is clear from the current resurgence of various infectious diseases that traditional and antibiotic-based therapies alone will not suffice. The continued study of bacterial interactions as they occur *in vivo* will inevitably lead us to more naturally occurring effector strains for the replacement therapy of various infections. Hopefully, the success of using genetic engineering to tailor an effector strain for replacement therapy of dental caries will encourage similar efforts to prevent other infectious diseases.

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©Operative Dentistry Supplement 6, 2001, 51-60

Potential for Vaccines in the Prevention of Caries Lesions

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Summary

A large body of experimental work over several decades has demonstrated the feasibility of inducing protective immunity against oral colonization by mutans streptococci and the subsequent development of dental caries in animal models. Current approaches focus on two principal protein antigens, the adhesin AgI/II and glucosyltransferase and the generation of salivary secretory IgA antibodies by novel strategies for the delivery of immunogens to effectively stimulate the common mucosal immune system. Alternative approaches include the development of antibodies suitable for passive application. Further advances to make immunization against caries practicable will depend upon clinical trials aimed at establishing whether appropriate immune responses can be safely generated in humans, particularly in the susceptible age groups, and whether such responses will afford desirable levels of protection.

Introduction

The concept of preventing dental caries by vaccination has existed for almost as long as dental caries has been known to be an infectious disease process, and considerable progress towards that goal has been accomplished during the past three decades (Krasse, Emilson & Gahnberg, 1987; Michalek & Childers, 1990; Russell, 1992; Russell & others, 1999). Numerous milestones can be cited to establish the scientific basis for this proposition (Table 1). Chief among these are the recognition of "mutans streptococci," principally *Streptococcus mutans* and *Streptococcus sobrinus* as the primary organisms responsible for the initiation of human dental caries (reviewed in Loesche, 1986), and the development of the concept of the common mucosal immune system (reviewed in Mestecky, 1987). Indeed, it is interesting to recall that one of the earliest demonstrations of the generation of mucosal antibodies by oral immunization in humans involved the administration of *S mutans* and the detection of IgA antibodies

Table 1: Milestones in Caries Vaccine Development

S mutans rediscovered and established as the primary etiologic agent of dental caries
Secretory IgA discovered as a distinct form of IgA predominant in secretions including saliva
S mutans classified into serotypes (now separate species) based on cell wall polysaccharides
Role of glucosyltransferases in the formation of extracellular adherent glucans from sucrose
Animal models of dental caries for evaluating immunity (rats and monkeys)
Surface proteins identified as major antigens; AgI/II as a major adhesin
Common mucosal immune system as the major pathway for eliciting secretory IgA antibodies
Mother-infant transmission of mutans streptococci; "window of infectivity" in infancy

against it in saliva and lacrimal fluid (Mestecky & others, 1978). However, with the benefit of hindsight, the responses induced in that experiment can be seen to be relatively modest; moreover, repeated administration of large doses of killed bacteria was necessary to induce salivary antibodies, and they did not persist for more than a few weeks. Progress towards the objective of developing a potentially useful vaccine against caries has centered on two main lines of work: the identification of appropriate antigenic targets, molecules of mutans streptococci involved in the cariogenic process against which antibodies would be expected to exert protective effects; and strategies for inducing potent mucosal antibody responses, especially in this context, salivary secretory IgA (SIgA) antibodies, while using only a few moderate doses of vaccine.

Antigens of Mutans Streptococci for Use in Vaccines

Investigation of the importance of dietary sucrose in the development of caries led to the discovery of glucosyltransferases (GTF) as the enzymes responsible for the synthesis of soluble and insoluble adherent glucans from sucrose (Guggenheim & Schroeder, 1967; Gibbons & Nygaard, 1968). As these glucans were shown to be important for the tenacious adherence of cariogenic streptococci to tooth surfaces and the accumulation of plaque, GTFs became obvious candidates for vaccine development with the expectation that antibodies would inhibit their enzymic activity. Progress was hampered by the difficulty of purifying and characterizing GTFs by conventional biochemical means until recombinant DNA technology enabled them to be cloned and sequenced, and thereby recognized as a family of at least three separate enzymes having distinctive properties in terms of their glucan products and requirements for preexisting 'primer' glucan chains (Russell, 1979b; Kuramitsu & others, 1991). Nevertheless, immunization experiments in rodent and primate models of caries using available preparations of GTF showed that significant protective immunity could be induced, even though this was not always correlated with antibody-mediated inhibition of GTF enzyme activity (Russell, Challacombe & Lehner, 1976; Smith, Taubman & Ebersole, 1979; Russell & Colman, 1981).

Studies on the role of sucrose and glucans derived from it in the adherence of mutans streptococci to hard surfaces led to the further identification of glucan-binding proteins (GBP) which lack the enzymic activity of GTFs but retain the ability to bind to glucan (Ma & others, 1996; Smith & others, 1998). GBPs are now thought to be important, along with GTFs themselves, in the binding of mutans streptococci to glucans deposited on tooth surfaces, thereby contributing to the sucrose-dependent adherence of these organisms to teeth. As such, GBPs are also candidates for vaccine antigens, and despite some sequence homology with GTFs, they appear to possess distinct antigenic epitopes (Smith & Taubman, 1996).

Meanwhile, it became clear that the sucrose-dependent tenacious adherence of mutans streptococci was preceded by a sucrose-independent phase of reversible adherence dependent on the presence of the salivary protein pellicle on tooth enamel (Peros & Gibbons, 1986). Separate and independent lines of investigation partly based on the analysis of crude preparations of GTF resulted in the identification of other protein antigens on the cell wall of *S mutans* designated AgI/II and AgIII (Russell & Lehner, 1978; Russell, 1979a; Russell & others, 1980a), or antigens A and B (Russell, 1980), which appeared to be involved in protective immunity against caries in monkey models (Russell, Challacombe & Lehner, 1980b; Lehner & others, 1981; Russell, Beighton & Cohen, 1982; Russell & others, 1983). Subsequently, it was found that AgI/II (antigen B) was a surface fibrillar protein important for the initial sucrose-independent adherence of *S mutans* to saliva-coated surfaces (Moro & Russell, 1983; Crowley & others, 1993; Hajishengallis, Koga & Russell, 1994) and was thus an important vaccine antigen candidate. This was strengthened by the finding that AgI/II of *S mutans* was homologous to SpaA cloned from *S sobrinus*, as well as other variants of the same protein identified and cloned from other strains and serotypes of mutans streptococci (Brady & others, 1991; Ma & others, 1991). AgI/II is now recognized as the prototype of a family of fibrillar surface proteins that are widely distributed on oral streptococci (Jenkinson

& Demuth, 1997). Antigen A (=AgIII), whose biological function remains unknown (Russell, Harrington & Russell, 1995), was also pursued as a vaccine antigen and proposed for a human clinical trial that ultimately did not take place (Hughes & others, 1986). Its disadvantage is that it occurs only in *S mutans* (and *S rattus*) but not *S sobrinus*, and so would be of limited utility against human caries.

Strategies for Effective Mucosal Immunzation

Numerous laboratory studies over the past two decades have led to the development of a variety of approaches towards enhancing the effectiveness of mucosal immunization (Table 2). These strategies include: (1) co-administration of mucosal adjuvants including heat-labile enterotoxins and their nontoxic derivatives, other bacterial products and cytokines; (2) coupling antigens to cell-binding proteins such as the B subunits of heat-labile enterotoxins; (3) incorporation of antigens into various micro-particles or membrane-bound vesicles that promote uptake of the antigens and protect against digestion; (4) expression of antigens in attenuated or commensal bacteria that colonize mucosal tissues; (5) expression of antigens in engineered viruses that undergo limited replication in mucosal tissues and combinations of these methods (Mestecky & others, 1997).

Table 2. Strategies for Enhancing Mucosal Immune Responses

Principle	Examples
Mucosal adjuvants	Cholera toxin (CT) etc, saponins, lectins, derivatives of lipid A or muramyl dipeptide
Coupling to carriers	CTB etc, chemical conjugates, or genetically engineered
Microparticles	Biodegradable polymers, liposomes, cochleates, multiple emulsions, ISCOMs
Live bacterial vectors	Attenuated Salmonella, BCG, commensals (lactobacilli, oral streptococci)
Live viral vectors	Vaccinia, adenovirus, polio replicons

Among these strategies, the author has explored the use of *S mutans* AgI/II coupled to the nontoxic B subunit of cholera toxin (CT) either by chemical conjugation to CTB (Russell & Wu, 1991) or by the genetic construction of recombinant chimeric proteins of the form: Ag-CTA2/B (Figure 1) (Hajishengallis & others, 1995). When delivered by intragastric (i.g.) or intranasal (i.n.) routes, such an immunogen constructed from the 40-kDa saliva-binding region (SBR) of *S mutans* AgI/II induced potent mucosal SIgA and circulating IgG antibodies to AgI/II (Table 3). The i.n. route was more effective than the i.g. route in requiring lower doses and in being less dependent on the co-administration of CT as a mucosal adjuvant. I.n. immunization also effectively induced SIgA antibodies in saliva of monkeys (Russell & others, 1996). Some evidence of compartmentalization of mucosal responses was revealed since i.g. immunization induced better intestinal responses, whereas i.n. immunization was better at inducing salivary, respiratory and genital responses (Russell & others, 1991; Wu & Russell, 1993). Moreover, i.g. and i.n. immunization induced cytokine-secreting T cells in the corresponding MALT and draining lymph nodes (Wu & others, 1996; Toida & others, 1997; Wu & others, 1997). Antibody responses persisted for prolonged periods, although booster immunizations after four to six months elicited mainly serum IgG antibodies (Russell & Wu, 1991; Wu & others, 1993; Hajishengallis, Michalek & Russell, 1996), and antigen-responsive T-cells could be detected particularly in the draining cervical lymph nodes after i.n. immunization (Wu & others, 1997). Recent findings indicate that immune responses can still be recalled two years after

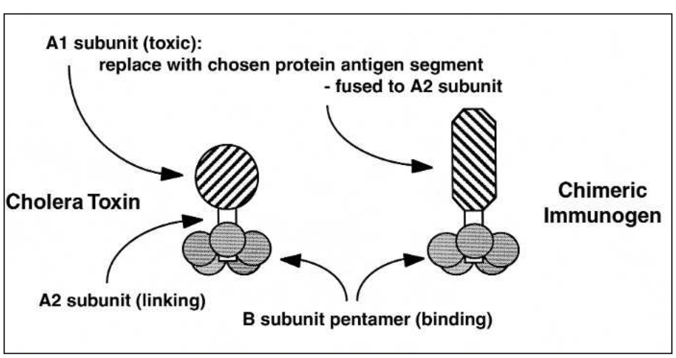

Figure 1: Principle of the construction of recombinant Ag-CTA2/B chimeric immunogens (reproduced from Russell [1998] by permission of S Karger AG, Basel, Switzerland).

Table 3. Serum and Salivary Antibody Responses to AgI/II After Intragastric (i.g.) or Intranasal (i.n.) Immunization with SBR-CTA2/B Chimeric Protein, With or Without Additional Cholera Toxin (CT) as Adjuvant

Immunogen	Route	Serum IgG (μg/ml)	Serum IgA (μg/ml)	Salivary IgA (%Ab/Ig)
SBR-CTA2/B	i.g.	88 x/÷4.0	0.5 x/÷3.8	0.4 x/÷2.8
SBR-CTA2/B + CT	i.g.	363 x/÷1.8	3.7 x/÷2.1	4.7 x/÷1.5
SBR-CTA2/B	i.n.	38 x/÷1.6	1.5 x/÷1.7	2.8 x/÷1.6

Data are geometric means x/÷SD; N = 4 or 5

primary mucosal immunization (Harrod, Martin & Russell, 2001). Such long-lasting immunity may be particularly important for a slowly developing condition such as caries, and also because it may be necessary to maintain protection over many years from infancy through childhood and adolescence. As an alternative, the ability to recall a salivary SIgA antibody response by booster immunization may be desirable, particularly if it should be found that besides the principal "window of infectivity" for mutans streptococci during the second year of infancy (Caufield, Cutter & Dasanayake, 1993), additional opportunities for infection arise at later times, such as when children enter school or when the permanent teeth erupt.

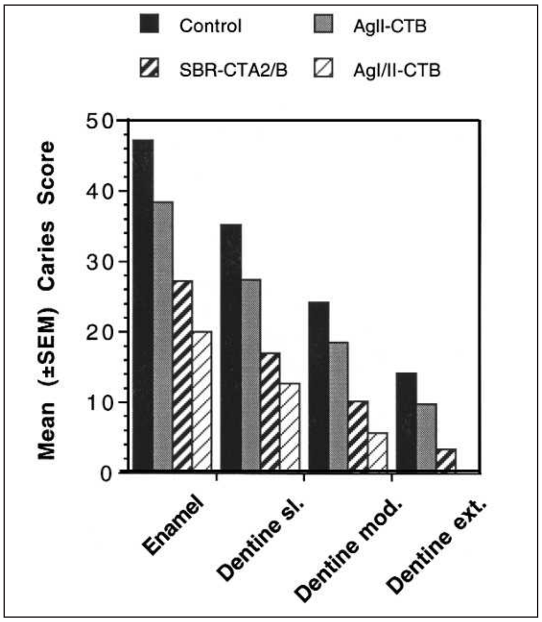

Figure 2. Caries scores in rats immunized i.n. with SBR-CTA2/B chimeric protein, or with AgI/II-CTB or AgII-CTB conjugates, and in unimmunized controls. Rats were infected orally with S mutans and fed a cariogenic diet containing sucrose. Caries scores were significantly lower in animals immunized with SBR-CTA2/B chimeric protein or AgI/II-CTB conjugate, compared to the control group. (Data from Hajishengallis, Russell & Michalek [1998]).

Protection against dental caries has been demonstrated in a rat model where weanlings were immunized with AgI/II-CTB conjugates or SBR-CTA2/B chimeric protein, infected orally with *S mutans*, and fed a sucrose-containing diet (Figure 2) (Katz & others, 1993; Hajishengallis, Russell & Michalek, 1998). Compared to controls, immunized animals developed salivary SIgA as well as serum IgG antibodies to AgI/II, the numbers of recoverable *S mutans* were diminished and caries development was reduced. Interestingly, animals immunized with SBR-CTA2/B showed comparable protection to those immunized with AgI/II-CTB conjugate, whereas those immunized with the C-terminal portion of AgI/II, that is AgII coupled to CTB, developed antibodies to this part of the molecule but showed little or no protection against *S mutans* infection or caries (Hajishengallis & others, 1998). This finding supports an earlier observation in monkeys that the N-terminal portion of AgI/II, AgI (which includes the SBR segment) induced protective immunity, whereas AgII did not (Lehner & others, 1981). Moreover, it suggests that an effective antibody response should be directed against the N-terminal part of AgI/II which is distal to the bacterial cell wall and appears to be where adhesin determinants are located.

A Composite Vaccine Against Caries?

The use of GTF as a vaccine antigen has been pursued particularly by Smith and Taubman in an extensive series of studies (Smith & others, 1979; Taubman & others, 2000). Recently, they have developed the approach of identifying conserved consensus segments from the amino acid sequences of these molecules, focusing on the glucan-binding (GLU) and catalytic (CAT) domains (Taubman, Holmberg & Smith, 1995). Peptides representing the CAT sequence have been engineered into "multiple antigenic peptides" which have been shown to be effective for eliciting GTF-inhibiting antibodies upon injection into rodents (Smith & others, 1997; Smith & others, 1999).

In order to develop this approach for mucosal immunization, the author has collaboratively attempted the construction of Ag-CTA2/B chimeric immunogens using similar segments cloned from the *gtfB* gene which encodes GTF-I, the enzyme responsible for synthesizing water-insoluble glucan (Jespersgaard & others, 1998). However, expression of CAT-CTA2 or GLU-CTA2 fusion proteins in *E coli* was problematic, as both CAT and GLU segments were deposited in insoluble inclusion bodies that resisted efforts at resolubilization. Thus they could not be co-expressed with CTB and assembled into the complete chimeric immunogens. However, immunization of rabbits with CAT or GLU segments generated antibodies, which, particularly in the case of anti-GLU antibodies, strongly inhibited GTF activity. Mice immunized in with GLU developed salivary IgA and serum IgG antibodies and revealed protection against challenge with *S mutans* and the subsequent development of caries (Jespersgaard & others, 1999).

Since both AgI/II and GTF are involved in different ways in the colonization process, the author has proposed that a vaccine designed to elicit salivary SIgA antibodies against both will be doubly effective in inhibiting oral colonization by mutans streptococci. A fusion protein constructed from parts of AgI/II (PAc) and GTF-I has been found capable of inducing antibodies that inhibit both GTF activity and the sucrose-independent as well as sucrose-dependent adherence of *S mutans* to saliva-coated hydroxyapatite (Yu & others, 1997).

Application to Humans: Future Prospects

An important question is whether such approaches to immunization, which have been amply demonstrated in a variety of rodent models over many years, can be applied to humans. This is not a trivial matter because it cannot be taken for granted that results obtained in one species can be extrapolated to another. Besides obvious differences in their teeth and dietary habits, there are subtle but significant differences in the immune systems of humans and rodents. The rodent models usually depend on implantation of mutans streptococci often under conditions of the suppression of other components of the oral microbiota and artificially high sucrose diets, and as a result, caries develops rapidly in a few weeks. Numerous efforts have been made to investigate caries vaccination in monkey models because their dentition closely resembles that of humans, they are phylogenetically closely related and caries develops slowly over several months on a sucrose-containing diet. Early attempts focused on the use of parenteral immunization, which was successful in demonstrating protective immunity associated with serum IgG antibodies (Lehner, Challacombe & Caldwell, 1976; Cohen, Colman & Russell, 1979). However, this systemic approach inevitably ran into questions concerning its safety, particularly because of the association of group A streptococcal infections with acute rheumatic fever. Fears that systemic immunization with antigens derived from mutans streptococci might induce antibodies capable of cross-reacting with heart tissue were exaggerated beyond the capability of the evidence to sustain them (Russell & Wu, 1990), and no purified mutans streptococcal antigen has been shown to generate this effect. Nevertheless, regulatory authorities are cautious about streptococcal vaccines and the burden of proof of safety is on the proponents. The problem, in essence, is that no injectable vaccine is 100% safe and caries is not a life-threatening condition.

Mucosal immunization in which no material is systemically injected may represent a substantially safer alternative. However, for reasons not clearly understood, this has been difficult to demonstrate in monkeys, especially by the intragastric route, even using such potent immunogens as cholera toxin or antigens co-administered with CT as an adjuvant or antigens coupled to CTB (Michalek & others, 1995). Moreover, despite a close phylogenetic relationship, there are subtle but significant differences in IgA and the mucosal immune system between humans and primates other than the anthropoid apes (Peppard & Russell, 1999). However, the author has been able to demonstrate that immunization of rhesus macaques with AgI/II-CTB induces IgA antibodies in saliva and other secretions, as well as circulating IgG antibodies (Russell & others, 1996).

Human experimentation has largely been limited to adult populations, but it has served to demonstrate the concept of the common mucosal immune system and the generation of salivary SIgA antibodies after i.g. immunization with mutans streptococci (Mestecky

& others, 1978; Czerkinsky & others, 1987). In some cases, evidence for suppression of re-colonization by mutans streptococci after oral immunization has been obtained (Smith & Taubman, 1990). Adults have also been immunized i.n. with an antigenic mixture of GTF and AgI/II, which induced a modest salivary IgA response (Childers & others, 1999). However, as dental caries occurs at younger ages, it will be necessary to evaluate vaccines in children. Attention has therefore turned to the possibility of immunizing infants, with the objective of preventing oral colonization by mutans streptococci in the first place (Taubman & Smith, 1992; Russell & others, 1999). This is founded on the concept of the "window of infectivity," when infants appear to be most susceptible to colonization by mutans streptococci during their second year of life (Caufield & others, 1993). Accordingly, it is proposed that mucosal immunization designed to induce salivary SIgA antibodies to such antigens as AgI/II and GTF in infants prior to colonization would inhibit colonization, or at least suppress the numbers of mutans streptococci below a critical level and result in diminished caries development. This can only be answered by carefully planned clinical trials in progressively younger age groups as safety and immunogenicity are demonstrated. The challenge is not only scientific, but depends on whether the resources can be marshaled and sustained to accomplish it. Additional questions, however, concern the duration of salivary antibodies sufficient to maintain suppression of mutans streptococci in the oral microbiota and whether salivary antibodies can be recalled or elevated by booster immunizations at later stages when further opportunities for infection may possibly arise, such as when children enter school or when the permanent teeth erupt.

Alternatively, given that infants acquire mutans streptococci almost entirely from their mothers (Li & Caufield, 1995), consideration might be given to mucosal immunization of pregnant or nursing mothers. Two objectives might be attainable in this way: (1) suppression of the mother's own oral load of mutans streptococci that would diminish the dose transferred to the infant; and (2) the concomitant provision of salivary SIgA antibodies or antibodies coated on the transferred bacteria that might diminish the colonizing capacity of the organisms in the infant. It is perhaps unlikely that a third potential objective is realistic in this case—the passive transfer of maternal SIgA antibodies in milk by breast-feeding since oral colonization by mutans streptococci depends on the presence of erupted teeth and the window of infectivity appears to open well after the cessation of breast-feeding. However, passive immunization against mutans streptococci might be achievable by other means. A mouse monoclonal antibody raised against AgI/II has been genetically engineered to replace the mouse IgG constant regions with human IgA constant regions, thereby constructing a human IgA antibody against AgI/II. This was expressed in tobacco plants and by cross-breeding these first with other transgenic plants expressing J chain (to generate polymeric IgA), then with plants expressing secretory component "humanized" SIgA antibodies to AgI/II were generated (Ma & others, 1995). Agricultural-scale growth and post-harvest processing then allows the purification of large quantities of these antibodies at economic cost sufficient to apply them in humans. Small-scale experiments have suggested that the passive application of such antibodies in volunteers who first received extensive oral hygiene can suppress the re-emergence of mutans streptococci in the oral microbiota for a prolonged time (Ma & Lehner, 1990; Ma & others, 1998). Whether this approach can be developed into a clinically useful treatment remains to be determined, and the results of double-blind placebo-controlled clinical trials are awaited with interest. Additional methods of producing antibodies for passive application against caries include immunization of cows or chickens to generate antibodies in milk or eggs, respectively (Hamada & others, 1991; Hatta & others, 1997; Loimaranta & others, 1998).

Questions remain as to whether vaccination against caries is desirable, and what must be accomplished to make it a practical reality. The question of desirability often elicits divergent opinions reflecting personal attitudes (on the part of investigators as well as potential recipients) to different control measures and may ultimately depend on economics and commercial considerations. Apart from such non-scientific factors, it is clear that, despite the undoubted success of fluoride, better awareness of simple preventive measures and the availability of high-quality dental care (at least in affluent communities), dental caries remains unacceptably prevalent even in the United States (Kaste & others, 1996) and a vaccine could contribute significantly to its reduction.

Acknowledgments

The author thanks numerous colleagues who have contributed extensively to the experimental findings and ideas discussed in this article. Laboratory studies were supported by USPHS grant DE06746 from the National Institute of Dental and Craniofacial Research.

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Footnote

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Biomaterials, Biomimetics and Tissue Engineering Programs at the National Institute of Dental and Craniofacial Research/National Institutes of Health

Eleni Kousvelari

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Introduction

The National Institute of Dental and Craniofacial Research (NIDCR) belongs to the family of institutes that constitute the National Institutes of Health (NIH). The NIH is one of the world's leading biomedical research facilities. Its mission is to discover new knowledge that will lead to bettering the health of people everywhere. Founded in 1887, the NIH today consists of 25 institutes and centers. About 83% of the NIH budget supports biomedical research in more than 2500 public and private institutions throughout the US and worldwide. About 11% of the NIH budget is for intramural research conducted on the NIH campus.

Dental and craniofacial diseases and disorders are among the most common health problems affecting people around the world. These conditions range from birth defects such as cleft palate and lip, injuries to the head and face, dental caries and periodontal disease, temporomandibular joint (TMJ) disease and head and neck cancers. The NIDCR was established in 1948 to support basic and clinical research and research training on diseases and disorders affecting the oral, craniofacial and dental tissues and organs.

To accomplish its mission, the Institute has two Divisions: the Division of Intramural Research (DIR) and the Division of Extramural Research (DER).

The DIR includes the Office of the Scientific Director and seven research branches:

- Craniofacial and Skeletal Diseases Branch
- Craniofacial Developmental Biology and Regeneration Branch
- Craniofacial Epidemiology and Genetics Branch
- Gene Therapy and Therapeutics Branch
- Oral and Pharyngeal Cancer Branch

- Oral Infection and Immunity Branch
- Pain and Neurosensory Mechanisms Branch

A majority of NIDR resources are spent for research grants and contracts to institutions outside the NIDR. These monies are distributed through a competitive process that involves two levels of peer review for scientific merit and relevance to the Institute's mission. The different branches and offices of the DER administer the grants. The DER includes the Office of the Division Director, five scientific branches and two offices:

- Craniofacial Anomalies and Injury Branch

This branch supports basic and clinical research to understand the development of the head, face and neck, and identifies the genetic and environmental contributions to craniofacial anomalies. The objective of this scientific program is to understand the underlying causes of craniofacial anomalies, thereby, advancing the fields of diagnosis, treatment and prevention.

- Infectious Diseases and Immunity Branch

This branch supports basic, applied and developmental research in four broadly based scientific areas that provide the basis for rapid development of knowledge of the etiology, pathogenesis, diagnosis, treatment and prevention of oral infectious disease and AIDS.

- Neoplastic Diseases Branch

This branch supports and encourages basic and applied research related to the etiology and early detection of oral cancers, progression of oral cancers, invention and metastasis and therapy of oral cancers.

- Chronic and Disabling Diseases Branch

This branch supports basic and clinical research on acquired and disabling conditions. It includes, but is not limited to, osteoarthritis, salivary gland autoimmune diseases (that is, Sjogrens syndrome), osteoporosis and temporomandibular disorders.

- Biomaterials, Biomimetics and Tissue Engineering Branch

This branch was created to embrace new paradigms and technologies in order to provide biological solutions for the replacement, restoration and repair of hard (teeth and bone) and soft tissues of the orofacial complex as well as early diagnosis of disease.

- Office of Clinical, Behavioral and Health Promotion Research

The overall mission of the office is to foster clinical, behavioral and health promotion research related to oral, dental and craniofacial health. Of specific interest are clinical and community-based studies aimed at documenting, understanding and eliminating craniofacial, oral and dental health disparities among the diverse populations and subpopulations of the US.

- Office of Training and Career Development

This office supports various institutional and individual national research service awards and career development awards to increase and retain the supply of outstanding investigators in basic, behavioral and clinical research pertinent to the mission of the NIDCR.

Detailed descriptions of the scientific research programs in each of the DIR and DER branches and offices can be obtained by visiting the NIDCR's web page: http://www.nidr.nih.gov/.

Biomaterials, Biomimetics and Tissue Engineering Branch

This paper discusses some of the supported research projects by the Biomaterials, Biomimetics and Tissue Engineering as well as what research should be encouraged to meet the future challenges in designing and developing new synthetic and biologically-derived materials for repair, reconstruction, alignment and regeneration of dental, oral and craniofacial tissues.

The Biomaterials Program of the Branch

Historically, the NIDCR has supported and continues to support the development of synthetic dental biomaterials for the restoration of teeth and for dental implants. These studies have led to better dental restorative materials that are currently used in dental practice. Some currently supported research projects focus on:

- the expansion and modification of existing dental materials to make them more biocompatible and clinically durable;
- the development of new alloy combinations, especially those that are mercury free;
- the modification of glass ceramics and dental composites for improved clinical durability;
- the modification of polymers for enhanced clinical usefulness;
- the design of adhesive dental materials using computer modeling and combinatorial library approaches;
- the enhancement of performance and longevity of dental implants; and
- the understanding of the basic biology of biointegration and the prevention of adverse biofilm formation on the surface of implants.

Two relatively new and highly multidisciplinary fields of science and technology are emerging. They hold promise to create functional, naturally biocompatible and durable replacements for diseased or otherwise damaged or deficient tissues and organs, and thus revolutionalize medicine and dentistry. These fields, Biomimetics and Tissue Engineering, are highly multidisciplinary and require biologists, chemists, clinicians, computer scientists, engineers and physicists to work cooperatively towards creating such replacement biomaterials.

The Biomimetics Program of the Branch

What is Biomimetics? Biomimetics is a relatively new field of science that studies how nature designs, processes, assembles and disassembles molecular building blocks to fabricate high performance mineral-polymer composite hard materials (for example, mollusk shells, bone, tooth) and soft materials (for example, skin, mucus, cartilage, tendon), and then takes inspiration from these designs and processes to engineer new molecules and materials with unique properties.

One well-studied example of biomimetic approach from nature is the fabrication of silica-based materials, such as resins and ceramics that draws inspiration from the marine sponge. The marine sponge produces large amounts of silica spicules under mild aqueous conditions at low temperature and pH. Each of these spicules contains a filament of similar protein subunits called silicateins. Silicatein α is homologous to a known enzyme cathepsin L of the papain family of proteolytic enzymes. In neutral pH, silicatein catalyzes the *in vitro* polymerization of silica from tetraethoxysilane and organically modified silicon triethoxides. Synthetic block copolypeptides that mimic the properties of silicatein were able to produce *in vitro* two different structures: hard silica spheres and well-defined columns of amorphous silica. These findings have led to the development of new low-temperature biomimetic routes to the synthesis of advanced mineral-organic composites *in vitro*. It is envisioned that it will be possible for *in situ* regeneration of such composite materials in bone and teeth since synthesis of silica can be done in an aqueous environment, at neutral pH and low ambient temperatures (Cha & others, 1999; Cha & others, 2000).

Biomimetic approaches are also used in the development of bioreactive scaffold materials, which then permit the proper formation of reparative tissues. The principles for the fabrication of such scaffolds were utilized from lessons learned from spiders. Spiders make their webs and perform a wide range of tasks with up to seven different types of silk fibers. To date there is a renewed interest in silks as biomaterial scaffolds due to their unique mechanical properties, opportunities for genetic tailoring of their structure and function and because of their biocompatibility. Native silk proteins from the cocoons of B mori silk worms were used for the preparation of silk fibroin films. Using molecular engineering, the fibroin was decorated with integrin (extracellular matrix receptors) recognition sequences (RGD), the first 34 amino acids of parathyroid hormone (PTH-34 amino acids) and a modified PTH1-34 (mPTH). These molecules help stimulate recruitment and anchorage of osteoblasts and subsequent bone formation (Sofia & others, 2001).

For tooth structure (for example, enamel), repair and regeneration scientists are utilizing the knowledge gained from years of scientific research on tooth development and enamel formation in order to design and develop strategies for tooth repair and regeneration. Genes and their encoded structural proteins as well as their expression, localization and function have been discovered for all tooth structures. In the case of enamel, the functions of long-known enamel proteins have been better characterized. Enamel is first created as a protein template, being synthesized and organized by ameloblasts as discrete rods of enamel proteins, resembling the threads of a fabric. Specialized regions of the ameloblast, called Tomes' process, serve to control the secretion of the organic portion of the organic matrix, allowing adjacent rods of organic matrix to join to one another in a continuum. The self-assembly of enamel proteins within this matrix provides the capacity to direct mineral crystal structure. The resulting fabric of enamel proteins forms the organic template around a core of dentin composite. The organic template (enamel proteins) controls the formation of long-, thin-, substituted-, hydroxyapatite-crystallites arranged parallel to one another under the influence of a single cell. Tomes' processes weave the ameloblast-defined matrix boundaries to one another, resulting in crystallites arranged between boundaries, forming a continuum of hydroxyapatite crystals. In the end, the organic matrix is almost entirely replaced with inorganic material. The ameloblasts oversee the final maturation of the inorganic phase, then cease to exist (Fincham & others, 2000).

Would it be possible in the future to utilize the principles of hierarchical self-assembly ("bottom-up" approach for the construction of a particular tissue for a unique function) to produce, for example, polymer scaffolds based on intact enamel protein and/or synthetic copolypeptide frameworks that mimic the function of enamel proteins in order to direct enamel biomineralization *in situ*? A group of scientists supported by the NIDCR are addressing this question. So far, scientists are able to make chick embryos grow tooth buds, while others generate dentin-like tissue from adult human dental pulp stem cells (Gronthos & others, 2000).

Some of the supported research projects in the Biomimetics program are focused on:

- examples from marine biology for applications to bone and tooth biomineralization, development of adhesives for tooth sealants and surgical replacement of sutures;
- biomimetic approaches to enamel biomineralization, to the engineering of tooth crowns and to oral mucosa, conjuctiva and skin regeneration;
- use of the dentin enamel junction as a biomimetic model for material-tissue interfaces;
- development of phospholipid-based scaffold materials that can be used in drug and cell delivery; and
- biomimetic approaches to designing bioreactive, polymer-inorganic composites for replacement of enamel, dentin and bone and for the regeneration of the periodontal tissues.

The Tissue Engineering Program of the Branch

Tissue Engineering is an emerging interdisciplinary field which applies the principles of biology and engineering to the development of viable substitutes which, while replacing lost or impaired tissue function, also promote the growth of new tissue to replace that lost to disease, trauma or congenital defects. Tissue Engineering thus promises to provide new opportunities for clinical treatment.

Although synthetic prostheses have been provided a solution for replacements for craniofacial tissues, these materials do not replace most functions of the tissue. They can also lead to infection and fail over a relatively short time. Conductive approaches to tissue repair have been widely used in dentistry (for example, guided tissue regeneration). This is a fairly passive approach to tissue replacement. To date, in an effort to actively promote tissue formation, investigators have been developing inductive and cell transplantation approaches. Inductive approaches involve the delivery of bioactive molecules, typically growth factors and/or extracellular matrix molecules, to the site at which one desires the tissue to form. These molecules bind to cells present in the surrounding tissue and promote their movement to the site, multiplication and specialization to form the desired tissue. A novel approach has been recently developed to incorporate these molecules into biodegradable synthetic polymers that allow the continuous release of fully active molecules at the implant site. Polymeric, biodegradable scaffolds were spiked with plasmids for bone formation. It has been demonstrated that plasmid DNA encoding the inductive proteins can be incorporated into these polymers for sustained delivery *in vivo* (Mooney & Mikos, 1999; Bonadio & others, 1999). This approach leads to the uptake of DNA by cells at the implant site, and the synthesis and secretion of the growth factor that promotes bone regeneration in this case.

Cell transplantation is an attractive approach to engineer tissues when inductive factors are unknown, a large defect must be filled or the tissue is needed immediately. In this approach, a small biopsy is typically obtained from a patient and the cells multiplied *in vitro*. This produces a large cell number from a small initial tissue sample, thus allowing a large tissue mass to be created. The cells may then be combined with an inductive biodegradable polymer scaffold. The cell-polymer combination may be grown in the lab for a period or immediately placed in the patient. The polymer degrades over time as the tissue forms, leading to the formation of a completely natural tissue.

Both approaches are being utilized for the management of large mandibular defects due to head and neck cancers, periodontal disease and craniofacial defects and genetic disorder.

An area that has benefited from the advances in materials (that is, biodegradable polymers) for tissue engineering is that of drug delivery. An example is the development of a novel degradable polymer implant that will be used to reduce inflammation and help restore periodontal tissues by locally releasing salicylic acid. The implant is fabricated in such a way that the polymer backbone breaks down into salicylic acid (SA). This approach has already been tested in a mouse model. It was shown that the active poly (anhydride-ester) polymers reduced inflammation and stimulated new bone formation. Clearly, this active polymer is an important new method to actively deliver salicylic acid to a specific side and reduce inflammation and pain while simultaneously restoring bone (Eldermann, Macedo & Uhrich, 2001).

Biomimetics and tissue engineering are opening new avenues to the treatment of patients. Clearly, we have entered an era where we can begin to use biological solutions to design and fabricate new materials. Advances in material sciences, coupled with the sequencing of the human genome, offer a number of solutions for the repair, reconstruction, maintenance and regeneration of tissues and organs.

Currently, the Tissue Engineering Program of the Branch supports research projects focused on:

- gene therapy approaches for engineering craniofacial bone and for reconstruction of periodontal tissues;
- tissue engineering of the temporomandibular joint (TMJ);
- principles of osseointegration of bioimplants;
- development of "smart" oral mucosal grafts *ex-vivo* for the reconstruction of major oral defects due to oncologic resection, traumatic events and/or developmental disorders;
- tissue engineering for the regeneration of orofacial muscles, periodontal regeneration and treating bony dental defects;
- the role of mechanical forces in guided tissue regeneration; and
- development of control release/site specific drug delivery systems.

Research Training Programs at the NIDCR

To be able to do multidisciplinary/interdisciplinary research in Biomimetics and Tissue Engineering, training programs and curricula must be modified. The NIDCR, through the Office of Training and Career Development, supports various institutional and individual national research service awards and career development awards to support and encourage research training programs in the areas of Biomimetics and Tissue

Engineering pertinent to the mission of the NIDCR. More information on training programs can be obtained by visiting the NIDCR's web site: http://www.nidcr.nih.gov/research/career.htm.

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Acknowledgments

The author thanks her colleagues Dr William M Johnston and Dr Kenneth Gruber for their valuable suggestions.

Note

This paper does not represent the depth and breadth of the Biomaterials, Biomimetics and Tissue Engineering Branch but rather provides few examples of the sciences supported by each program in the Branch.

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Assessment of Factors Affecting Current Approaches to Dental Education

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Abstract

Curricular content in dental education should be evidence based. Unfortunately, there is general agreement that innovative curricula that introduce non-traditional approaches to clinical problems are difficult to inculcate into dental schools. The burden of blame is often placed at the feet of rank-and-file dental faculty, when in fact the factors influencing curricula are complex and multi-factorial. The history of dental education has documented from the 1926 Gies report to the 1995 Institute of Medicine summary a series of consistent and persistent issues which merit attention. While some burden for change must be born by current dental educators, many of the challenges facing dental educators are complicated by factors outside the school environment. This paper documents some of the factors affecting education and the barriers in addressing these factors, with eight specific recommendations to be considered by dentists, educators, researchers and dental organizations in an effort to improve the climate for incorporating new concepts in patient care in dental curricula.

Introduction

A prevalent paradigm in dental education states that the curricular content put forth by most dental educators, particularly clinical educators, is dated and has not kept pace with the rapid expansion of new knowledge generated by dental scientists. The argument goes that since approaches to clinical care (and thus the teaching of such clinical principles) should be evidence-based, that non-traditional approaches should be inculcated into curricula in a contemporaneous fashion. Clinical educators are severely criticized for their lack of innovation by practitioners, opinion leaders, health care policy makers and dental researchers. It is often said that a negative result of this lack of innovation is the prevention of introducing new and potentially superior approaches to patient care (Garrison, 1993).

On the surface there may appear to be inconsistencies with including this topic in a symposium on Alternatives to Caries Management geared to a wide audience dominated by practitioners, not educators. It may also seem odd that a research-oriented academic is addressing this issue instead of a formal educator. Yet, incorporating new approaches to patient care into dental curricula is critical not only to the health of patients but also to maintaining the dental profession as one worthy of confidence and trust. It is this author's belief that issues in education affect the whole profession and that identifying and implementing solutions must include all constituents in the profession, not just educators.

However, since the focus is on the educational process, let us begin in the dental school. In most educational environments, the assumption is that clinical educators are stodgy and slow to change, while researchers are sleek, fast and modern. This creates a chasm in the culture of the dental school environment and breeds a class system with the clinical educators often viewed as second-class citizens. So, let us begin with the assumption held by most professionals that education is bland, outdated and in need of an overall change. Placing all or the majority of blame on the clinical educator is akin to the conclusions made by researchers in a famous amphibian experiment. In that study, researchers sequentially amputated the limbs of a frog and observed the jumping behavior after stimulation with a loud noise. After the first three amputations, the frog responded to the noise by jumping, albeit abnormally. After the fourth amputation, the frog did not respond to the noise stimulus by jumping and the researchers concluded that amputating all the frog's appendages makes it deaf! The facts observed are correct—that more current evidence-based information *should* be taught. It is a faulty conclusion in that only educators should assume the burden.

The reality is that dental school educators are at the center of a maelstrom of complicated and often-competing imperatives. These factors include, but are not restricted to, the influence of licensing boards, government agencies, dental manufacturers, university administrators, third-party payers and lay media. We will return to some of these issues in more detail, but as with many issues, it may be useful to evaluate the history of the evolution of dental education to assess where it needs to go.

Historical Influences on Dental Education

The Carnegie Foundation for the Advancement of Education funded a series of reports on the status of professional education in the United States. In 1910, Abraham Flexner published a report on medical education, which was considered a landmark and influences both medical and dental education even today. This report discussed and supported what, at the time, were medical education innovations, including rationalizing the relationship between the professional school and the university, creating higher standards for student admission and faculty, and perhaps most importantly, moving towards a system of education grounded in scientific thinking (Wheatley, 1988). In 1926, William Gies published a report that focused on dental education. This in-depth study included a detailed description and evaluation of each existing dental school. Gies' report summarized five conclusions paraphrased below:

1. Dentistry deserves respect and attention from universities as an oral specialty.
2. Dental research should be as effectual as any in the university and the status of dental educators raised accordingly.
3. Dentistry is not a trade, and the preparatory curricula for dental students should be the same as medical students.
4. General practice should be the focus of pre-doctoral education.
5. Post-graduate training should be provided in all areas of oral science and include hospital and research experience.

While Gies' report had a significant effect on dental education, the weaknesses in dental education that he identified have been inconsistently addressed. In the Institute of Medicine's report, *Dental Education at the Crossroads-Challenges and Change* (1995), it is noted that in the intervening 70 years since Gies' report, numerous surveys and reviews of dental education have identified persistent curricular problems. *The Institute of Medicine Report* was a comprehensive review of dental education, and in part, sought to set a framework for constructive change and evolution leading to better models for teaching and research. However, some specific observations made in the conclusion of the report are remarkably similar to those made by reports going back to the original Gies research, namely:

1. There should be greater collaboration between the parent university and academic health centers;
2. there needs to be a commitment to research programs and building research capacity; and
3. curricula should be enriched in a timely fashion to incorporate new scientific knowledge into clinical applications.

They summarize these weaknesses in five areas. First, the report cites the weak link between basic science and clinical education. Second, current and emerging practice is insufficiently addressed in curricula. Third, comprehensive patient care models remain problematic in implementation. Fourth, medicine and dentistry are weakly linked. Fifth, the student's development of critical thinking is placed secondary to the volume of material covered in dental curricula.

Understanding these criticisms requires a view of how medical education has changed since the Flexner and Gies reports. Since these reports elevated scientific method as being critically important for clinical education, they promoted the idea that students should master scientific methods before beginning clinical training. This resulted in the "departmental" curricular model, which is still prevalent today. While this structure was a great advance over the non-scientific curriculum previously in place, it is criticized today for being a barrier to integrating science into clinical practice. Because of the weak link between medicine and dentistry, changes in medical education were not reflected in dental schools. Following the Flexner-induced changes, the next major changes in medical schools were spawned with the formation of academic health centers and the generation of "academic physicians" (Mandan & others, 1997). These individuals taught, provided clinical patient care and conducted research, actually implementing in their daily professional lives the principles espoused by leading educators. Later in the 1960s, medical education began to focus on problem-solving ability as an indicator of clinical competence and expertise. Barrows & Tamblyn (1981) described the two primary educational objectives of this approach as: 1) the acquisition of integrated knowledge related to clinical problems and 2) the development of problem-solving skills.

Dental education, in general, has been much slower to change the models of education delivery. One reason may be the need for dental students to simultaneously assimilate both didactic knowledge and perceptual motor skill to begin to identify and execute appropriate treatment regimens (Field, 1995). Certainly, critics of traditional educational models cite the over-emphasis of procedure-driven, requirements-based systems as a key barrier in developing critical-thinking skills in dental graduates. However, given the external pressure on dental educators to prepare students for regional licensing exams, it is no surprise that dental school clinical models are still highly influenced by focusing on providing students with repetitive experiences (requirements) at the expense of a more integrated and comprehensive approach.

The American Dental Association's Commission on Dental Accreditation made a highly significant policy change in an effort to begin addressing some persistent concerns noted in the Institute of Medicine report. In 1998, the Council shifted focus to outcome measurement in a "competency-based" curriculum. With respect to clinical education, the new standards are geared toward comprehensive patient care with much less emphasis on numerical requirements. Following the ideas of Hendricson and Kleffner (1998), the competency-based curriculum asks three questions. First, what knowledge, skills and values should entry-level practitioners possess? Second, which learning experiences do students need to acquire these competencies? Third, what is the proof of the student-establishing competency? In addition to the move towards comprehensive care, the Council also emphasized curricular objectives that include developing the critical thinking skills necessary for life-long learning. Formicola (1991) described traditional and alternative basic and clinical education models, which focus on developing a comprehensive and integrated model for dental education. Figure 1 shows the traditional,

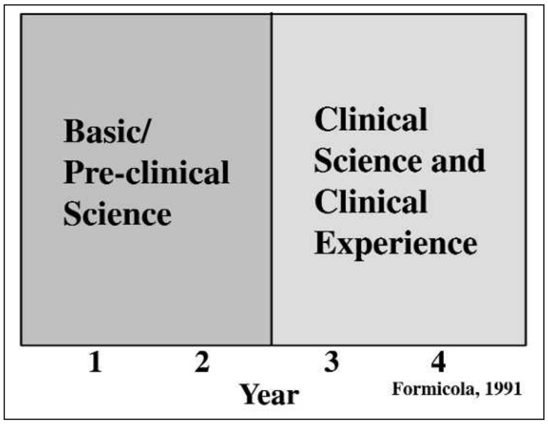

Figure 1. Traditional Curriculum.

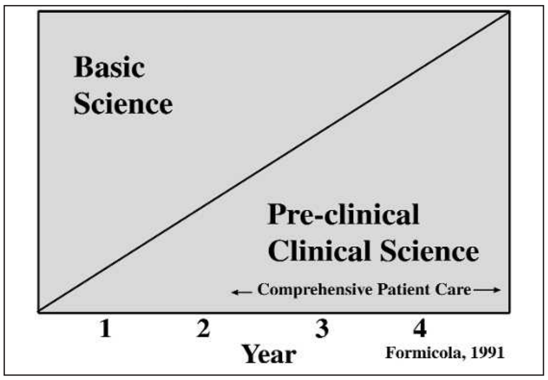

Figure 2. Diagonal Curriculum.

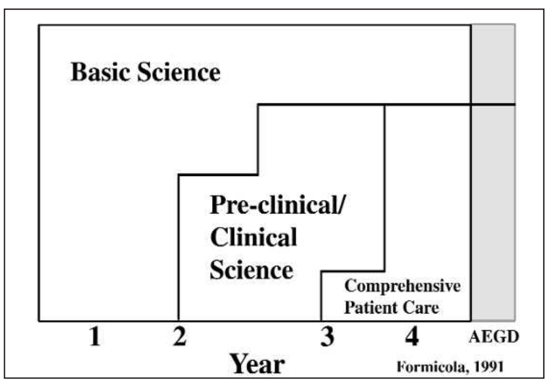

Figure 3. Integrated Curriculum.

Table 1. Traditional vs Integrated Learning

• Fact-oriented science	• Concept/problem oriented science
• Discipline focused	• Interdisciplinary
• Abstract knowledge	• Clinically-related
• Larger classes	• Smaller classes
• Lectures	• Guided discussion
• Multiple-choice exams	• Analytical exams

"Dental Education at the Crossroads" 1995

Table 2. Traditional vs Comprehensive Care

• Specialist role model	• Generalist role model
• Student-centered instruction	• Patient-centered education
• Segment patient care	• Continuity of patient care
• Procedure focus	• Evaluation and management focus
• Numerical requirements	• Competency criteria

"Dental Education at the Crossroads" 1995

non-integrated structure. Figure 2 illustrates a diagonal structure of basic and clinical sciences as a way to better integrate the basic and clinical sciences. Figure 3 outlines an integrated model of basic science and clinical education. Figures 2 and 3 propose a more gradual shift in emphasis from basic science to clinical education and are attempts to correlate the two areas more uniformly throughout the predoctoral program.

Structural changes in curriculum are not enough to improve the educational process. The link between science and practice must be consistently demonstrated in the didactic and clinical arenas. One emphasis in this area is the changing mode of education to the previously mentioned "problem-based" learning. Traditional and problem-based learning characteristics are summarized in Table 1. While a number of dental schools have initiated problem-base learning, there is little research that documents the success of this educational approach. One study documented a favorable response from faculty and students involved in pilot problem-based curriculum but were unable to demonstrate a better outcome when compared to a traditional approach (Walton, Clark & Glick, 1997). Medical education has used problem-based teaching models for nearly 20 years. Medicine's sophisticated development and testing would greatly benefit tailoring strategies for improving dental education (Mandan, & others. 1997).

The final piece in a more optimized curriculum is the move from a traditional, segregated clinical care model to an integrated, comprehensive care model. The ideal is to provide care in the school environment similar to that found in private dental practice. Table 2 compares the key components of this model to the traditional one.

To this point, we can see the historical roots of the issues in education and specific efforts to remedy them through changes in curriculum structure, education modeling and accreditation standards. The Institute of

Medicine report, however, notes a resistance to curricular changes and places most of the blame on conservative faculty who: 1) lack graduate training and are not involved with students who question tradition, 2) are unwilling or unable to participate in private practice and 3) are not involved in research. As noted above with the frog experiment, the data is correct—curricular changes are warranted and a more vibrant, evidence-based curriculum is warranted, but inditing faculty for the slowness of change ignores many critical factors in education.

The "Other" Factors Affecting Education

Clinical dental faculty struggle daily to provide an environment for teaching complex skills in what is essentially an apprenticeship educational model. While "standardized patients" are used extensively in medicine and may be valuable for the development of diagnosis and treatment planning skills, on graduation, dental graduates, unlike their medical counterparts, are expected to be operationally (surgically) proficient. Developing psychomotor skills requires some repetitive activity. It is a considerable challenge for dental faculty to treat the comprehensive needs of the dental school patient population, yet still provide the requisite repeated experiences needed for student competency. Schools have an ethical obligation to prepare their graduates for practice today and in the future. This includes preparing students to pass regional licensing exams. One may argue that these exams are outdated, but the fact remains that they are still required for practice and students must be ready for their challenge. Until the focus of exams is fundamentally changed, dental schools must address these demands.

A second significant factor is the basic economic model of dental education. Medical and dental models are fundamentally different in that supervising clinical medical faculty deliver clinical care while teaching. This care can be billed at provider reimbursement levels. Supervising clinical dental faculty, on the other hand, are monitoring student delivery of care. Typical dental school fees are lower than fee-for-service partly to attract patients to provide treatment opportunities for students and partly to execute the service mission of many schools. The net economic result is that the giant group dental practices run by dental schools are both expensive to operate and staff. Pre-doctoral dental clinics are generally loss leaders from a financial perspective. Moving towards comprehensive care models and problem-based learning modes of education may require increases in space and faculty for many schools, thus further increasing the cost of the educational environment.

Another often overlooked factor is a tension among school faculty, a tension which may often lie just below the surface but that contributes to a culture that resists meaningful change. While the ideal of a "triple-threat" faculty member who excels at clinical practice, teaching and research is set as a standard, the reality is that many faculty are forced by training, interest or the needs of the particular school to be less balanced in their academic life. The segregation, particularly of the science/research faculty from the clinical teaching faculty, particularly in pre-doctoral programs, creates a "class" society. Often, researchers view the teaching clinicians as second-class citizens within the school. The clinician's practical orientation is often viewed as not worthy of the "scientific" methodology practiced by formally trained researchers. In turn, clinicians view research-oriented faculty as totally out of touch with clinical care, especially with respect to preparing students to pass licensing boards and actually earning a living in the way dentistry is practiced and reimbursed in today's environment. Thus, even when new treatment approaches are supported by evidence-based research, the lack of communication (and often mutual respect) become a barrier within the school for promoting meaningful curricular and practice change. Even when clinical faculty are oriented to new advances, this lack of trust causes them to doubt the information, the practicality of teaching the information, the relevance of the information to the licensing gauntlet and the value of the information in helping graduates actually earn a living.

If there is a consensus that new education models are needed and new information must be taught, then the implementation cannot be done merely by saying that faculty should "just do it" without addressing the other factors that schools must handle.

Unfortunately, many of these factors are outside the control of the dental school and require a collaborative effort by educators, regulators, private practitioners and even the consumer public to effect changes.

What is Worth Researching and Teaching?

Assuming that new education models based on developing critical thinking skills in a comprehensive clinical care environment are adopted and funded, the question of what to teach students still looms large. In the 1980s, this author heard Dr Jack Preston boldly state that 50% of what is taught in dental schools is useless. His caveat, however, was that the challenge was determining which 50% should be eliminated. The new millennium answer, particularly for clinical education, is to base practice concepts on "evidence-based" research. Simply stated, evidenced-based decisions begin with the articulation of a clinical question that can be answered by human testing. It encompasses a review of all pertinent research to collate and review available information and critically analyze results and concludes with a recommendation directly related to decision-making and treatment in clinical care. Thus, asking the clinical question, "Can composite restorations be used as reliably as amalgam for posterior intra-coronal restorations?" presumably has an evidence-based answer. Yet in the sequence of determining what are the important questions, doing clinical trials, evaluating data and disseminating the conclusion is a void. Knowing what to do may be clear but determining who will do it, and perhaps more relevant, *who* will pay for the research, is not as clear.

A variety of entities: government, foundations, organized dentistry and private industry fund clinical research. However, it seems that no coordinated effort is in place to systematically identify and answer meaningful clinical questions. Federal funding through the NIDCR can be credited for advances in basic science areas and for advancing "biomimetics" as a future breakthrough. However, I believe the average dental practitioner sees little relevance of the funding priorities compared to the more immediate questions and issues facing dentists and patients now and in the near future. Just as there appears to be a deep rift between clinical and basic science faculty in dental schools, a great gap appears between the questions of importance to dentists today and the current NIH/NIDCR research emphasis.

This does not suggest that there is no value to the basic science research being funded. However, a better balance between basic science and applied clinical science research must be met to provide the resources to generate answers to the "evidence-based" questions facing educators and practitioners today. Leaders in dental education and research often perpetuate this lack of balance and perspective. In the first-ever Surgeon General's report on Oral Health released in May of 2000, one of the major findings was that scientific research is the key to reducing the burden of diseases and disorders that affect the face, mouth and teeth. A special task force was appointed by the American Dental Education Association (ADEA) to respond to the Surgeon General's report. In response to the Surgeon General's findings with respect to research, the task force recommended that the ADEA provide leadership to ensure incorporation of new science into dental academic institutions (Ferrillo & others 2000). Unfortunately, they only emphasized the links between oral and systemic health as a focus and centered their emphasis on improving "genetic literacy" in the dental curriculum. They suggested that human genomics would be the foundation for future oral health disease control. This author has no doubt that unlocking the molecular and genetic basis for disease will be the future foundation for oral care. However, the unbalanced emphasis on these long-term initiatives serves to disenfranchise a whole generation of dentists and their patients from the research resources needed to address the practical problems of the next 10-20 years. This author shares the view of the Institute of Medicine's report that recognized the lack of practical, evidence-based research initiatives and encouraged all funding agencies to more aggressively evaluate opportunities for expanded use of "simple" clinical studies.

While it seems that funding practical, evidence-based studies is largely ignored, some agencies should be recognized for their efforts in this area. The American Dental

Association Health Foundation and the Paffenbarger Research Center at the National Institute of Science and Technology consistently provide support for the practicing dentist. But the role of the NIDCR in addressing these unmet but important initiatives still needs to be clarified.

The Role of "Opinion Leaders" in Continuing Education

If dental clinical faculty are viewed as behind the times, and if graduating dental students are not trained to be critical thinkers and evaluators of the scientific literature, then where do practicing dentists get the information they need to stay current and evaluate new treatment strategies and techniques? As educators, we may resent the most influential sources, but the fact is that practitioners focus on the evening "expert" seminar speaker and the "throw-away" news journal for the bulk of their "scientific" information. Often, these lecturers' champion approaches they have "researched" in their own practices and discredit the dental faculty as being outdated, behind the times and not "practical." The "evidence-base" provided by these speakers and the non-refereed journals may be purely anecdotal, but the practitioner seems drawn to these sources as a moth to a flame. We may be critical regarding the lack of discriminating thought on the part of dental graduates, but as educators, we may in fact be the cause. If clinical faculty and basic science faculty communicate poorly and do not exhibit mutual respect in the school environment, it might be that we train our graduates to seek information from other sources. No matter what the reasons for the influence and success of the opinion leader seminars, it is our obligation as a profession of educators, researchers, dental leaders and practitioners to assure in some way that true evidence-based information is disseminated.

Summary and Recommendations

The fact that new and innovative techniques and technology are not inculcated into dental curricula in a robust and timely way is related to a host of factors, many not under the control of dental educators. While dental faculty can take responsibility for improving the dialogue between clinical and basic science educators, the profession as a whole must take initiatives to address licensure requirements, research funding priorities, dental insurance reimbursement policies and control of valid information dissemination. Having raised so many barriers, it is only appropriate that this author address these issues with specific recommendations:

1) Seek to change the culture of dental academia to give both science and clinical faculty their due respect and influence.
2) Seek to change the paradigms of practice to reward practitioners using care, skill and judgement, not just procedures.
3) Improve the academic curricula to improve the development of critical thinking and life-long learning skills for graduates.
4) Allocate resources and money to train all educators in problem-based learning strategies and at least cover the basics of understanding evidence-based research.
5) Plan and implement a coherent, evidence-based research plan to address issues of direct concern to today's dentists and patients.
6) Develop a national plan to peer-review and certify all continuing education given for licensure credit.
7) Create an Internet-based "virtual clearinghouse" review by panels which quickly and accurately disseminate evidence-based conclusions to practitioners.
8) Normalize dental licensure requirements to a national standard and periodically review the exam for relevance to current standards of care.

While these suggestions may not be radical or groundbreaking, this author offers them as a framework for initiating a dialogue that might lead to improvements in curricula and ultimately better patient care.

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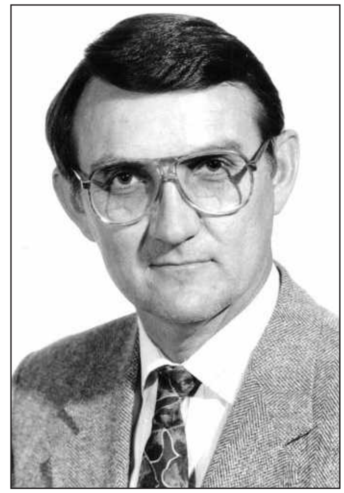
New Approaches for the Underserved

CR Hook



Charles R Hook

Traditionally, the dental profession has been committed to providing oral health care for "all people." No other health profession has worked more diligently to eradicate the health problems associated with its discipline. In recent years, dentistry has placed emphasis on target groups, including the medically compromised, the geriatric and those suffering from infectious diseases such as AIDS and hepatitis. Dental education has traditionally focused on providing a high quality educational environment for dental students in a school setting where students spend approximately four years learning philosophical and factual information and developing technical skills to become a competent practitioner. Little emphasis, however, has been placed on access to dental care for the underserved. The goals of this paper are to stimulate thought concerning the role that research and education can play to combat dental caries among those who cannot afford to pay and to reawaken the profession's responsibility for this enormous task.

A review of the socioeconomic history of dental caries in undeveloped countries reveals some interesting information. Areas in Africa, South America and China have a lower decayed, missing and filled rate (DMF) than newly industrialized countries such as Taiwan, Mexico, Chile and Peru (0.2 - 1.7 DMF and 1.6 -5.9 DMF, respectively) (Ettinger, 1999). A relationship seems to exist between increased industrialization, consumerism, refined sugar consumption and dental caries. However, highly industrialized countries such as the United States, Britain and Japan have shown some progress towards a decrease in the DMF rate. This reduction can be attributed to an increased emphasis on research technology, oral hygiene, water fluoridation and oral health care spending by consumers and the government. The success is not due to surgical intervention. Instead, it is attributed to knowledge, education and preventive services.

"Even though a consistent decline in dental caries has been observed in the US since the 1960s, it is still the most common childhood disease that is not self-limiting."

Even though a consistent decline in dental caries has been observed in the US since the 1960s, it is still the most common childhood disease that is not self-limiting (Vargas, Crall & Schneider, 1998). In South Carolina public elementary schools, the South Carolina Department of Health and Environmental Control estimate that dental problems are the number one excuse for missing school (next to the common cold), and 80% of all children in the United States are affected by dental caries by age 17 (Vargus & others, 1998) (SC-DHEC, 2000).

Maxwell Anderson, David Bales and Karl-Ake Omnell wrote a landmark paper in 1993 entitled, "Modern Management of Dental Caries: The Cutting Edge is Not the Dental Bur" (Anderson, Bales & Omnell, 1993). This paper clearly pointed out that dental caries is an infectious disease, which should be managed as such; however, dentistry has been treating the symptoms instead of the disease. In fact, we have known since 1905 that bacteria cause dental decay (Miller, 1905). In 1927, an article appeared in *The Dental Cosmos*, entitled, "The Bacterial Invasion of the Enamel in Dental Caries" (Bodecker, 1927). And in 1931, an advertisement appeared in the same journal entitled, "Reduction of Oral Bacteria Considered of Major Importance by Scientists in Prevention of Dental Caries" (Advertisement, 1931). So, we have known for at least 90 years that bacteria cause this disease, yet we have failed to formulate an effective and efficient way to deal with this reality.

We know the predictors for people at risk for dental caries. They include past caries experience (DMF rate), fluoride exposure, tooth morphology, microbial agents and socioeconomic status. Children from families with low socioeconomic means who live in isolated rural areas or come from overpopulated urban areas comprise a significant at-risk group. Children from families with little formal education, those with single parents and families who have recently immigrated to the US are included in this group (Vargus & others, 1998).

There is no doubt that the incidence of caries in the US depends on socioeconomic status. Eighty percent of all permanent teeth with carious lesions are found in 25% of the population (Drury & others, 1996), and 12% of the children in the US have one-half of all the carious teeth (Ettinger, 1999). Vargus has reported that decreased income equals increased caries. The percentage of 6 to 12 year-olds with a carious lesion can be related to income versus poverty levels (41% of children living at the poverty level have a carious lesion, whereas only 17.1% of the children whose family income is three times that of the poverty level have a carious lesion) (Vargus & others, 1998).

Barriers to providing traditional dental care to the underserved are many, but a lack of adequate funding sources and an uncertainty as to who is responsible for the health care of the underserved are significant. Who should take the lead? The government, the dental provider, the community or the individual?

Dental health and dental epidemiological research are not high priorities for most federal programs, and dental care is a low priority among the indigent. Only 20% of Medicaid-eligible children receive routine preventive dental services (Vargus & others, 1998). There are a number of reasons that our current dental workforce has been unable to address the problem of the underserved. Among them are limited access to indigent communities, high debt among new graduates and low reimbursement by Medicaid.

Our present dental delivery system offers some avenues for service to the general public, including education, water fluoridation, new restorative materials, preventive techniques and general medical advancements. Education is certainly a key. It is from this platform that all other services arise. Both public agencies and dental providers have a responsibility to educate the public. Marketing tools, such as television, should be used. Dental schools also have a duty to educate future dental providers so that preventive and restorative services can be made available to those who traditionally have been on the fringe of dental care. Dental education has traditionally focused on teaching ideal treatment, but in the area of public health, it must be understood that all services cannot be offered to all people. Economic realities must be appreciated and managed. Curriculums have to be developed that teach dental students the need that exists and ways to remove barriers to access of care. At the Medical University of South Carolina an example of this type of program has been the development of a program that sends dental students into underserved communities in a mobile dental van. Students see the need, provide care and gain an appreciation for the problems associated with access to care.

Likewise, continuing education courses for graduate professionals often focus on ways to increase revenue, manage and promote office efficiency and new materials and techniques for paying customers. Rarely does a course on public health attract large numbers of paying professionals intent on learning ways to better deliver services to people with limited ability to pay. The profession of dentistry has a responsibility to society to develop systems that teach and promote oral health to everyone, not just the affluent. This duty stems from the very definition of "professional." Profess means to teach. Society, through licensure, grants a monopoly to those trained in health care. With this privilege comes the responsibility to serve.

As we have noted, the surgical model of dental care has not been a cure for dental disease, only a short-term solution. For years, the dental profession has treated caries as a symptom instead of a disease. Confounding this approach has been the fact that socioeconomic status dictates access to this expensive surgical model of care. There has been little emphasis on an integrated plan to combat social, health and economic issues facing low-income families.

A new model of oral health care is slowly being advanced throughout the world. A number of terms have been used to describe this approach, such as minimal intervention dentistry, preservation dentistry and the medical model for treatment. With this in mind, we must ask ourselves how can the profession of dentistry enter this new age with a revised, enlightened approach to this ancient problem.

So what can be done? Certainly, we should continue to refine traditional treatment and make it available to all people. This includes water fluoridation, which has already halved tooth decay in five year-old children and reduced the dental caries divide between the rich and poor (Jones & Worthington, 1999). School programs, including oral hygiene education in underserved communities, as well as pit and fissure sealant placement in primary school children, need to be expanded. An emphasis should be placed on recruitment of minority applicants who demonstrate a greater tendency to return to minority communities where many of the underserved reside. And finally, it is our responsibility as a profession to be aware of new advances in treating the disease of caries and to incorporate the advances into our practices and our public health delivery systems.

Exciting work is progressing in the area of technology. Gene replacement therapy holds great promise, and research conducted at leading universities is providing hope. Strains of streptococcus mutans that are not virulent may replace pathologenic strains and literally stop dental decay as we know it. This work is reviewed by Dr Jeff Hillman in an article contained in this supplement.

Until such time as this and other therapy is available, there are innovative steps that can be considered today. Listed below are methods and materials that can be brought into play today to help members of our society who for various reasons do not benefit from traditional treatment.

Restorative materials can be used to combat the socioeconomic disparity in access to oral health care. Most clinicians are familiar with glass ionomer restoratives that release fluoride and can be used effectively in high-risk patients. Quick-setting glass ionomers are available, which can be used in a specific caries control program known as ART (atraumatic restorative treatment). Under this protocol, lesions in patients at high risk are quickly and efficiently excavated and "restored" with these "self-retentive," "preventive" materials to remove nidi of infection as the underlying disease is managed (Mjör & Gordan, 1999).

Other work is being conducted on materials that act as "smart" materials. One such material detects when the pH of the mouth reaches a critical pH, then releases a buffering agent to raise the pH above that, which results in demineralization (Baranska-Gachowska, Borkowski & Ziaja, 1999).

Other scientists are developing remineralizing solutions in the form of dentifrices, chewing gums and toothpastes (see Laurence Chow's article also featured in this supplement).

Fluoride varnishes (5% NaF in an alcoholic suspension of natural resins) are now available and used worldwide to deliver concentrated levels of fluoride directly to teeth in a very simple, effective and cost efficient way. Six monthly applications have resulted in a 37% caries inhibition in children with high caries risk (Zimmer, Robke & Roulet, 1999).

The relationship between refined sugar and dental caries is well documented. Diet counseling emphasizing simple concepts, such as eating cheese as a snack, has shown remarkable effectiveness (Herod, 1991). Avoiding sugary snacks and carbonated sodas is accepted dietary counseling but unfortunately is under-prescribed by many clinicians (Ettinger, 1999).

When we recognize that bacteria cause dental decay, it seems obvious to bring into play antimicrobials, such as chlorhexidine (.12%) rinses. These rinses can play an important preventive role when combined with a comprehensive preventive program (Bowden, 1996).

A simple, yet effective preventive and remineralization technique is the chewing of xylitol gum. Xylitol is a polyol and can be used as a sugar substitute. Habitual xylitol consumption appears to select for mutans streptococci, creating impaired adhesion properties. That is, they shed easily to saliva from plaque. A 40-month study in Belize showed a 43% decrease in carious lesions (Makiinen, 1995). These compounds contain an extra hydrogen and have shown remarkable effectiveness in numerous clinical studies. Chewing these gums for five minutes three times a day has shown consistently positive results. Techniques such as this provide a simple, inexpensive control in battling the disease of dental decay; however, it is surprising how few dentists recommend this therapy.

Conclusions

Although recent advances in dental equipment, materials and techniques have advanced the quality of service given to the dental patient, these services, by and large, are limited to those who can afford them. The profession's commitment to "all people" implies that the practicing dentist has a responsibility and an appreciation for the dental needs of those who cannot afford the services. If the profession does not take the leadership in efforts to meet the oral health care needs of the underserved, then the door is left open for other organizations to step in and control the access to care, including the government and managed care.

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Metallic Restorative Materials and Historical Standards

Metallic Restorative Materials and Historical Standards

THEME 2

©Operative Dentistry Supplement 6, 2001, 81-85

Performance Standards for Competitive Dental Materials

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As we move through time, we are continually faced with the opportunity to change. This is as true for our restorative material selection as it is for anything else. In order to know whether or not we should change, we must have an understanding of where we are currently. If the change will not provide improvement, is it wise to pursue?

How we determine improvement depends on our paradigm, our view of the objectives of restorative dentistry. Traditionally, dentists have believed that slowing down the restorative cycle as much as possible is the ideal pursuit of restorative dentistry. We live in a time that challenges that paradigm. The challenge comes through a push for esthetics and the increased predictability of implant dentistry. Lectures are being given which teach that our concern for the disease process should be secondary to improving the self-esteem of our patients by maximizing the esthetic result as rapidly as possible, even if it means re-restoration within a short period of time. Much of that thought is driven by the idea that implant dentistry is always available and is as comfortable, functional and esthetic as a natural dentition.

This paper provides some insight into where we are in terms of restorative dental materials standards. The hope is that we will be better able to pursue changes that will move us in a positive direction. It is written with the belief that in some way the new must resolve to be an improvement over the traditional before we can justify the change. The preservation of tooth structure is an important characteristic of restorative dentistry until proven otherwise.

The Longevity Standard

The traditional performance standard is centered on the concept of longevity. How long will our restorations last? The longer a restoration lasts, the fewer the number of times a tooth will require restoration in a lifetime. Therefore, pursuing a material that will withstand the rigors of the oral environment has long held our attention.

Gold was used as a restorative material as early as the 4TH century BC (Ring, 1985). Gold and its alloys have seen widespread use for decades. The expected lifetime of modern gold restorations has been investigated by Mjör & Medina (1993). They investigated the mean age of 2,564 cast and compacted gold restorations., and found longevity of 16 and 18 years, respectively. In the case of 111 restorations, they also reported a mean failure age of 18.5 years for both types of gold. Stoll & others (1999) reported on the longevity of cast gold inlays and partial-coverage gold crowns by providing 10-year survival rates. They found that 85.7% of 3,518 cast gold restorations placed in a dental school clinic survived 10 years. Bentley & Drake (1986) found similar results when they reported a 10-year survival rate of 91.1% in a dental school clinic.

It may be desirable to view something other than gold as the benchmark for our restorative treatment. Dental amalgam has a long history of use and has been a more financially attractive alternative for many people. An argument could be made that the new restorative materials should only have to compete with the standard set by dental amalgam. A search of the literature provides varying results. Hawthorne & Smales (1997) looked at 2,931 restorations in three private practices. The median survival time for the amalgam restorations investigated was 22.5 years. Mjör, Dahl & Moorehead (2000) looked at 6,761 restorations and reported a median survival time of 11 years for dental amalgam. Thus, two different study populations provided very different results. To further complicate the issue, Smales (1991) reported 15-year survival rates of 72% for amalgam restorations which replace cusps. It has been taught that cast gold restorations are indicated when cusps are involved (Baum, Phillips & Lund, 1981). From the results of reported survival rates, it appears that this decision should be based on personal abilities and preferences.

The same types of problems appear when evaluating the longevity of composite resin restorations. Hawthorne & Smales (1997) reported a median survival rate of 16.7 years, while Mjör & others (2000) reported median longevity of eight years. They also reported that glass-ionomer restorations have a median survival of four years. In contrast, Matis, Cochran & Carlson (1996) showed a 10-year survival rate in the range of 76% for glass ionomers.

Upon reading these studies, it becomes very evident that study design significantly impacts the reported numbers. Things which may influence the results include the number of restorations evaluated, the number of operators used in placement, the type of practice involved, the sex of the operator, whether the design was prospective versus retrospective and whether or not a randomized and controlled design was utilized (Mjör & others, 2000). One method used to investigate this evidence is a meta-analysis of the literature. This analysis can be viewed as a study of the studies. It critically evaluates the validity and quality of the literature on a given topic. Few actually exist in dentistry. However, Downer & others (1999) have published a meta-analysis reviewing the topic of Class I and Class II restoration longevity. Amalgam, composite resin, glass ionomer and cast gold restorations were included. The authors searched all the available literature and located 124 research reports on the topic. Of those, only eight were considered relevant and of satisfactory validity and quality to be included in the analysis. They were unable to provide any statistical validity to their findings due to the low number. What they did report was that 50% of these restorations probably last 10-20 years, regardless of the type of material used.

Studies that evaluate ceramic systems are available (Fuzzi & Rappelli, 1999; Kreulen, Creugers & Meijering, 1998; Roulet, 1997). However, these studies are for relatively short periods of time or use small sample sizes. Kihn & Barnes (1998) reported promising results with a 100% survival rate at four years for 53 porcelain veneers. A six-year clinical trial evaluated 49 Class I and II ceramic inlays and onlays (Hayashi & others, 1998) and reported a 92% longevity. Sorenson & others (1998) reported on three-unit In-Ceram fixed partial dentures in a three-year prospective study. The failure rates were 0% for anterior, 11% for premolar and 24% for molar regions.

The evidence for longevity seems to indicate that the materials available to restorative dentists today can provide predictable performance for a reasonable amount of time if the placement parameters are well-monitored. Another perspective in looking at materials standards evaluates the mode of failure of the restorative material. If significant destruction of the remaining tooth structure occurs during the failure process, the objective of maintaining a tooth for the lifetime of the patient may be significantly compromised.

The Caries Standard

Despite good historical performance of many materials, all types of restorations do exhibit failure. Longevity can be increased by understanding and preventing the failure mechanism. One mode of failure common among many types of materials is the presence of caries. Mjör & Medina (1993) reported that for replaced restorations, 22% of the cast gold restorations and 21% of the compacted gold restorations were replaced due to caries. Stoll & others (1999) stated that the most frequent reason for failure of gold restorations (34%) was caries. Dental caries was reported to be the most frequent cause of failure (38%) in an evaluation of fixed partial dentures (Libby & others, 1997). Burke & others (1999) reported the reason for placement or replacement of 9,031 restorations in the United Kingdom. Their study included amalgam, resin composite and glass ionomer restorations. Regardless of the material, the most common reason for restoration replacement was the presence of caries (22%).

One means of trying to reduce the presence of decay around restorations has been the use of fluoride-releasing materials. Hicks & Flaitz, 2000 reported a decrease in caries activity around these restorations. Tooth structure adjacent to these materials would then require fewer restorations. Qvist & others (1997) reported that the surfaces of primary teeth adjacent to glass ionomer restorations required significantly fewer (12%) restorations resulting from caries than did primary teeth adjacent to amalgam restorations (21%). It appears that fluoride-releasing materials can reduce caries activity but will not eliminate it.

The Wear Standard

Early resin composite restorations had a history of exhibiting problems resisting wear and degradation (Phillips, 1991). Hybrid composite systems minimized the concern about wear resistance. The 1993 ADA Specification #27 on Resin Based Filling Materials states, "Wear tests and surface hardness tests have been considered, but evidence suggests that wear, *per se*, is not a problem with the new generation of Class A materials." (Class A materials are intended to restore occlusal surfaces.) No wear testing was included in this specification. A recent study by van Dijken (2000) indicates that this statement may not be correct. He reported that a main reason for failure in both direct and indirect composites after 11 years was occlusal contact area wear. A new ADA Acceptance Program entitled Resin Based Composites for Posterior Restorations is considering adding requirements on wear resistance. These requirements would call for loss of no more than 50 microns of material between 6 and 18 months of service when evaluating occlusal contact and contact-free wear for 20-30 restorations. While this represents a short clinical study of small sample size, it acknowledges that wear for composite restorations continues to be an issue of concern.

The Economic Standard: Trends and Practice

An evaluation of scientific studies to determine standards for restorative materials is a valuable exercise. Another factor of considerable importance is the driving force behind the introduction of new materials to the marketplace. What are dentists looking for in new materials? Ivoclar/Vivadent Company, Inc (1999) conducted a significant survey of practicing dentists. Dentists were asked to disclose their reasons used for selecting a resin composite. Twelve percent of the respondents reported wear resistance as a factor, but the most frequently reported selection criteria were handling and versatility (48%). For these dentists, the actual physical properties of the material were less important than the handling and versatility of the material. Is this response consistent with a changing paradigm? Is longevity still of primary importance? The ability to handle a composite easily should provide increased longevity. However, is that the motivating factor behind the survey response? What is forcing the maintenance and improvement of the physical properties of these materials? Scientific evidence provides some ammunition for continued materials development based on longevity. But, the growing esthetic and implant-based paradigms *might* be having a far greater and a far more subtle impact.

Conclusions

In order to identify a standard of performance, your paradigm must first be identified. Your perspective will have tremendous impact upon this question. Assuming that longevity of restorations is important, there are many materials available today which should provide adequate performance for 10-20 years. This includes many esthetic materials. Continued efforts need to be made to reduce the number of failures, particularly those associated with mechanisms destructive to the life and support of the tooth. Better understanding of the carious process, better diagnosis and more conservative treatment options will continue to transform restorative dentistry from a discipline that treats symptoms to a therapeutic discipline that treats a disease process.

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Mercury, Its Impact on the Environment and Its Biocompatibility

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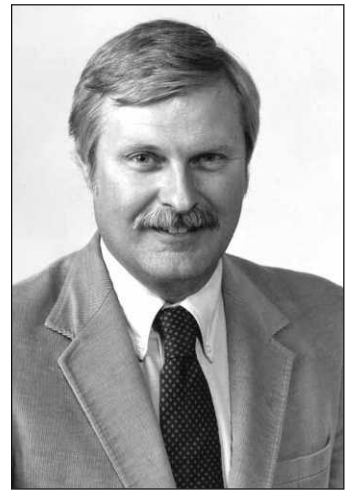

John W Osborne

Abstract

The metal mercury is widely used in our society. Some of its unusual properties include that it is a liquid at room temperature, has a high specific gravity, acts as a catalyst in certain reactions and is toxic in multiple forms to living organisms. Dentists should be aware of the broad parameters of mercury's toxic properties, and specifically its hygiene and vapor hazard in the dental office. Dentists should examine the forthcoming technology for reducing mercury discharge from their offices. They should also understand the complex aspects of medical/psychological profiles of patients with "amalgam illness" and the needs of such patients for proper treatment.

Introduction

Mercury is an element that has been known for at least 4,000 years (Chang, 1985). It is an intriguing metal that is liquid at room temperature and widely used in our modern society. Its medical aspects are well understood; yet, it is highly reviled by the general public for its misunderstood and/or misrepresented toxic properties.

In an effort to narrow and condense what is a very broad subject, this paper is divided into several sections. They include: mercury, its history, the compounds found in the Merck Index, biocompatability, toxicity of elemental mercury and its compounds, disposal of mercury (related to the dental office), release of mercury from dental amalgams and the medical consequences of its release. In addition, a section is included on the psychological profiles of individuals with "amalgam illness" and how to address this complex, yet sensitive issue.

Mercury

Mercury is the 80TH element in the periodic chart. Its synonyms are quicksilver and hydrargyrum (water metal), hence, its symbol Hg (Sunderman, 1988). It is a silvery-white metal with a mirror-like surface when it is a liquid and has an atomic weight of 200.6. Mercury has a specific gravity of 13.55, melts at –38.8°C and boils at 356.7°C (Merck Index, 1996). It is a rather poor conductor of heat compared to other metals and a fair conductor of electricity (Lide, 2000). The commercial unit of mercury is a "flask," which weighs 76 lbs. (Lide, 2000). As a vapor, it is odorless and colorless and has a high vapor pressure (Putman & Madden, 1972). These combinations make mercury a potentially serious inhalation hazard (Patnaik, 2000). Air passing over a 10 cm^2 surface at 1 L per minute at 25°C becomes 15% saturated and acquires about 3 mg/cm of mercury vapor (Giese, 1940). Pure mercury does not tarnish when exposed to air at ambient temperatures (Patniak, 2000). It forms alloys, a process called amalgamation, with most metals other than iron (Merck Index, 1996). In nature, it has seven isotopes and 35 additional isotopes and isomers are known (Lide, 2000). Interestingly, mercury is the only metal that has a planet named after it (Sunderman, 1988).

Mercury occurs naturally and is found throughout the environment (Chang, 1985; Lide, 2000). It is in the air, water and the food we consume. Although extremely rare in nature as an unreacted metal, it is commonly found as cinnabar (HgS) (Merck Index, 1996; Lide, 2000). Sources of this element in the environment include: volcanic activity and evaporation from the oceans, 30,000-150,000 tons per year (Weiss, Koide & Goldberg, 1971; Korringa & Hagel, 1974; WHO, 1976; WHO, 1989); burning of fossil fuels at 20,000 tons per year (Gavis & Ferguson, 1972; National Academy of Science Panel, 1978) agriculture contributes 3,000 tons per year (WHO, 1989); smelting and mining operations at another 10,000 tons per year (WHO, 1990); and sewage releases 15,000 tons per year (WHO, 1976). The earth's crust contains 0.5 µg mercury/g and soil-forming rocks contain 10-300 µg mercury/g (International Atomic Energy Agency 1972). Interestingly, the mercury levels in air are generally highest over humus topsoil (WHO, 1976). Because of mercury's high vapor pressure, air-mercury levels are highest in the summer and mid-day, and lowest in the winter and midnight (Schroeder, 1974). The average atmospheric mercury level is 1.5 $\mu g/m^3$, but in industrial areas the mercury level can exceed 50 $\mu g/m^3$. The major pathway for the global transport of mercury is via the atmosphere (WHO, 1976). The daily consumption of mercury from air, food and water is 10-20 µg, and this is on a low fish diet (Williams, 1981; Vostal, 1972)

History

Mercury's many unique properties have made it a curiosity for man since the beginning of history. Its toxic properties were known in early recorded history (Maurissen, 1981). The Chinese used it in many areas in ancient times (Bidstrup, 1964); it has been found in the tombs of Egyptians dating from 1500 BC, and in 500 BC, Hindus used salts of mercury for therapeutic purposes (Lide, 2000). The Greeks and Romans were aware of the toxic effects of mercury, and in 400 BC Aristotle is credited with calling it quicksilver (Sunderman, 1988). Paracelsus' book (1988) on medicine in 1538 had a whole section on mercury that included symptoms of poisoning, and his explanation of "dose makes a poison" is directly related to mercury (Cumings, 1959). The 14TH century English nursery rhyme, "Rub, a dub, dub. Three men in a tub…" (*Treasury of Mother Goose*, 1984) is a political satire on the middle class being infected with syphilis. The treatment for syphilis in those days was sitting in a heated tub of mercury and breathing the mercury fumes (Bidstrup, 1964).

Industrial poisoning from mercury mines was well known centuries ago (Cumings, 1959). Hunter (1943) reported that in 1804 a fire in a mercury mine in Austria sent vapors into the countryside, affecting 900 people. Use of mercury nitrate in the preparation of fur felt led to 'the hatter's shakes' (Aronson, 1998; Sunderman, 1988). Physicians, prior to the 18TH century, regarded mercury and its compounds as one of the few true medicines they had to treat diseases (Sunderman, 1988). Even as late as 1940, calomel and Mercury Blue Mass, elemental mercury mixed with honey and licorice, were commonly used as cathartics (Merck Index, 1996; Sunderman, 1988). Although mercury toxicity is relatively rare in individuals not associated with mining or industry, famous people such as Isaac Newton (Lieb & Hershman, 1983), Paganini (O'Shea, 1988a & b), President Andrew Jackson (Cernichiari & others, 2000; Deppisch & others, 1999), and Edgar Allen Poe (Shoemaker, 1997) possibly suffered from mercury intoxication.

Today, the unique chemical and physical properties of mercury are widely used in industry, agriculture, medicine, mining, dentistry and other areas of everyday life (Sunderman, 1988).

Merck Index

This author found 57 compounds that contain mercury in the Merck Index (1996), an encyclopedia of chemicals, drugs and biologicals. Some of these are used in the manufacture or processing of felt, fireworks, batteries, blackening brass, photography, pigments for rubber and plastics, wine coloring, destroying phylloxera and medicine. The latter group of medical compounds comprised 75% of the list and included antibacterial, antisyphilitic, topical antiseptic, immunosuppressant, anti-infective, fungicide, diuretic, cathartic and preservative agents.

The website: chemicalfinder.com lists more than 250 mercury-containing compounds.

Biological Activity

The human body has 70 known trace elements. Of these, 35 are known to have some biological activity, but mercury is not one of these trace elements (WHO, 1996). Zinc, iron, calcium, magnesium, copper and chrome are well recognized as having biological activity. Mercury, cadmium and lead have no known function (Conning, 1987; Chang, 1985). The research on carcenogensis of mercury and its compounds has indicated no positive results in humans, (Boffetta, Merler & Vainio, 1993), but teratogenesis of organic mercury compounds has been observed in numerous systems (Leonard, Jacquet & Lauwerys, 1983; Hansteen & others, 1993).

Mercury Compounds a) Inorganic

Inorganic mercury compounds are highly toxic, and poisoning is usually the result of accidental or intentional ingestion (Winship, 1985; Mucklow, 1989; Weiss, Trip & Mahaffery, 1999). Mercury chloride ($HgCl_2$) is listed as a “violent poison” in the Merck Index (1996). Because of the caustic nature of this compound, when ingested, the lining of the GI tract is lost. The patient exhibits severe pain, nausea, vomiting and diarrhea (Yoshida & others, 1997). Cardiovascular collapse may occur within several hours after exposure (Seu, 1998). Patients do not generally die from just mercury toxicity, but from renal failure due to the severe loss of fluids and proteins. Patients that die do so in six to 23 days (Seu, 1998). Oral burns are noted in 13% of the cases where mercury chloride was ingested (Troen, Kaufman & Katz, 1951). Mercury chloride is also irritating to the skin (Aberer, 1991) and exposure in this manner causes urticaria and vesication. Preparations of mercury chloride (calomel) have been known to cause a toxic reaction in patients (Kang-Yum & Oransky, 1992; Balluz & others, 1997; McRill & others, 2000). It has been used as a teething powder for children (Seu, 1998). Chronic use of calomel as a laxative has caused renal failure, severe colitis and dementia (Wands & others, 1974). Chinese herbal medicines have been shown to have mercury compounds that can cause death (Kang-Yum & Oransky, 1992).

Children have swallowed small button batteries and had the contents spilled into the gut (Mant & others, 1987). Mercury oxide is a constituent in many of these batteries, and the absorption of mercury can cause elevated blood and urine levels (Mant & others, 1987; Litovitz & Schmitz, 1992). Other compounds include mercury sulfide, Chinese vermilio (used as the red color in tattooing and can cause an allergic reaction) and mercury fulminate (a detonator widely used in explosives) that can cause systemic contact dermatitis (Goldfrank & others, 1990).

b) Organic Compounds

Organic mercury compounds are short- and long-chain alkyl and aryl compounds. Of alkyl compounds, methyl and ethyl are the most common and very toxic (International Atomic Energy Agency, 1972; Dales, 1972). These compounds are absorbed 90% into the gut (Seu, 1998; Klassen, 1990) and have a biological half-life of 70 to 90 days (Winship, 1986). Methylation of mercury by micro-organisms is well-accepted (Renzoni, Zino & Franchi, 1998; Jernelov, 1972). These forms of organic mercury get into the food chain, are generally concentrated as they move up the food chain and finally are consumed by humans (Renzoni & others, 1998). Episodic methyl mercury poisoning has occurred to large groups of people where fish and/or shellfish are a major part of their diet (Takeuchi, 1982). Industrial discharge of mercury in the waterway is converted into methyl mercury, and during chronic consumption degenerative neurological disorders are found in the population (Putman & Madden, 1972; Powell, 1991). The classic example is Japan's Minamata Bay episode in the 1950s. The consequences of this environmental disaster have been thoroughly documented (Takeuchi, 1982; Moutinho & others, 1981; Tsubaki & Irukayama, 1977; Powell, 1991).

The consumption of wheat seed and/or other grains treated with aryl mercury compounds for their anti-fungicidal properties has caused serious environmental disasters. The treated seed is ground into flour or fed to livestock instead of being planted (Putman & Madden, 1972). When the bread or meat is ingested, the aryl organic mercury is converted into mercuric ion and symptoms of the mercury poisoning occur within two months of exposure (Seu, 1998). Depending on the mercury compound, the patient will exhibit visual, cerebellar and sensory dysfunction or may exhibit renal and gut toxicity (Bauer & Fuortes, 1999).

Mercurochrome, a topical antiseptic, has caused mercury toxicity in infants (Goldfrank & others, 1990; Yeh, Pildes & Firor, 1978). Thimerasol, 49% mercury by weight, is a widely used preservative in pharmaceuticals. A wide spectrum of antibacterial activity with Thimerasol can be obtained when concentrations are 0.02-0.1%. It is used in ophthalmic solutions; soaps; hypoallergenic cosmetics; and flu, rabies, diphtheria, gamma globulin and various vaccination shots (Seu, 1998). The American Pediatric Association has debated its use in vaccinations (Anonymous, 1999).

c) Elemental Mercury

Elemental mercury has little or no toxic effect when swallowed (Cintron-Rodriguez & Lugo-Rodriguez, 1982; Langford & Ferner, 1999; Fryer, 1999). Patients undergoing a diagnostic procedure for bowel blockage using a Miller-Abbott tube have had the mercury balloon break (Kummer & Michot, 1984). The patient is usually sent home with little or no consequences. This author was told that prior to the turn of the 20^{TH} century, physicians recommended drinking a pound of mercury for constipation. One report (Lin & Lim, 1993) showed that elemental mercury was cleared from the gut in 10 days, even though 7 lbs of mercury (about 1/2 pint) was ingested.

However, some bizarre forms of elemental mercury poisoning can occur when the mercury is injected subcutaneously, intramuscularly (Krohn & others, 1980) and/or intravenously (Chodorowshi & others, 1997; Johnson & Koumides, 1967). Some of these are the result of suicide attempts or self-administered experiments; others are in a mistaken effort to build muscle mass. For instance, boxers in Latin American countries have injected mercury into their hands (Seu, 1998). Reports (Chodorowshi & others, 1997; Bleach & McLean, 1987) have shown that individuals have injected elemental mercury into their arms, legs and abdomen. In many cases, the patient does not see a doctor for years (Hohage & others, 1997). Initially, the mercury may cause local inflammation, abscess and gangrene, and only later can the mercury become a systemic problem. Even then, it rarely creates severe mercury toxicity (Chodorowshi & others, 1997). Accidental aspiration of elemental mercury has caused narcotizing bronchitis and progressive pulmonary fibrosis (Celli & Kahn, 1976; Naidich & others, 1973; Dzau, Szabo & Chang, 1977).

d) Mercury Vapors

Significant toxicity can occur when vapors of mercury are inhaled (Houeto & others, 1994; Langford & Ferner, 1999). Elemental mercury vapor accounts for most occupational and accidental exposures in mercury intoxication episodes (Anonymous, 1992; Langford & Ferner, 1999; Browning, 1969). Eighty percent of mercury vapor inspired is absorbed in the lungs (Hurch & others, 1976) and the toxic exposure is generally cumulative (Seu, 1998). Acute toxicity can occur, but is infrequent. When it does occur, the large dose of mercury vapor can cause acute pneumonitis, renal failure, seizures and neurological dysfunction (Bluhm & others, 1992; Seu, 1998). The sources of mercury in domestic intoxication usually occur when mercury is spilled in the house or other enclosed area (Anonymous, 1995; Schwartz, Snider & Montiel, 1992; McClanahan, 1996). Typically, intoxication occurs when vacuum cleaners are used to clean up the spill and create an aerosol of mercury vapor (Cambell, Gonzales & Sullivan, 1992; von Muhlendahl, 1990; Etzel, 1995; Bonhomme & others, 1996), when the mercury compounds are heated, such as smelting of lead and/or gold (Kanluen & Gottlieb, 1991; Snodgrass & others, 1981; Donoghue, 1998) or during paint removal (Anonymous, 1990).

Table 1: Potential Occupational Exposures to Mercury (Adapted from Goldfrank's Toxicological Emergencies, 1990)

Elemental	**Salts**
Amalgam makers	Disinfectant makers
Barometer makers	Dye makers
Battery makers, mercury	Explosives makers
Boiler makers	Fireworks makers
Bronzers	Fur processors
Calibration instrument makers	Ink makers
Caustic soda makers	Percussion cap makers and loaders
Carbon brush makers	Tannery workers
Ceramic workers	Taxidermists
Chlorine makers	Vinyl chloride makers
Chemistry teachers	
Dental amalgam manufacturers	
Dentists and their operating staff	
Diffusion pumps makers	
Direct current meter workers	**Organic**
Electric apparatus makers	Bactericide makers
Electroplaters	Drug makers
Fingerprint detectors	Embalmers
Gold extractors	Farmers
Jewelers	Fungicide makers
Lamp makers, fluorescent and mercury arc	Histology technicians
Lighthouse keepers	Insecticide makers
Manometer makers	Pesticide workers
Mercury workers, miners, refiners	Seed handlers
Paint makers	Wood preservative workers
Neon light makers	
Paper pulp workers	
Photographers	
Pressure gauge makers	
Silver extractors	
Thermometer makers	

There is a wide range of original sources for chronic exposure to mercury vapor (van Netten & Teschke, 1988) (a list is presented in Table 1). Exposures can be from broken fluorescent light bulbs (Tunnessen, McMahon & Baser, 1987), thermometers (Langford & Ferner, 1999), sphygmonanometers (Patterson & others, 1985; Rennie & others, 1999), mercury-containing clock pendulums and antique barometers. It can also occur in poorly ventilated areas where mercury is used in manufacturing. Manufacturing of such items as electric relay switches, pesticides, furniture polish or vinyl chloride materials are potential sources for mercury contamination. Even dental offices have the potential for chronic mercury vapor exposure. The European Union has passed new laws that will eliminate many clinical-medical instruments, such as the sphygmomanometer and the thermometer that uses mercury because of the potential exposure hazard (Langford & Ferner, 1999).

In vapor exposures, mercury, once absorbed, causes alveolar edema and is quickly transported via the blood to the organs of the body. It can be converted to the Hg^{+} ion in the blood and/or in tissue (Seu, 1998). Mercury will readily pass the blood-brain barrier, and if there are sufficient quantities, will cause neurological dysfunction (Kishi & others, 1994). The pervasive disruption of normal cell physiology by mercury can be from several mechanisms (Seu, 1998). These include binding to sulfur, which replaces the body's sulfhydryl groups, and reactions with phosphoryl, carboxyl and amine groups. These reactions with mercury disrupt enzyme and transport mechanisms, membrane and structural proteins (Klassen, 1990).

Chronic exposure to mercury vapor manifests as mild-to-moderate CNS dysfunction with irritability, memory loss, insomnia, renal failure, anorexia and tremor (Smith, 1978, Fahn, 1972). There is considerable overlap among concentrations of mercury found in the normal population, asymptomatic exposed individuals and patients with clinical signs of mercury toxicity (Seu, 1998). There are many conditions that can mimic mercury toxicity, such as alcoholism, lead and arsenic poisoning, Parkinson's, cerebellar lesions, senile dementia and vascular degenerative diseases (Fahn, 1972). Only testing mercury-urine levels can make a final diagnosis of mercury intoxication (Seu, 1998). A level of 10 µg mercury/L is normal, 100 µg/L indicates a significant exposure and patients with symptoms typically show 300 µg mercury/L in urine (Seu, 1998; Elberger & Brodey, 1998).

Precautions need to be taken in any environment that uses mercury. The American Dental Association (ADA Council on Scientific Affairs, 1999) has set forth recommendations for mercury hygiene in the dental office. These include: 1) training all office personnel regarding the potential hazard of mercury and its sources, 2) making sure that the work area is well ventilated with a fresh air supply, 3) periodically checking operatories for mercury vapor, 4) designing operatories to facilitate spill containment and cleanup, 5) using only precapsulated amalgam alloys and, if possible, recapping after use, 6) using an amalgamator that has an enclosed arm, 7) using high volume evacuation when removing and finishing amalgam and cleaning the traps frequently, 8) salvaging, then storing all scrap amalgam in a closed container and recycling when possible, 9) disposing of mercury-containing items in sealed bags, 10) cleaning up spilled mercury and 11) removing professional dress before leaving the office.

In addition to mercury hygiene information, it has recently been reported that amalgamators are contaminated with mercury (Roberts, 1999). In a recently published article Roberts, Leonard & Osborne (2001) found that the mercury level was high when tested within the small confined space of the amalgamator (0.044 µg/m^3). But above the triturator in the work area, the time-weighted mercury vapor level was only 0.0008 µg/m^3, magnitudes below any government guidelines. They reported that maintenance personnel were not unduly exposed to mercury during repairs of the amalgamators and that the level for an eight-hour TWA was 0.001 µg/m^3. Limits for TLV-TWA are 0.05 µg/m^3 for mercury vapor (Patnaik, 2000). The authors did suggest that amalgamators be treated as a hazardous waste product when consideration is given to disposal.

Disposal of Mercury from the Dental Office

Discharge of mercury into the environment has come under increasing scrutiny, especially from dental facilities (Roberts, 2000). Mercury is classified as a Persistent Bioaccumulative Toxin (Stone & others, 2000) and the Environmental Protection Agency (US EPA, 1995; 1997a; 1997b) has stressed a need to eliminate mercury from medical and dental waste before entering the wastewater stream. It has been estimated that dental facilities in the United States annually discharge 40 tons of mercury (Roberts, 2000). Unfortunately, most publicly-owned treatment facilities are not designed to treat toxic pollutant discharges. Fortunately, they are not enforcing the limits set by government agencies. In the future, dental treatment centers will be required to pre-treat their effluent prior to discharge into the public waste stream (Roberts, 2000).

Use of efficient centrifugal separators in removing amalgam particulate matter larger than 10 microns can reduce amalgam and mercury discharge from dental facilities (Cailas & others, 1994). Foreign government agencies, especially the Europeans, require dental clinics to recover 90% of dental amalgam mass from wastewater in this manner (Stone & others, 2000). Centrifugal separators, however, will not address wastewater issues in the US, for the EPA methodology measures total mercury concentration in discharges, whether particulate matter, suspended colloidal material or dissolved ionic or molecular species (Stone & others, 1999). Dental amalgam constituents below 10 microns in size present special challenges to sedimentation and centrifugal methods of removal (Stone & others, 1999; Cailas & others, 1994; Naleway & others, 1994). This particulate matter is colloidal and remains in suspension via electrostatic and Brownian forces. Removal of this colloidal suspension requires additional filtration with the assistance of chemical and/or electrochemical coagulation (Stone & others, 2000; Naleway & others, 1994).

Presently, there are two available mercury recovery technologies available that address both filtration of amalgam particles and removal of dissolved mercury (Roberts, 2000). Both technologies rely on particulate filtration and/or sedimentation to remove particulate matter, and the dissolved mercury is removed by processing the filtrate through either proprietary activated charcoal elements or specially formulated resins (Roberts, 2000).

One technology is the Mercury Recovery Unit marketed by ADA Technologies/Dental Recyclers of North America (DRNA), Denver, CO. The mercury recovery system is designed for a four-unit or less dental operatory (Roberts, 2000). This recovery unit proposes to collect wastewater and particulate matter. For best function, the unit requires several hours between the conclusion of dental operations and the start of recovery unit and requires approximately 90 minutes for full function. At the conclusion of the operating day, a timer-activated pump discharges the collected wastewater from the system. Solid amalgam particles remain in the separator while soluble mercury is removed via an adsorbent column containing a mercury-specific chelating agent (Turchi, Albiston & Stewart, 1999). ADA Technologies/DRNA states that the MRU does not require routine cleaning and maintenance and the adsorbent columns and separators are shipped to the user when it is time to recycle those components. The used components are placed in containers that are provided, then shipped to appropriate recycling agencies that the recovery the mercury. For larger facilities, ADA Technologies is in the process of building a commercial unit that is said to serve as the template for large clinics and dental schools (Roberts, 2000).

Another technology is based on a resin-bead filtration/coagulation process marketed by SolmeteX (Roberts, 2000). This mercury removal technology is based on a proprietary resin, Keyle:X, which is described as a polymeric bead that is a mercury-specific binding chemistry. Keyle:X Mercury Removal Resin contains modified sulfur reaction groups that are grafted on the resin structure and claims to remove mercury to below 0.010 ppb effluent concentration. SolmeteX says that Keyle:X Mercury Removal Resin has been evaluated and documented by the State of Massachusetts (Massachusetts Water Resources Authority, 1997) and has proved to remove mercury to below 1 ppb in wastewater, clinical laboratory waste, histology/pathology waste and groundwater (Roberts, 2000).

Dental Amalgam, Mercury and Medical Issues

For many years the idea that mercury was released from dental amalgam was not understood and, in fact, denied. Technology had not been developed to detect low levels of mercury coming from the amalgam restoration. In 1985, Vimy and Lorscheider reported that 27 µg Hg/12 amalgams/day are released. It was quickly shown, however, that their calculations overestimated exposure by about 16 times since they had estimated the patients' mercury exposure from oral concentrations as if they were exposed to room air concentrations (Olsson & Bergman, 1987; Mackert, 1987). Skare and Engqvist (1994) estimated that 7.3 µg mercury is released from 10 amalgam surfaces per day. The World Health Organization (WHO) in 1991 stated that 10 µg mercury/day are released from dental amalgam. These estimates have also been shown to be high (Mackert & Berglund, 1997). A variety of difficulties in determining the amalgam-derived mercury have complicated the issue. Collection volume and flow rate of measuring instruments, and breathing rate differences between patients, as well as other factors, generally have resulted in over-estimations of the absorbed dose (Mackert & Berglund, 1997).

Berglund's (1990) carefully monitored and controlled human study provides an estimate of 1.7 µg mercury/12 amalgams/day. Other data (Langworth, Elinder & Akesson, 1988) has substantiated this assessment. Interestingly, if one corrects the Vimy & Lorscheider data (1985) by the factor of 16 as others recommended (Olsson & Bergman, 1987; Mackert, 1987), the amount is the same as reported by Berglund (1990).

Several clinical studies have also shown that tissue fluid mercury levels attributable to amalgams are very low (Bjorkman & Lind, 1992; Berglund & Molin, 1996; Molin, 1900; Nilsson, Gerhardsson & Nordberg, 1990; Molin & others, 1987). Kingman, Albertan & Brown, (1998) in the largest study to date, with more than 1,100 men, has indicated that 10 amalgam surfaces will increase the urine mercury level less than 1 µg/l or one part per billion.

Based upon occupational exposures to mercury, the WHO (1991) sets an upper limit of 30 µg/g creatinine urine mercury level to illicit the most subtle preclinical effect in the most sensitive individuals. Mackert & Berglund (1997) point out that it would take 450-530 amalgams in a patient to produce this level of mercury derived from amalgams. Clearly, the likelihood of mercury toxicity from the presence of dental amalgam in the mouth is extremely remote.

There have been studies on the release of mercury vapor during removal of amalgams (Engle & others, 1992; Powell & others, 1994; Ferracane & others, 1994; Pohl & Bergman, 1995). The grinding procedure when the amalgam is removed, as well as the resultant generated heat, release mercury vapor and amalgam particles of various sizes. Engle & others (1992) studied mercury vapor levels generated during amalgam removal and concluded that cutting with air-water spray produces 15-20 µg mercury vapor for a Class I restoration. However, use of high volume evacuation and extending the suction after cutting reduced this mercury vapor level by 90%. This reduction would apply to larger restorations as well. As this study and others (Powell & others, 1994; Ferracane & others, 1994; Pohl & Bergman, 1995) point out, the total amount of mercury vapor released was far below the maximum level established as permissible for occupational exposure.

Dental operatory personnel experience multiple episodic exposures to mercury vapor, and this fact serves to demonstrate the patients' level of safety (Osborne & Albino, 1999). Dentists have more mercury exposure than the general population, yet health and morbidity studies indicate that they have no unusual diseases and, in fact, live longer than their physician colleagues who are not generally exposed to mercury in the workplace (Langworth & others, 1997; McComb, 1997; American Dental Association, 1975; Eccles & Powell, 1967; Orner, 1978).

Several studies have examined patients who had all their amalgams removed in one dental session (Sandborg-Englund & others, 1998; Molin & others, 1990; Socialstyrelsen, 1994). In a study (Sandborg-Englund & others, 1998) conducted at the Karolinska Institute in Sweden, 12 patients with an average of 18 amalgam surfaces removed at one session were examined. The patients' tissue fluids were monitored prior to removal of their amalgams and up to 115 days after. Removal of the amalgam fillings resulted in a transient increase of mercury in both blood and plasma, but no increase in urinary mercury excretion.

Molin & others (1990) evaluated 10 patients who had all amalgams removed in one session and 10 matched controls that did not have amalgams removed. They examined 22 supplementary biochemical analyses for the 20 patients and concluded that mercury vapor generated during amalgam removal did contribute to slightly elevated plasma and urine mercury levels, but the biochemical analyses showed no influence on organ functions. Other papers (Mackert & others, 1991; Osterblad & others, 1995, Ahlquist, Berrgtsson, & Furunes, 1998; Bjorkman & Lind, 1992; Molin, 1990; Langworth & others, 1997) have shown that a patient's medical conditions cannot be related to the mercury released from dental amalgams in the mouth or during their removal.

The exception to the above medical/dental data is an allergic response to amalgam restorations (Catsakis & Sulica, 1978; Duxbury & others, 1982). This condition is extremely rare and the allergen/antibody response could be to metals other than mercury in the amalgam, such as copper, tin or zinc. A qualified physician should conduct the diagnosis of amalgam allergy.

Psychological Aspects of "Amalgam Illness"

Noting the highly remote possibility of mercury intoxication from dental amalgams poses serious questions regarding individuals who claim they have been poisoned by their amalgams. A term used to identify these patients' maladies is "amalgam illness" (Malt & others, 1997; Henningsson & Sundbom, 1996). Their symptoms are vague, or may be associated with a variety of medical conditions; they often receive no clear diagnosis in early consultations. Rather than live without an answer, they continue to search for treatment from a variety of practitioners. In the hope of a cure, they may even adjust their own perceptions of their health problems to fit the condition described by someone promising treatment (Osborne & Albino, 1999).

Stenman and Grans (1997) report that patients seeking treatment for suspected "amalgam illness" often have been encouraged to seek bogus care because of the hyper attention given this issue by the media. Many of these patients actually suffer from diagnosable medical conditions but look for an explanation and a cure by suspecting mercury. Individuals with neurological symptoms may be especially vulnerable. Their symptoms may be quite frightening, and the "amalgam illness" solution may seem preferable to the unknown consequences of some serious health problem. By missing the correct diagnosis, however, these patients can be placed in a dangerous situation.

Reports on psychological aspects (Malt & others, 1997; Henningsson & Sundbom, 1996; Bratel & others, 1997a,b; Herrstrom & Högstedt, 1993; Björkman, Pedersen & Lichtenstien, 1996; Bågedahl-Strindlund & others, 1997; Meurman, Porko & Martomaa, 1990; Langworth, 1997; Lindberg, Lindberg & Larrsson, 1994; Anneroth, Ericson & Johnsson, 1992; Sandborgh-Englund & others, 1994) provide profiles of patients presenting with "amalgam illness" that often include psychogenic problems, such as psychosomatic disorders, anxiety and depression, panic disorder and the inability to perceive and understand threatening situations. The frequency of these patterns across available studies is noteworthy (Osborne & Albino, 1999).

In two reports, Bratel & others (Bratel & others, 1997a; Bratel & others, 1997b) studied 100 Swedish patients, including a group presenting with "amalgam illness" and a control group matched for age, gender and residence. They examined mercury levels in blood, urine and hair. The patients were given oral, stomatognathic, psychiatric, and biochemical assays and they completed a checklist of medical symptoms. Mercury levels in both groups were similar and far below those levels causing negative health effects. Patients in the "amalgam illness" group reported more medical symptoms and also had more TMD disorders. Psychiatric diagnoses were established in 70% of the "amalgam illness" group compared with 14% in the control. Anxiety and mood disorders were the most frequent psychiatric diagnoses, and psychological tests confirmed related symptoms, such as illness behaviors, disruptive life events and emotional disturbance.

Herrstöm & Högstedt (1993) reported on 218 patients complaining of oral galvanism or alleged "amalgam illness." They found no cases of mercury intoxication and mean levels of blood mercury at 17.3 ηmol/l and none that exceeded 50 ηmol/l. Psychological disorder was diagnosed in 42.7% of the cases, with anxiety disorder the most commonly reported problem, followed by panic disorder. There was no correlation with blood mercury level and oral galvanism or general health and, in fact, patients with psychological disorders as the primary diagnosis had lower mercury levels in the blood than those with no psychiatric problems.

In another Swedish study, Henningsson & Sundbom (1996) evaluated 20 patients with self-diagnosed "amalgam illness" and 37 controls using a projective technique, the "Defense Mechanism Test." The most characteristic traits of people with alleged "amalgam illness" appeared to be difficulty in perception of threats and inappropriate emotional response to such threats, probably reflecting "denial" as a primary coping mechanism. The control group did not show these characteristics and in fact were completely separated from the "amalgam illness" group. They suggested that people with alleged "amalgam illness" may have major psychological difficulties with threatening situations.

A well-controlled study (Bågedahl-Strindlund & others, 1997) presented in the *Scandinavian Psychiatric Journal* (*Acta Psychiatric Scandinavia*) compared 67 patients diagnosed with possible "amalgam illness" with 64 matched controls. A battery of psychological tests was used within the context of a semi-structured interview, along with dental and medical examinations. Eight-nine percent of the patients with alleged "amalgam illness" met the criteria for psychiatric diagnoses of the somatoform–anxiety-affective types, whereas only 6% of the control group exhibited psychiatric problems. Affective disorders were common among the "amalgam illness" group, which also reported more psychological services and use of psychotropic drugs. Alleged "amalgam illness" patients also received higher scores on tests of somatic anxiety, muscular tension, psychasthenia and low socialization. As in the Henningsson & Sundbom study (1996), the patients had difficulty in expressing emotions. The multiple signs and symptoms of distress could not be explained either by dental or medical examinations. About 50% of the alleged "amalgam illness" patients, and only 4% of the controls, thought their general health was poor.

These studies (Bratel & others, 1997a,b; Henningsson & Sundbom, 1996; Bagedahl-Strindlund & others, 1997; Herrstom & Hogstedt, 1993) and others (Björkman & others, 1996; Meurman & others, 1990; Langworth, 1997; Lingberg & others, 1994; Anneroth & others, 1992) have found that many patients with alleged "amalgam illness" often manifest psychological problems, such as anxiety, depression and neurotic difficulties. The data further suggest that these patients have difficulty in dealing with threats and expressing emotions, and therefore may lack coping skills for dealing with life's difficulties.

What to Do for Patients Wanting Amalgam Removed

The dentist who is asked by a patient to remove amalgam restorations for medical reasons is confronted with an important task (Osborne & Albino, 1999). Professional responsibility requires that a practitioner work with the patient to gain an understanding of the presenting health concerns. Noting the remote possibility that mercury is the causative agent, most dentists are not prepared to evaluate or diagnose potential medical or psychological problems. What the dentist can do is rule out potential dental causes for the symptoms reported and ensure the patient's optimal oral health. The dentist also has the responsibility to inform and educate the patient about "amalgam illness."

The dentist needs to recognize that the patient presents biological, psychological and social components to this complex problem. For this reason, the presence of psychological symptomatology should not be taken to mean that there are no physical or medical problems. The pain, discomfort or other symptoms experienced are real. The possibility that they are related to mercury intake from dental amalgam is essentially nonexistent.

Concern should be expressed about the patient's complaints and an offer should be made to help by contacting the patient's primary care physician or appropriate caregiver. A physician should give a diagnosis of mercury toxicity or other medical problem. Given the low probability of a clear medical diagnosis based on dental examination, the rationale that removing amalgams could provide a beneficial placebo effect is not acceptable and would be questionable in terms of professional ethics. Needless to say, the same "removal of amalgam for placebo effect" is true for patients with diagnosed medical conditions such as cancer, Alzheimer's, MS or ALS.

Many physicians may not be familiar with the concept of "amalgam illness" and would no doubt welcome an overview of what is known on this topic. The dentist would also want to report the results of the dental examination and let the physician know that it is highly unlikely that the patient's presenting complaints are dental in origin.

The fact that many patients complaining of "amalgam illness" also manifest psychological symptoms does not necessarily mean that the only appropriate diagnosis is psychiatric. It may be that undiagnosed pain or discomfort are related to some very real medical problem that has resulted in such problems as anxiety, denial or even depression. Recognize that from a patient's standpoint, thinking it is mercury may be easier to face than the real problem. In addition, the lack of social support in dealing with medical issues may also have resulted in maladaptive behaviors.

All these factors make this situation very difficult and yet critical for the patient to obtain proper care and relief of their symptoms.

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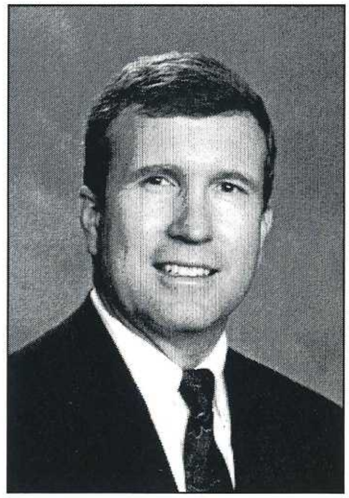
Gold as a Historic Standard and its Role for the Future

CT Smith



Cleveland T Smith

Introduction

Since antiquity and the dawn of civilization, man has used gold as a dental material. It has always had a very special intrinsic and practical value in dentistry and will continue to do so. Of all the dental restorative materials in use, gold to this day has had the best combination of physical properties that make it a premier restorative material for today as well as tomorrow. In addition, clinical research and experience has shown no other material demonstrates the superb long-term prognosis as properly placed gold restorations. Many of our patients have gold restorations, which have served them for decades, and these patients are walking archives of dental history. Gold restorations have withstood the test of time and to this day are the benchmark by which we judge many other dental restorative materials.

Discussion

Figure 1 is a remarkable example of a gold bridge fabricated by the Etruscans in 500 BC. Gold was used to splint and bridge the maxillary anterior teeth. This level of craftsmanship was not seen again until the 1700s. The first record of the use of gold leaf for filling teeth was by Arculenus (1412-1484) (Weinberger, 1948). In his writing "Practica in Aarte Chirurgica," he wrote that carious teeth should be filled with gold leaf after the removal of putrefied dentin with files and scalpels, emphasizing that teeth should not be treated by barbers or charlatans but by qualified men only.

Figure 1. *Etruscan bridgework fabricated around 500 BC.*

Gold foil fillings were introduced into America by either John Baker, MD or Robert Woffendale (Weinberger, 1948). Woffendale arrived in New York from England in 1766. Dr Baker arrived in New York from Boston in 1767, where he had established a practice of more than 2,000 patients. His 1768 advertisement stated, "...he fills teeth with lead or gold." In 1855, Dr Robert Arthur discovered that cohesion could be induced to gold by the simple

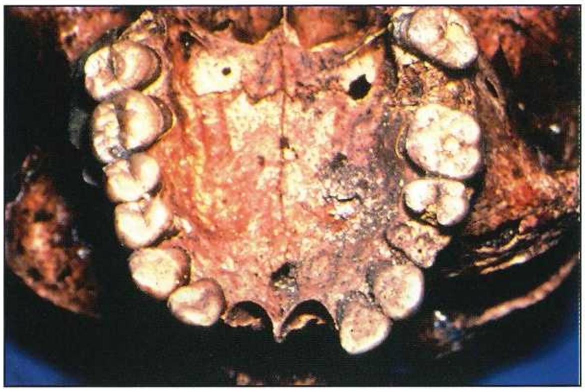


Figure 2. *Class I and II gold foils placed on the maxillary premolars and molars in 1850, Charleston, South Carolina.*

process of passing it over an alcohol flame, after which it could be welded in the cold state (Weinberger, 1948). This increased the popularity of gold foil as a filling material, but its usefulness was dramatically improved upon the invention of the rubber dam in 1864 by Sanford C Barnum. Figure 2 illustrates some very remarkable gold craftsmanship when one considers these foils were done in 1850 without rotary dental instruments or modern lighting. Gold foils were placed on the occlusals of the maxillary right first and third molars, the maxillary left first molar and a Class II on the mesial of the maxillary right second premolar. The remains of the skull were excavated from one of the historical churchyards in Charleston, South Carolina.

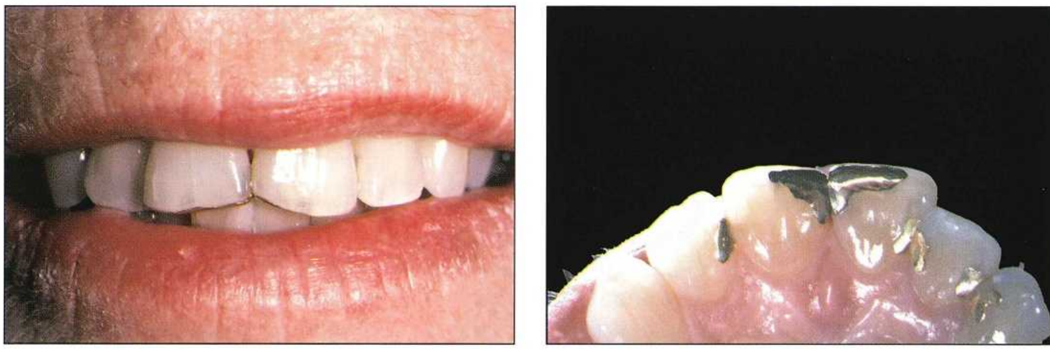


Figure 3-4. *Facial and incisal views of Class IIIs and IVs done in 1930. These gold castings were fabricated from direct wax-ups in the oral cavity.*

In the dental practice it is not uncommon to see older patients with gold restorations which have been in function for many years under severe conditions that would have destroyed most other dental materials early on. Figures 3 and 4 are post-operative photographs taken in the year 2000 of gold Class III and Class IV inlays done in 1930. These restorations were placed by the patient's grandfather, a dentist, and according to the patient, a direct wax technique was used to fabricate the inlays. This is one example of the many cases that illustrate the long-term prognosis of properly executed gold restorations.

Figure 5. *Cast gold preparations: Full veneer preparation on the maxillary second molar, 7/8 crown preparation on the first molar, 3/4 crown preparation on the second premolar and a distal occlusal inlay preparation on the first premolar.*

Gold restorations have fallen out of popularity among dental practitioners in favor of composites and tooth-colored restorative materials. This is largely due to economic market pressures and misconceptions. Composites, ceramics and gold restorations all have their place in the practice of dentistry. Each one has individual characteristics that make it superior to the other. Unfortunately, some dental practitioners fail to see or acknowledge the physical and technical limitations of composites and ceramic hybrids. There is a place and time to use each of these materials, but in some situations common sense dental treatment planning and treatment has been blurred by market and peer pressure to the point that it has impaired good judgement in treating

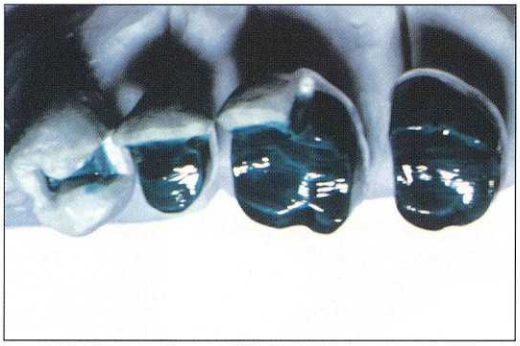


Figure 6. (left) *Model work prior to the wax-ups.*

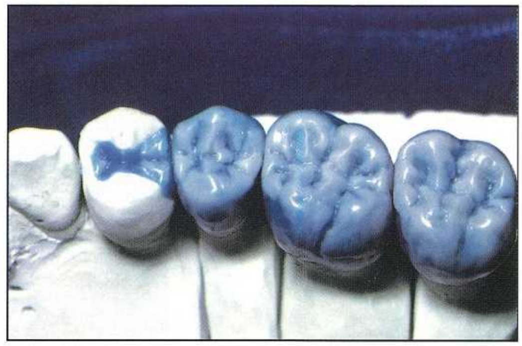


Figure 7. (right) *Final polished wax-ups ready for investing and burnout procedures.*

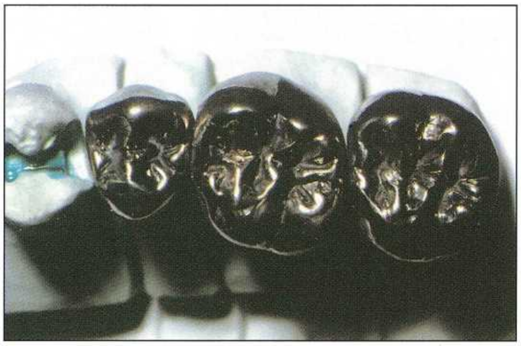


Figure 8. (left) *Partial veneer castings after investment removal with acid. These castings have not been polished and will need very little polishing because of the fine surface finish and the accuracy of the laboratory investment and casting procedures.*

Figure 9. (right) *The unpolished or adjusted casting seated on the die seen at 20x magnification. Extremely accurate castings can be obtained on a consistent basis with good laboratory technique and require minimal adjustments.*

the patient. Traditionally, tooth preparations for gold casting have been full, partial veneers or inlays. Figure 5 shows a full veneer preparation on the maxillary second molar, a 7/8 preparation on the first molar, a 3/4 preparation on the second premolar and a distal occlusal inlay preparation on the first premolar. Whenever possible, one should preserve tooth structure and keep margin placement supragingival. These basic concepts aid in periodontal health and provide easy cleansability. Excellent preparations and model work are quintessential for long-term success. Ideally, the laboratory technician requires clean, continuous finish lines with no undercuts (Figures 6 and 7) (Christensen, 1966). All gold castings can be fabricated with extreme accuracy and detail (Figures 8 and 9) (Krug & Markley, 1969). The intimate fit and durability of cast gold restorations are the underlying reasons for the long-term success of these restorations. A poorly executed laboratory technique will assure failure even with best of dental practitioners at the chairside. The gold castings are adjusted and polished, then cemented with the aid of a rubber dam. The rubber dam aids in moisture control, tissue retraction and field of vision (Figure 10).

Figure 10. *Occlusal view of the castings seated at delivery.*

Gold castings may also be used for customized overdenture abutments when dental implants are not an option (Figures 11 and 12). These are cast post- and core-overdenture abutments with zest attachments in the mandibular canines. They have substantial strength as a foundation for the complete overdenture and biocompatibility with soft tissue. The use of gold in this case has salvaged the remaining tooth structure and preserved the bone and soft tissue.

An additional use for gold is in dental ceramics. Esthetically, gold ceramic alloys, when used with modern porcelains, can provide a harmonious and natural look if correctly handled in the laboratory phase. Ceramic gold alloy is biocompatible and exudes a warm color that gives the porcelain a more natural look (Chiche & Pinault, 1993). In

Figure 11. (left) *Gold overdenture abutments on the mandibular canines and premolars.*

Figure 12. (right) *Mandibular complete overdenture with zest male attachments.*

Figure 13. (left) *Maxillary centrals incisors prepared for porcelain fused to gold crowns with porcelain butt joints.*

Figure 14. (right) *Post cementation of the maxillary central crowns.*

the maxillary anterior dentition, porcelain butt joint margins aid in light conduction and illumination if used with ceramic gold copings. Figure 13 represents prepared two maxillary central incisors with butt joints. Both centrals have been endodontically treated. The right has discoloration that could create a low value problem for an all-ceramic crown system due to the translucency of the ceramic. Figure 14 shows the porcelain fused to gold crowns at the time of cementation. In this case, the gold metal coping and opacious porcelains inhibited the transmission of the dark tooth understructure. Gold alloys offer distinct advantages when used in conjunction with dental implants. The most notable advantage is the low electropotenial of the alloy. Non-precious alloys can create galvanism if used over dental implants due to the difference in the electropotenials between metals. This may result in failure of an implant-supported prosthesis because of the attachment breakdown at the bone implant interface due to galvanism.

Customized gold implant abutments can be a simple solution for a variety of difficult cases, such as the improper angled placement of the implant. This is a very common problem caused by surgical error, lack of surgical planning or insufficient osseous contours. Figure 15 shows an implant placed too far to the buccal with a mesial slant in a large osseuos defect. Under an ideal clinical setting with proper ridge height, width and implant placement, this would still be a difficult restorative case. In Figure 16, the ridge was augmented and a custom gold abutment and crown were fabricated (Figure 17).

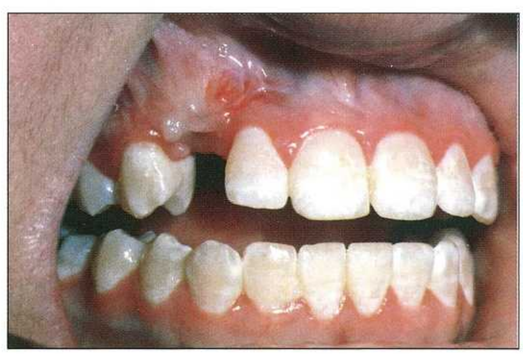


Figure 15. (left) *Pre-prosthetic treatment of the maxillary right canine edentulous area, prior to ridge augmentation.*

Figure 16. (right) *Post-ridge augmentation of the maxillary right canine edentulous area.*

Figure 17. (left) *Porcelain fused to gold coping on the custom gold abutment after laboratory fabrication.*

Figure 18. (right) *One and half weeks post-operative after the porcelain fused to gold crown and abutment were delivered during the uncovering of the implant.*

The abutment and crown were delivered at the surgical uncovering of the implant, which allowed for tissue contouring on the proximal surfaces for the papilla. The gold abutment is subgingival and supports the facial tissue without casting a gray shadow through the gingival (Figure 18). This is one and one-half weeks post operative and the tissue has conformed well to the abutment because of the compatibility of the gold and porcelain against the soft tissue. Esthetically, this is much improved in large part due to the custom gold abutment and crown. Overall, there are many more applications for gold in the restorative phase of dental implants. This case only represents a small sample of the use of gold alloys for dental implants in the clinical setting.

Conclusions

This discussion has been limited to a brief synopsis of the history of gold in dentistry and clinical cases prepared and fabricated by the author in his private practice. There are many other creative uses of gold in dentistry that are not mentioned in this article due to time and space. Durability, biocompatibility, inertness and fit are the characteristics that have made gold a premier restorative material of the past, the present and for the future. Ultimately, history will judge the quality and longevity of a dental material, and gold has superbly withstood the test of time when compared to other materials. It remains to be seen whether the newer restorative composites and hybrids will survive in function and serve as long as gold materials. One has to keep an open mind and use a common sense approach when evaluating all dental restorative materials for use on their patients.

Acknowledgment

Special thanks to Dr TL Welch, Department of Operative Dentistry, Medical University of South Carolina, for historical data and his guidance in the field of gold restorations.

Materials

JRVT, J-IV gold alloys
Jensen Industries Incorp
50 Stillman Road
North Haven, CT 06473
1-203-239-2090

Aquarious ceramic gold alloy
Williams/Ivoclar North America
175 Pineview Drive
Amherst, NY 14224
1-800-533-6825

Creation Porcelain
Jensen Industries Incorp
50 Stillman Road
North Haven, CT 06473
1-203-239-2090

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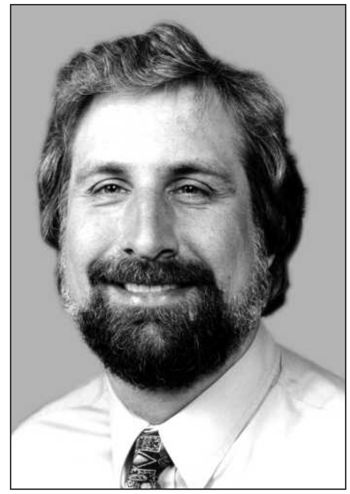
Research into Non-Mercury Containing Metallic Alternatives

FC Eichmiller



Frederick C Eichmiller

Abstract

Many attempts have been made over the years with varying degrees of success to developing metallic alternatives to dental amalgam. Much of the difficulty in achieving success is the inability to meet the physical, mechanical and clinical criteria for an "ideal" alternative. An additional requirement for any new material is that it be "environmentally friendly"—both from a manufacturing standpoint and in use. Gold foil has been one of dentistry's most successful direct filling materials, but is only used by few/select clinicians and is largely considered a lost art. Metal-modified glass ionomers have achieved some success as crown buildup materials and direct restoratives in the primary teeth of children, but these are slowly being displaced by improved composites. Several attempts have been made to develop metal-filled composites, but only one product is available for use as a crown buildup material. There is a long history of attempts to formulate an acceptable gallium alloy. Early nickel-gallium formulations resulted in severe tumorgenicity in animal trials. Palladium-gallium-tin alloys were less toxic but still exhibited high latent expansion and severe soft tissue inflammation around implants and tissue-embedded particles. More recent attempts to formulate silver-copper-gallium-indium-tin alloys resulted in better biocompatibility, but clinical trials showed corrosion and latent expansion too severe for general clinical acceptability. Studies of consolidated silver materials have resulted in the development of a direct restorative system with favorable properties and biocompatibility, but no human trials have yet evaluated the material's clinical performance. The demands in today's market for esthetics and regulatory pressures to reduce heavy metals in wastewater have resulted in less interest in metallic alternatives for amalgam. Future development will likely focus on improving polymeric composites in an attempt to meet the call for an amalgam alternative.

Introduction

The search for a suitable alternative to dental amalgam has truly been the "holy grail" of dental materials research. Many approaches have been taken, with most recent efforts focusing on improving polymeric composites. Many attempts have been made to develop metallic alternatives, resulting in varying degrees of success. This paper describes the progress and status of several technologies for these metallic alternatives to dental amalgam.

From a materials engineering standpoint, design of the ideal "amalgam alternative" should be guided by several criteria that directly affect the clinical handling and performance of the final restoration. For physical properties, the first of these criteria is that the material must be fluid or plastic at room temperature to allow it to be shaped to conform to the cavity preparation and to form the final anatomical contour of the restoration. Once in place, it would need to harden rapidly, preferably under the control of the operator. The cured or hardened restoration should be chemically and mechanically stable; it would be an added advantage if the material had good adhesive strength to adhere to the surrounding tooth structure and cohesive strength to adhere to itself when repairs are needed. Resisting or preventing recurrent decay would also be preferable, as well as matching the surrounding tooth structure in color and texture.

In addition, the material should meet mechanical criteria, such as high tensile and shear strength, and a high fracture toughness to support cyclic functional loads. Compressive strength should be moderate, as should be the material's resilience. Creep or viscoelastic flow should be low to prevent time-dependent deformation under load. The wear of the material should be comparable to tooth enamel and should not erode opposing tooth structure or restorations more than enamel. The material should have low corrosion or galvanic potential and not promote or support colonization by dental plaque.

Once all these criteria have been met, the desired clinical criteria must be considered for successful placement and performance. The material should have handling characteristics such as viscosity, plasticity, resistance to condensation and low tackiness to make placement easy and convenient. The biocompatability must be adequate to make it considered safe for intraoral use. The clinician should have direct control of the setting reaction, and the material should achieve high early strength. Lastly, it should be easily shaped, contoured and polished to give a natural anatomical texture and appearance.

This is a tall order for any material because once many of these criteria have been met, today's environmental demands for any material used in dentistry need to be considered. The material should not be sensitive to extremes in environmental conditions, such as temperature and humidity. Its shelf life should be as long as possible to save resources and reduce disposal costs. There should be no known environmentally hazardous components and waste generated from manufacturing and use and any waste products should be recyclable. Lastly, the cost of manufacturing and disposal should be the lowest possible.

Direct Gold

A discussion of metallic alternatives would not be complete without first exploring what is already available. One of the oldest materials used for direct filling of dental cavities is gold. Stringfellow (1839) was the first to document direct placement of gold in the form of powders and foils. In reviewing our original criteria, it is evident why this technology has achieved such a long, successful history. Gold is relatively plastic when placed, intimately adapts to a cavity form, sets immediately upon consolidation, can be shaped and polished to anatomical form and surface texture, maintains an excellent seal to the surrounding tooth structure and has relatively high strength, toughness and durability (Figure 1). Unfortunately, it has lost its appeal due to the perceived complexity of placement, the need for detailed, retentive cavity preparations and its dependency upon

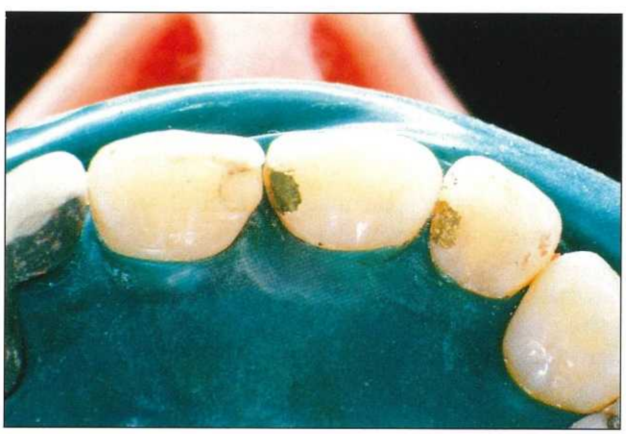


Figure 1. *Class III gold foil restorations placed from a lingual approach. No metal is visible from the facial side and the restorations are more than 15 years old. Clinical photograph courtesy of the author.*

operator skill and proficiency for clinical success. Add to this the lack of tooth-mimicking color and translucency. From an engineering perspective, direct gold is a wonderful material, but from a clinical perspective, it has largely fallen from favor.

Metal Modified Glass Ionomers

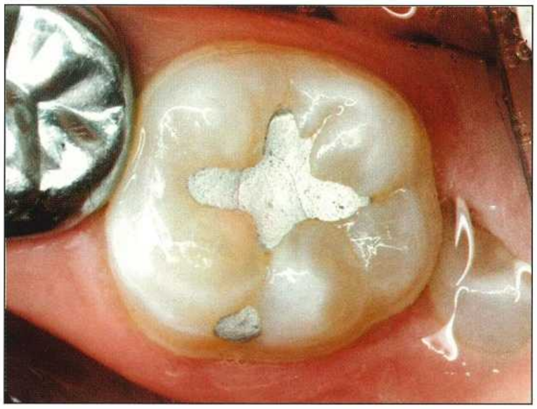


Figure 2. *A primary molar restored with a glass ionomer cermet restoration. The wear and durability of this material has been shown to be adequate for restorations with short service requirements, such as primary teeth. Clinical photograph courtesy of Dr Theodore Croll.*

Metal-modified glass ionomers are another alternative that has been available since the late 1970s. These materials largely fall into two classes. There are add-mixed materials, such as Miracle Mix™ (GC America, Alsip, IL 60658), that simply add a small quantity of intermetallic amalgam powder to the reactive glass filler of a conventional glass ionomer. The resulting filling is a composite composed of an aluminum fluorosilicate glass reacted with an acrylic acid that forms a polysalt matrix surrounding the remaining unreacted glass and the intermetallic powder. The second class is commonly referred to as a cermet and is composed of a reactive glass that has been thermally fused to silver prior to being commutated to a powder. This silver-enriched glass is then reacted with an acrylic acid to form a polysalt matrix surrounding unreacted particles. McClean & Gasser (1985) describe the process. The primary difference between cermets and admix materials is that cermets have no freestanding metal particles as part of the filler phase of the final composite structure. These metal-modified glass ionomers have been largely used as buildup materials because of their higher compressive strength, and in pediatrics (Figure 2), for the direct restoration of posterior primary teeth (Croll & Phillips, 1986). There have been reports of improved wear and compressive strengths over unmodified glass ionomers, but the material still lacks the strength and fracture toughness needed for permanent load-bearing restorations (Wasson, 1993; deGee & others, 1996).

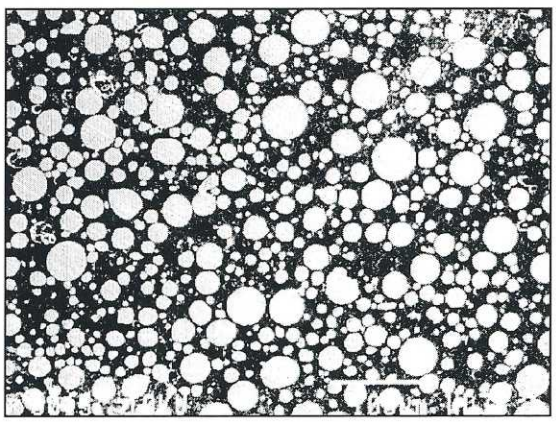


Figure 3. *A scanning electron microscopy image of the polished surface of an experimental metal-filled polymeric composite under development at BioMat Sciences in Rockville, MD. Micrograph courtesy of Dr Ivan Stangel.*

There has been some research into metal-filled polymeric composites. Bowen & Chandler (1973) experimented with a variety of metal fillers and surface coupling techniques in combination with different acrylic monomers to formulate metal-filled composites. They showed that coupling could be achieved with metal particles that readily formed a coherent oxide layer. Mechanical properties of some formulations approximated those achieved with conventional glass fillers (Bowen & others, 1978), but further development was not pursued and clinical studies were not done. One commercial product, Ti-Core™ (Essential Dental Systems, Hackensack, NJ 07606), has been marketed and recommended by the manufacturer as a core buildup material. This material uses a conventional polymer matrix with a mixture of glass and titanium particulate fillers. The properties do not differ significantly from a conventional dental composite, and it has not been recommended for use as a general restorative material (Combe & others, 1999). Hirano & others (1996) have also attempted to make a magnetic composite by incorporating stainless steel fillers. More recent developments have been introduced by Stangel (2000), who started BioMat Sciences (Rockville, MD), which formulates a metal-filled composite that uses a combination of submicron and micron-sized metal fillers in a polymeric matrix (Figure 3). The fillers are coupled to the matrix using proprietary functionalized couplers, just as silane is used on glass fillers. These composites are currently being optimized in preparation for clinical trials (Benhaddad & others, 1997; Stangel & others, 1997).

Research and development of gallium-based alloys has a long history. PuttKammer was the first to report on the use of gallium for a direct dental alloy in 1928. Investigators worked for several years to develop a suitable alloy, but largely abandoned their efforts until scientists at the Aluminum Company of America (ALCOA) patented a nickel-gallium formulation in 1952 (Lyle, 1952). Research also began at that time at the National Bureau of Standards, which revealed other potential combinations of metals to be used with gallium (Waterstrat, 1969). The most promising formulation was based on a palladium-gallium-tin alloy that showed physical properties very comparable to amalgam (Waterstrat & Longton, 1964). Pulpal studies conducted at the National Institute of Dental Research showed a favorable pulpal response, but anecdotal evidence of early postoperative sensitivity was described by the investigators but never formally reported (Swerdlow & Stanley, 1964; Stanley, 1998). Property measurements also revealed a five-day setting expansion of 1% with this alloy (Waterstrat & Longton, 1964) and when contaminated with water, it was later reported to reach 4.2% (Waterstrat, 1969). During this same period, subdermal implant studies in rats with the ALCOA nickel-gallium system resulted in nine out of 10 animals developing sarcomas (Mitchell, Shankwalker & Shazer, 1960). Similar studies were conducted with the palladium-gallium-tin alloy and although no sarcomas were present, the implants did elicit severe inflammatory reactions with tissue necrosis and localized infections (Lyon, Waterstrat & Paffenbarger, 1966). One pulpal trial on primates also reported severe pulpal reactions using the palladium-gallium-tin formulation. At this point the National Bureau of Standards halted research on gallium alloys and no further developments were reported until 1986, when a new formulation containing silver-copper intermetallic powders mixed with a liquid composed of gallium, indium and tin was reported (Horibe; Okamoto & Naruse, 1986). This combination was approved in 1991 for the Japanese market as Gallium Alloy GF (Tokuriki Honten, Tokyo, Japan). Biocompatibility data for this system was generally favorable, but an early clinical evaluation reported bulk fracture, tooth fracture and severe corrosion (Navaro & others, 1993). A second product of similar formulation came on the market in 1994 under the trade name Galloy (Southern Dental Industries, Bayswater, Victoria, Australia). It was submitted to the American Dental Association for the Seal of Acceptance and subsequently awarded the Seal based upon its physical and mechanical properties meeting the requirements for amalgam. The first clinical report on this alloy appeared in 1995 and 12-month data indicated some corrosion, but no adverse problems (Osborne & Summitt, 1995). By the time two-year data from this trial became available, it was obvious that corrosion was more severe and one tooth had fractured for some unknown reason (Osborne & Summitt, 1996). Others were noticing the corrosion problems and recommendations were made by several investigators to avoid contamination of the alloy during placement (Kaga & others, 1996; Knight & Berry, 1997; McComb, 1998). The clinical trials conducted on Galloy employed methods to protect it from water contamination. Each trial used a dentin adhesive as a cavity liner to protect dentin from directly contacting the alloy, and a post-placement coating of unfilled or adhesive resin was applied to prevent salivary contamination of the freshly placed alloy. By 1998, it became apparent that latent expansion, likely caused by corrosion, was resulting in alloy fracture and in some cases, tooth fracture (Neo, Chew & Osborne, 1998). A study by Venugopalan, Broome & Lucas (1998) described the corrosion process and demonstrated the latent expansion by contaminating the alloy *in vitro*. When these results were brought forward, the Galloy product was quickly withdrawn from the market and the ADA Seal of Acceptance withdrawn. Later reports by Osborne & Summitt (1999), Osborne (1999) and Neo & others (2000) confirmed the clinical fracture of teeth from alloy expansion (Figure 4) and demonstrated the expansion using photoelastics and extrusion from polycarbonate molds. A few studies are still investigating the corrosion process and

Figure 4. *A bicuspid fractured after 24 months, with a gallium alloy restoration. Clinical photograph courtesy of Dr John Osborne.*

expansion mechanisms of this alloy, but there is no current evidence in the literature of further development of gallium alloys.

In 1991, scientists from the metallurgy division of the National Institute of Standards and Technology (NIST, formerly the National Bureau of Standards) introduced their work on the formation of intermetallic compounds from powdered metals to the American Dental Association Health Foundation's Paffenbarger Research Center (PRC), also located at NIST. These scientists were developing copper-tungsten intermetallics for uses such as cutting tools and armor-piercing projectiles, and thought that some of their methods may also apply to silver-tin systems. In 1992, collaboration to investigate methods of forming silver-tin intermetallics from elemental powers began. Several early developments resulted from this effort. The first was the discovery of a process called "acid-assisted consolidation," where these elemental powders could be mixed with an acid to remove surface oxides and consolidated, while submersed in the acid (Dariel & others, 1996; Lashmore & others, 1998; Dariel, Ratzker & Eichmiller, 1999). The result was a diffusion reaction between the silver and tin powders that allowed for room-temperature formation of silver-tin intermetallics, their second discovery. As research progressed, it became apparent that the formation of these *in situ* intermetallics resulted in the inability to achieve adequate density at pressures delivered by dental hand instruments, and research shifted to more silver-rich systems. These systems used chemically precipitated silver powders that were further annealed to increase their ductility. These powders could then be mixed with additional intermetallic powders coated with a thin layer of pure silver, the third major discovery (Dariel, Lashmore & Ratzker, 1995).

In 1994, The National Institute of Dental Research called for proposals on the development of amalgam alternatives. This call was in response to increased pressure by US regulators to eliminate the use of mercury and by the World Health Organization to find a suitable alternative that could be used in third-world settings as direct restorative. The PRC-NIST collaboration continued development, with design criteria centering around:

- Direct placement
- Suitable biocompatibility
- Robust storage and stability
- Instrumentation and placement similar to amalgam
- Performance equivalent to amalgam
- Low manufacturing and processing costs

The project was a collaborative effort where the NIST metallurgists were responsible for alloy development and processing, and PRC scientists developed clinical methods for delivery and placement. As work progressed, it became apparent that the addition of coated intermetallic powders also prevented achieving adequate density because of their high yield strengths. Eventually, a composition greater than 98% chemically-precipitated silver powder was settled on. This powder had an agglomerated particle size of approximately 25 μm. The powder was immersed in a volume fraction of 2% fluoroboric acid (HBF_4) to form slurry that could be directly condensed into the cavity preparation. Condensation was done with a 1.5 mm diameter serrated amalgam condenser in increments of 0.1 mm to 0.3 mm in thickness to build up the filling mass (Figure 5). The powder would cold-weld during consolidation to achieve a mass with a density of approximately

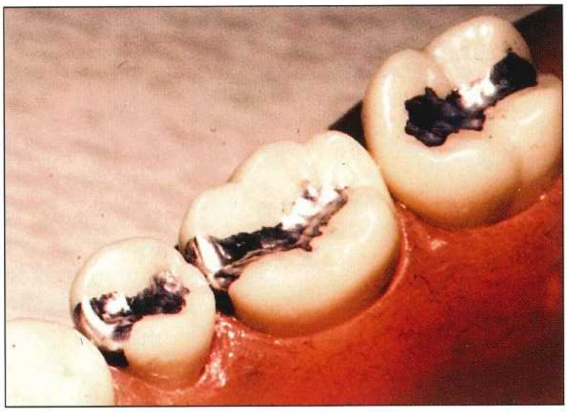


Figure 5. *Metallic restorations made from consolidated silver powders using hand instruments for condensation and cold-welding of the silver. The surfaces were polished with conventional amalgam polishing discs, burs and polishing points. Photograph courtesy of the Paffenbarger Research Center, NIST.*

75% that of theoretical Ag density (Eichmiller & others, 1998). The mass achieved maximum strength immediately upon consolidation, and polishing was accomplished using conventional amalgam polishing techniques (Geiger & others, 1998). Laboratory studies extensively evaluated the physical and mechanical properties of the material and most properties were equivalent to or exceeded amalgam (Xu, Liao & Eichmiller, 1998; Xu & others, 1998; Eichmiller & others, 1999a; Xu & others, 1999a; Xu & others, 1999b; Hoard & others, 2000). Biocompatibility was also evaluated with cell culture studies, dermal sensitivity, subdermal implants and pulpal response (Eichmiller & others, 1999b; Schumacher & others, 2000). The only severe response noted was in cytotoxicity testing, where the response was similar to that expected for pure silver or amalgam. This collaborative project ended in 1999. No clinical studies of this system have since been initiated, and further development will largely depend on whether the industry shows an interest in marketing a direct metallic filling material.

Summary

What does the future hold for metallic alternatives to amalgam? Gold foil continues to be sold and used by a small group of clinicians, but techniques for placement are no longer taught as a regular part of any dental school curriculum. Metal-modified glass ionomers are still being used as buildup materials and restorations in primary teeth, although composites and other fluoride releasing materials have largely taken their place. There is still some ongoing research into metal-filled composites, but the only product available is limited to a buildup composite. Development of gallium alloys appears to have ceased in response to the adverse results from clinical trials, and the one product available in the US market has been withdrawn. The consolidated silver project at NIST has been completed and moved to the technology transfer phase, should some company come forward with interest.

In the last 10 years there has been a tremendous shift in the market requirements for an amalgam alternative. With the current emphasis on esthetics, the market has practically eliminated the demand for new metallic materials and focused primarily on tooth-colored composites. The World Health Organization is focusing its efforts on reinforced glass ionomers with a method known as the Atraumatic Restorative Technique. Regulatory agencies are continuing to put pressure on the profession to reduce or eliminate the discharge of mercury and other heavy metals in dental wastewater. All this adds up to a diminishing interest in metallic alternatives by industry, the public and the profession. In today's market, it would be hard to envision any non-esthetic material being successfully introduced into practice. As such, development of alternatives to amalgam will continue to largely revolve around improving tooth-colored composites.

Disclaimer

Certain commercial materials and equipment are identified in this paper to specify the experimental procedure. In no instance does such identification imply recommendation or endorsement by the National Institute of Standards and Technology or the American Dental Association Health Foundation. Neither are any of the specific materials or equipment identified the best available for the purpose.

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Conservation Dentistry Through Adhesion and Non-Metallic Materials

Conservation Dentistry Through Adhesion and Non-Metallic Materials

THEME 3

©Operative Dentistry Supplement 6, 2001, 119-144

Adhesives and Cements to Promote Preservation Dentistry

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Introduction

During the last three decades clinicians have been confronted with a continuous and fairly rapid turnover in adhesive materials. It started in the mid-'60s with the advent of the first commercialized restorative resin composites, followed in the early '70s with the introduction of the acid-etch technique in clinical practice. Since then, there has been ongoing progress in developing more refined and diversified restorative composites along with the production of steadily improved bonding agents. Effective adhesion to enamel has been achieved with relative ease and has repeatedly proven to be a durable and reliable clinical procedure for routine applications in modern adhesive restorative dentistry. Although adhesion to dentin is not as reliable as adhesion to enamel, today's adhesives produce superior results in laboratories (Perdigão & Lopes, 1999; Inoue & others, 2000a,b; Tanumiharja, Burrow & Tyas, 2000), along with improved clinical effectiveness (Van Meerbeek & others, 1994b, 1996, 1998a; Brunton & others, 1999; Folwaczny & others, 2000; Tyas, 2000; Van Dijken, 2000), thereby, approaching enamel-bonding performance.

Early one-step dentin bonding agents became multi-step systems with more complicated, time-consuming and technique-sensitive application procedures. In the early '90s, the selective enamel-etching technique was replaced by a total-etch concept. Since then, universal enamel-dentin conditioners have been simultaneously applied to enamel and dentin. Now that today's total-etch adhesives have reached a clinically acceptable bonding effectiveness, most recent research and development efforts have focused on simplifying the multi-step bonding process and reducing its sensitivity to errors of inaccurate or incorrect clinical handling (Sano & others, 1998; Finger & Balkenhol, 1999; Inoue & others, 2000b).

In addition to interposition of a resin-based adhesive system between the restorative material and the remaining tooth structure, bonding to tooth tissue can also be clinically achieved directly using glass ionomer cements (Davidson & Mjör, 1999). Glass ionomer-based materials have an auto-adhesive capacity thanks to their specific chemical formula and structural nature (Wilson, Prosser & Powis, 1983; Van Meerbeek & others, 1998b; Yoshida & others, 2000). Parallel with the progress made in resin-based adhesives, glass ionomer technology has undergone many improvements and modifications of its original chemistry since being developed in the early '70s by Wilson & Kent (1971). A thorough discussion of self-adhering glass ionomer materials is beyond the scope of this paper. Nevertheless, some reference will be made to one of the latest trends in adhesive material development that converges both glass ionomer and composite technology into new adhesive systems and restorative materials with mixed characteristics.

This paper critically reflects on the current status of adhesives. An overview is provided with today's commercial adhesives classified according to their adhesive approach towards enamel and dentin. Some critical steps in the rather technique-sensitive bonding procedure are discussed in detail. Finally, bonding effectiveness of a selected group of adhesives is presented in terms of micro-tensile bond strength to enamel and dentin and by clinical retention rates in Class V non-carious cervical lesions.

Classification of Modern Adhesives

The most commonly used classification of adhesives is chronologically based, more or less on the time of their release into the dental market (Kugel & Ferrari, 2000; Van Meerbeek & others, 2000b). Typically, five or even six generations are considered. However, this classification in *generations* lacks scientific background and thus does not allow the adhesives to be categorized on objective criteria. Therefore, classification of adhesives is presented on the basis of the number of clinical application steps, and more importantly, how they interact with the tooth substrate (Figure 1 and Table 1).

The basic mechanism of bonding to enamel and dentin is essentially an exchange process involving replacement of minerals removed from the hard dental tissue by resin monomers that upon *in situ* setting become micro-mechanically interlocked in the created porosities (Figure 2). Depending on the clinical approach, three mechanisms of adhesion are currently in use with modern adhesive systems (Van Meerbeek & others, 1998a, 2000b; Inoue & others, 2000b).

Figure 1. *Classification of current adhesives according to their adhesion strategy towards enamel and dentin.*

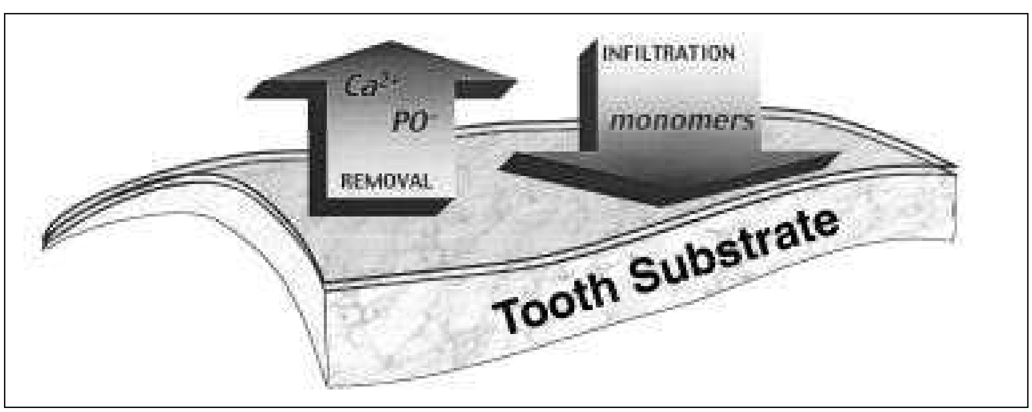


Figure 2. *Schematic presentation explaining the basic mechanism of adhesion to tooth substrate.*

Total-Etch Adhesives

Total-etch adhesives involve a separate etch-and-rinse phase. In their initial configuration, the conditioning step is followed by a priming step and application of the adhesive resin, resulting in *three-step total-etch* adhesives (Figure 1 and Table 1). *Two-step total-etch* adhesives combine the primer and adhesive resin into one application (Figure 1 and Table 1).

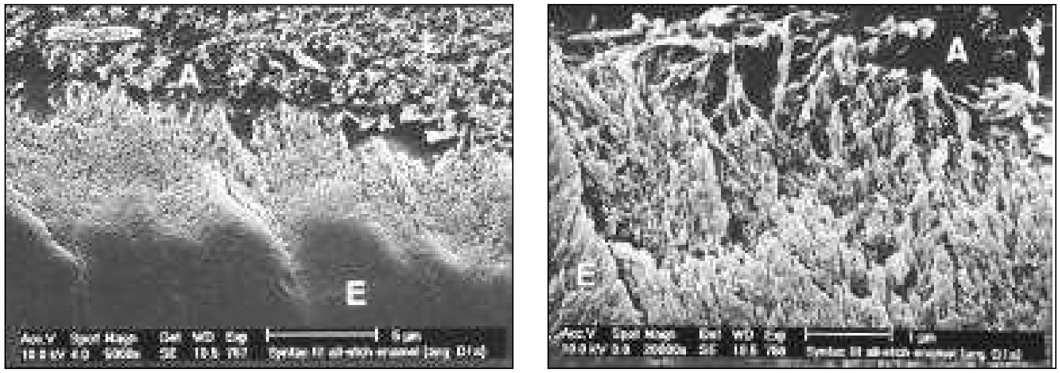


Figure 3Aand B. *Fe-SEM photomicrographs illustrating the enamel-resin interface produced by an experimental two-step total-etch adhesive (Ivoclar-Vivadent) that involved acid-etching of enamel with a 37% phosphoric-acid etchant. Etch-pits have been exposed at the enamel prisms up to a depth of about 5 µm. Macro- as well as micro-tags are formed at respectively the enamel prism peripheries and cores.*

Bonding to acid-etched enamel theoretically requires an air-dried surface to allow the photo-polymerizable hydrophobic bonding agent to be drawn by capillary attraction into the pits created by acid-etching. As a result, two kinds of tag-like resin extensions are formed (Peumans & others, 1999; Van Meerbeek & others, 2000b). Macro-tags are circularly formed between enamel prism peripheries. Microtags are formed at the cores of enamel prisms where the resin cures into a multitude of distinct crypts of dissolved hydroxyapatite crystals (Figure 3). Although most research dealing with adhesive techniques lately has focused mainly on bonding to dentin, the importance of enamel bonding effectiveness may not be neglected with the development of new adhesive systems. The bond to enamel remains the best that can be clinically achieved. Preserving adjacent enamel as much as possible, therefore, remains one of the most important guidelines when preparing cavities for adhesive restorations.

The underlying mechanism of adhesion to dentin is alike for the three- and two-step total-etch adhesives. The dentin smear layer produced during cavity preparation is removed by the etch-and-rinse phase, which concurrently results in a 3-5 µm deep demineralization of the dentin surface (Perdigão, 1995; Perdigão & others, 1996a). Collagen fibrils are nearly completely uncovered from hydroxyapatite (Figures 4-6), and form a micro-retentive network for micro-mechanical interlocking of monomers (applied successively with the primer and adhesive resin for three-step total-etch systems, or combined in one application for two-step total-etch systems). This interlock was first

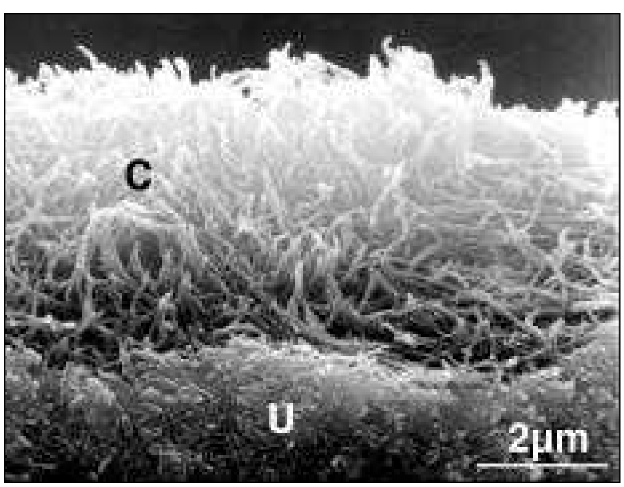


Figure 4. (left) *Fe-SEM of dentin etched for 15 seconds with 35% phosphoric acid (Ultra-Etch, Ultradent). C =Exposed dentinal collagen; U = Unaffected dentin; Bar = 2 µm.*

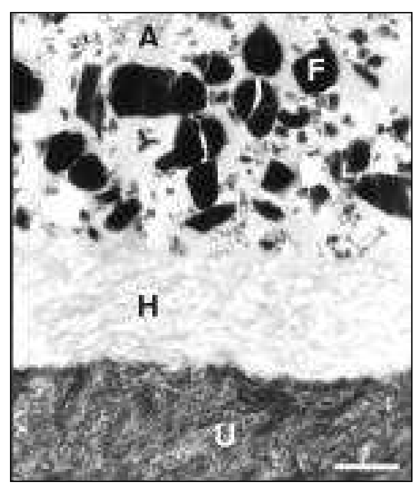


Figure 5. (right) *TEM photomicrograph of an unstained, non-demineralized section through the dentin-resin interface produced by the three-step total-etch adhesive OptiBond FL (Kerr). Note that a 2-3 µm hybrid layer (H) was formed that did not contain any residual hydroxyapatite crystals. A= Adhesive resin; F= Glass filler; U = Unaffected intertubular dentin; Bar = 1 µm.*

Table 1. *Classification of Modern Adhesive Systems According to Their Clinical Application Mode and the Resultant Mechanism of Adhesion to Tooth Substrate*

Brand Name	Manufacturer
One-Step Compomer Adhesives	
[Ariston Liner (Ariston)][1]	Vivadent, Schaan, Liechtenstein
Compoglass SCA(Compoglass)	Vivadent
F2000 Adhesive (F2000)	3M, St Paul, MN, USA
Hytac OSB (Hytac)	ESPE, Seefeld, Germany
Prime&Bond 2.1 (Dyract AP)	Dentsply, Konstanz, Germany
Prime&Bond NT[2] (Dyract AP)	Dentsply
Prompt L-Pop for compomers	ESPE
Solist (Luxat)	DMG, Hamburg, Germany
One-Step Self-Etch Adhesives	
AQ Bond - Touch&Bond	Sun Medical, Kyoto, Japan
Etch&Prime 3.0	Degussa, Hanau, Germany
One-up Bond F	Tokuyama, Tokyo, Japan
Prompt L-Pop for composites	ESPE
Prompt L-Pop 3 (exp)	ESPE
Syntac 3 (self-etch; exp)[2]	Vivadent
Xeno CF Bond	Sankin, Otahara, Japan
One-Step Glass Ionomer Adhesives	
FujiBond LC Liq-Liq (exp.)[2]	GC, Tokyo, Japan
Reactmer[2]	Shofu, Kyoto, Japan
Two-Step Glass Ionomer Adhesives	
FujiBond LC[2]	GC
FujiBond LC Liq-Liq (exp)[2]	GC
Photac Seal (exp.)[2]	ESPE
Two-Step Self-Etch Adhesives	
ABF[2] (exp)	Kuraray, Osaka, Japan
Clearfil Liner Bond 2[2]	Kuraray
Clearfil Liner Bond 2V[2]	Kuraray
Clearfil SE[2]	Kuraray
Imperva FL-Bond[2] (Fluorobond)	Shofu
NRC & Prime&Bond NT[2]	Dentsply
OptiBond (no-etch)[2]	Kerr, Orange, CA, USA
OptiBond FL (no-etch)[2]	Kerr
Sustel (F2000)	3M
Unifil BOND	GC
Coltène ART Bond[3]	Coltène, Altstätten, Switserland
Denthesive II[3]	Hereaus-Kulzer, Wehrheim, Germany
Ecusit Primer-Mono[3]	DMG
Imperva Bond (no etch)[3]	Shofu
Scotchbond 2[3]	3M
Solid Bond[3]	Hereaus-Kulzer
Superlux Universalbond 2[3]	DMG
Syntac[3]	Vivadent
XR-Bond[3]	Kerr

described by Nakabayashi, Kojima & Masuhara in 1982 and is commonly referred to as *hybrid layer* (Van Meerbeek & others, 1992, 1993a; Nakabayashi & Pashley, 1998). Concurrent with hybridization, resin tags seal the unplugged dentin tubules and offer additional retention through hybridization of the tubule orifice wall (Figure 7).

Three specific ultra-morphologic features have been described as resulting from this hybridization process. A *shag-carpet* appearance stands for the loose organization of collagen fibrils that are directed towards the adhesive resin and often unraveled into their micro-fibrils (Figure 8). This feature typically appears when the dentin surface, after being acid-etched, has been actively scrubbed with an acidic primer solution. A similar pattern of deeply tufted collagen fibrils has been observed to result from citric-acid burnishing of root surfaces as part of a tissue-regenerative periodontal treatment (Sterrett & Murphy, 1989). The physical rubbing action combined with the chemical action of the citric acid was found to enhance the removal of acidically-dissolved inorganic dentin

Table 1. *(continued)*

Brand Name	Manufacturer
Two-Step Total-Etch Adhesives – 'One-Bottle'Adhesives	
Bond 1	Jeneric/Pentron, Wallingford, CT, USA
Dentastic Uno	Pulpdent, Watertown, MA, USA
Dentastic Duo	Pulpdent
EasyBond	Parkell, Farmingdale, NY, USA
Everbond (exp)[2]	ESPE
Excite[2]	Vivadent
Gluma 2000	Bayer, Leverkusen, Germany
Gluma One Bond	Heraeus-Kulzer
Gluma Comfort Bond	Heraeus-Kulzer
One Coat Bond	Coltène
One Step	BISCO, Schaumburg, IL, USA
Optibond SOLO[2]	Kerr
Optibond Solo Plus[2]	Kerr
Prime&Bond 2.1	Dentsply
Prime&Bond 2.1 Dual Cure	Dentsply
Prime&Bond NT[2]	Dentsply
Prime&Bond NT Dual Cure[2]	Dentsply
PQ1[2]	Ultradent, South Jordan, UT, USA
Scotchbond 1 (Single Bond)	3M
Snapbond	Cooley & Cooley, Houston, TX, USA
Solist	DMG
Solobond M	Voco, Cuxhaven, Germany
Stae	Southern Dental Industries, Victoria, Australia
Syntac Single-Component	Vivadent
Syntac Sprint	Vivadent
Syntac 3 (total-etch; exp)	Vivadent
Tenure Quik with Fluoride	Den-Mat, Santa Maria, CA, USA
Three-Step Total-Etch Adhesives	
ABC Enhanced	Chameleon, Kansas City, KA, USA
Ælitebond	BISCO
All-Bond 2	BISCO
Amalgambond Plus	Parkell
Clearfil Liner Bond[2, 4]	Kuraray
Dentastic	Pulpdent
Denthesive	Hereaus-Kulzer
EBS	ESPE
EBS Multi	ESPE
Gluma Bonding System	Bayer
Gluma CPS	Bayer
Imperva Bond (total-etch)	Shofu
Mirage Bond	Chameleon
OptiBond (total-etch)[2]	Kerr
OptiBond FL (total-etch)[2]	Kerr
PAAMA[2]	Southern Dental Industries
Permagen	Ultradent
Permaquik[2]	Ultradent
Quadrant UniBond	Cavex Holland, Haarlem, Netherlands
Restobond 3	Lee Pharmaceuticals, South El Monte, CA, VS
Scotchbond Multi-Purpose	3M
Scotchbond Multi-Purpose Plus	3M
Solid Bond	Heraeus-Kulzer
Super-Bond D Liner	Sun Medical
Tenure S	Den-Mat

[1]One-step adhesive used in combination with an ion-releasing restorative material; [2]Adhesives providing filled adhesives; [3]Early self-etch adhesives developed to be applied on dentin only, whereas enamel is etched separately with a phosphoric acid (>30%) conditioner; [4]Because of the application of a silica-filled low-viscosity resin (Protect Liner) in addition to the application of the adhesive resin, Clearfil Liner Bond is applied in four steps.

material and surface debris. This resulted in a deeply tufted collagen fibril surface topography, similar to the appearance of a *shag carpet*. In this way, the dentinal root surface became more receptive to the attachment of cells from new connective tissue-formation. Likewise, the combined mechanical/chemical action of rubbing the acid-etched dentin with an acidic primer (or primer/adhesive combination) probably

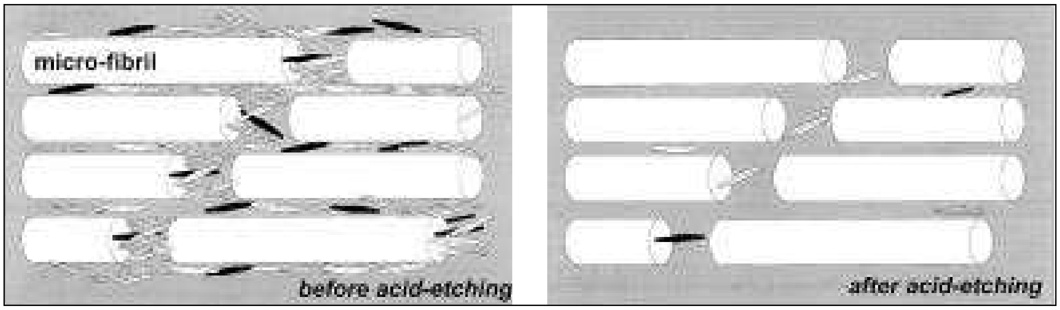


Figure 6. *Schematic drawing presenting a mineralized collagen fibril with its micro-fibrils before and after being etched with a conventional phosphoric acid etchant.*

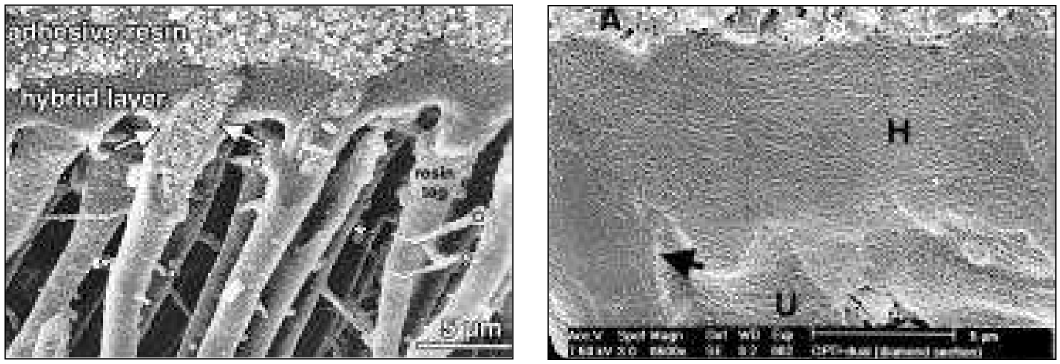


Figure 7. (A) (left) *Fe-SEM photomicrograph illustrating the dentin-resin interface produced by the three-step total-etch adhesive OptiBond FL (Kerr) after removal of the adjacent unaffected dentin. An acid-resistant hybrid layer of 3-5 µm was formed along with particle-reinforced resin tags. The hybrid layer triangularly extends within the tubule orifice walls, representing "tubule wall hybridization" (arrows). Micro-tags (asterisks) are formed within the tubule lateral branches and branch off the main resin tags. Bar = 5 µm.*

Figure 7 (B) (right) Fe-SEM photomicrograph of a diamond-knife sectioned dentin-resin interface produced by Optibond Dual Cure (Kerr). Aclear loosely organized collagen fibril network can be observed within the 4-5 µm hybrid layer (H). A= Adhesive resin (particle-filled); U = Unaffected intertubular dentin; Arrow = Tubule wall hybridization; Bar = 5 µm.

dissolves additional mineral while fluffing and separating the entangled collagen at the surface (Figure 9). This active rubbing application is thought to promote infiltration of monomers into the loosened collagen scaffold by a kind of "massaging" effect.

Asecond typical hybridization characteristic has been termed as *tubule-wall hybridization* and represents the extension of the hybrid layer into the tubule wall area (Figure 10). Resin-tag formation in the opened tubules is circularly surrounded by a hybridized tubule-orifice wall that is thought to be favorable in hermetically sealing the pulpo-dentinal complex against microleakage and the potential subsequent ingress of micro-organisms. This effect may be especially protective when the bond fails either at the bottom or top of the hybrid layer, which are considered the two weak links in the micro-mechanical attachment. Then, the resin tags usually break off at the hybrid layer surface keeping the dentin tubules and thus the direct connection to the pulp sealed (Figure 11). In particular, the resin-tag necks at the top 5-10 µm of the tubule orifices are thought to contribute most to retention and sealing effectiveness (Figure 10). The actual length of the resin tags must probably be regarded as being of secondary importance.

Thirdly, *lateral tubule hybridization* has been described as the formation of a tiny hybrid layer into the walls of lateral tubule branches (Figure 12). This micro-version of a hybrid layer typically surrounds a central core of resin, called a *micro-resin tag*.

A plus-minus balance featuring three-step total-etch systems is given in Table 2. Although the clinical application procedure of the newest generation of "one-bottle" or two-step total-etch adhesives might be simpler due to the reduction by one step, the eventual application time may not have been substantially reduced as compared to con-

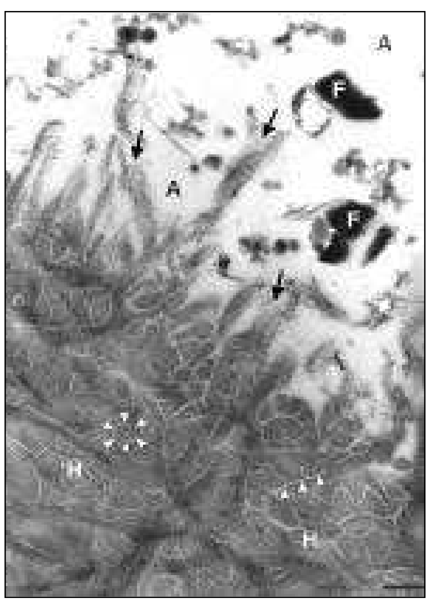


Figure 8. *TEM photomicrograph illustrating the typical* shag-carpet *appearance at the transition of the hybrid layer (H) to the adhesive resin (A) when the three-step total-etch adhesive Optibond Dual Cure (Kerr) was used. The collagen fibrils are directed towards the adhesive resin and are frayed at their ends into their micro-fibrils (arrows). This ultra-morphologic feature is ascribed to result from actively rubbing the etched dentin surface using an acidic primer solution. F= Glass filler incorporated within the adhesive resin; Arrow heads = 10-20 nm resin-filled interfibrillar spaces; Bar = 0.2 µm. (Reprinted from Van Meerbeek & others, 1998c).*

ventional three-step systems (Table 3). In conventional three-step systems, the primer should assure efficient wetting of the exposed collagen fibrils, displace any residual surface moisture, transform a hydrophilic into a hydrophobic tissue state and sufficiently carry monomers into the interfibrillar channels. The adhesive resin should fill up the remaining pores between the collagen fibrils, form resin tags that seal the opened dentinal tubules, initiate and advance the polymerization reaction, stabilize the formed hybrid layer and resin tags and provide sufficient methacrylate double bonds for co-polymerization with the successively applied restorative resin. In simplified one-bottle systems, the functions of the primer and the adhesive resin should be perfectly combined. As a consequence, higher technique sensitivity has often been ascribed to the use of these one-bottle systems (Finger & Balkenhol, 1999; Perdigão, Swift & Lopes, 1999; Inoue & others, 2000a,b; Blunck, 2000). As these combined primer/adhesive resin solutions have a higher solvent-to-monomer ratio, a realistic risk exists that such adhesives are applied in a too thin layer (Table 3). To achieve adequate bonding, it is of major importance, however, that the *one-bottle* solution is abundantly applied. Monomers should be sufficiently supplied not only to saturate the exposed collagen fibril network, but also to establish a satisfactorily thick resin layer on top of the hybrid layer. Such a distinct resin layer (that definitely must be pre-cured prior to applying the restorative composite) must be regarded as a flexible, intermediate *shock-absorber* (see below). In light of an *elastic bonding concept*, it is expected that this shock-absorber may help to protect the adhesive joint against early failure caused by the shrinking composite cured on top. Therefore, when using one-bottle adhesives, it is recommended to apply multiple layers to ensure a sufficiently thick resin film on top of the hybrid layer. They are particularly necessary when using primer/adhesive resin combinations with high acetone content. The so-called *nanofiller* added to certain *one-bottle* adhesives (Prime&Bond NT, Dentsply; Excite, Vivadent) may also help to establish a uniform resin film that stabilizes the hybrid layer. After priming, the surface should appear glossy without so-called *dry spots*, the clinical indication that resin was adequately and sufficiently applied. Especially in the latter respect,

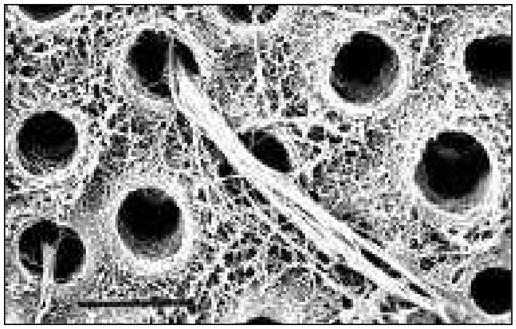


Figure 9. *Fe-SEM photomicrograph demonstrating the effect of Non-Rinse Conditioner (Dentsply) on dentin (top view) that resulted in a typical "shag-carpet" appearance. Note that due to smear layer preparation, a bundle of intratubular collagen was pulled out of the dentin tubule and smeared over the exposed intertubular collagen fibril network. Bar = 5 µm.*

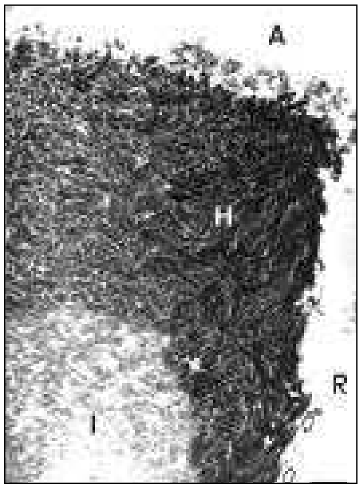


Figure 10. *TEM photomicrograph of a demineralized section through the dentin-resin interface produced by Optibond Dual Cure (Kerr). The loosely organized hybrid layer (H) typically contains collagen fibrils separated by resin-filled interfibrillar spaces and extends triangularly into the tubule wall area (open black arrows). This "tubule wall hybridization" firmly attached the resin tag (R) to the tubule orifice wall and most importantly contributed to a hermetic seal of the tubule. A= Adhesive resin; I = Lab-demineralized intertubular dentin (I). Bar = 500 nm.*

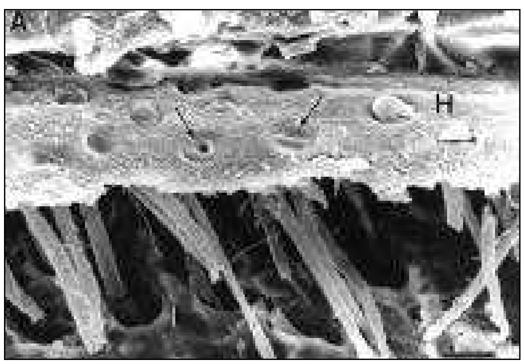


Figure 11. *Fe-SEM photomicrograph of a dentin-resin interface that was produced by the three-step total-etch adhesive Permagen (Ultradent). The interface was separated between the adhesive resin (A) and the hybrid layer (H), while the resin tags (arrows) kept the tubules sealed as they broke off at the level of the hybrid layer. This must be attributed to the tubule wall hybridization that ensures a leakage-free seal of the tubules and strong bond to the tubule orifice walls. I = Intertubular dentin; Bar = 4 µm.*

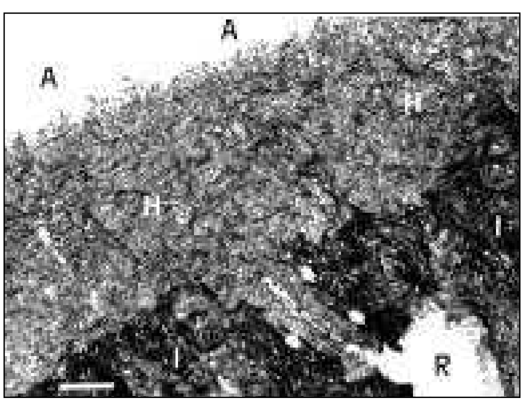


Figure 12. *TEM photomicrograph of a non-demineralized section demonstrating the resin-dentin interface produced by the three-step total-etch adhesive Optibond Dual Cure (Kerr). Note the formation of a micro-resin tag (arrows) into a lateral tubule branch. Acore of resin is surrounded by a hybridized wall* (lateral tubule hybridization) *A= Adhesive resin; H = Hybrid layer; I = Intertubular dentin; R = Resin tag; Bar = 1 µm. (Reprinted from Van Meerbeek & others, 1998a).*

Table 2. *Plus-Minus Balance of Three-Step "Total-Etch" Adhesives*

Plus	Minus
• Separate application of conditioner, primer and adhesive resin	• Risk of "over"-etching dentin (highly concentrated phosphoric-acid etchants)
• "Lowest" technique-sensitivity	• Time-consuming three-step application procedure
• *In-vitro* and *in-vivo* proven effectiveness of adhesion to enamel and dentin	• Post-conditioning rinse phase required (time-consuming and risk on surface contamination when not using rubber dam)
• Best bond to enamel	• Sensitive to "overwet" or "overdry" dentin surface conditions
• Most effective and consistent results	• Weak monomer-collagen interaction (which may lead to nano-leakage and early bond degradation; Figure 6)
• Possibility for particle-filled adhesive ("shock-absorber")	

Table 3. *Plus-Minus Balance of Two-Step "Total-Etch" Adhesive*

Plus	Minus
• Basic features of three-step systems (Table 2)	• Not substantially "faster" application (multiple layers)
• "Simpler" application procedure by reduction with 1 step	• More technique-sensitive (multiple layers)
• Possibility for "single-dose" packaging • Consistent and stable composition • Controlled solvent evaporation • Hygienic application (>< cross-infection)	• Risk of a too thin bonding layer (no glossy film, no "shock" absorber, insufficiently polymerizable due to oxygen inhibition)
• Possibility for particle-filled adhesive ("shock-absorber")	• Effects of total-etch technique (Table 2) • Risk of "over"-etching dentin • Post-conditioning rinse phase required • Sensitive to degree of dentin wetness • Weak monomer-collagen interaction
	• Insufficient long-term clinical results

the addition of nanofiller must be regarded as beneficial, rather than perceived that the nanofiller would infiltrate the exposed collagen fibril network and thus reinforce the hybrid layer, as has been hypothetically claimed. TEM (Transmission Electron Microscopy) of unstained sections has clearly demonstrated that the collagen fibril network mostly filters out the nanofiller, holding them at the hybrid layer surface (Tay, Moulding & Pashley, 1999; Inoue & others, 2000b). Besides, it is not obvious that penetration of the nanofiller in the hybrid layer would strengthen the bond or improve the bond stability. Even simply providing evidence that this effect may occur must be extremely difficult, if not impossible.

Self-Etch Adhesives

The alternative approach is based on the use of non-rinse acidic monomers that simultaneously condition and prime dentin and enamel. The concept of self-etch primers was first introduced with Scotchbond 2 (3M) in the early '90s (Table 1). However, this system was advocated only to be applied on dentin alone, and therefore required clinically selective-enamel etching in a separate step. The current self-etch adhesives provide monomer formulations for simultaneous conditioning and priming of both enamel and dentin. Most common self-etch adhesives involve two application steps with the self-etch primer followed by an adhesive resin, resulting in *two-step self-etch* adhesives (Figure 1 and Table 1). Most recently, *one-step self-etch* or so-called *all-in-one* adhesives combining the conditioning, priming and the application of an adhesive resin into a single application have been marketed (Figure 1 and Table 1). Besides, on the basis of the number of application steps, self-etch adhesives should also be subdivided into *mild* and *strong* self-etch adhesives, depending on their pH and thus etching potential (Table 4).

Table 4. *Classification of "Self-Etch" Adhesives Following Their Etch Potential**

Mild (pH = ± 2)	Strong (pH ≤ 1)
Clearfil Liner Bond 2V (Kuraray)	Non-Rinse Conditioner & Prime&Bond NT (Dentsply)
Clearfil SE Bond (Kuraray)	Prompt L-Pop 1,2 (ESPE)
F2000 Primer/adhesive (3M)	Vivadent experimental self-etch adhesive
Imperva FL-Bond (Shofu)	
Mac-Bond II (Tokuyama)	
One-up Bond F (Tokuyama)	
Experimental PQ/Universal (Ultradent)	
Unifil Bond (GC)	

* Some of the self-etch adhesives mentioned in Table 1 were not included in this table, as their interfacial interaction with dentin has not yet been studied.

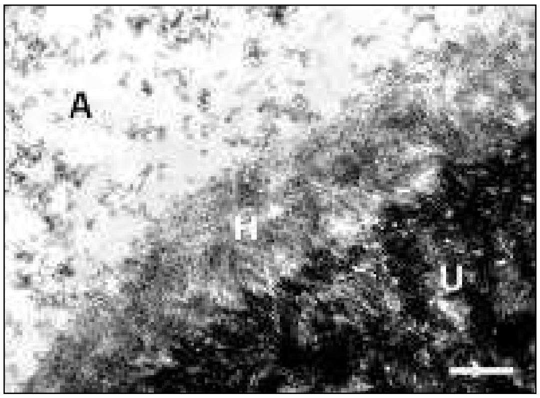


Figure 13. *TEM photomicrograph of an unstained, non-demineralized section illustrating the interface between dentin and the "mild" self-etching adhesive Clearfil Liner Bond 2V (Kuraray). A hybrid layer (H) with the depth of on average 600 nm was formed with only partial demineralization and exposure of collagen fibrils (not visible because this section was not stained). Hydroxyapatite crystals are clearly scattered within the hybrid layer. A= Adhesive resin (particle-filled); U = Unaffected intertubular dentin; Bar=500 nm.*

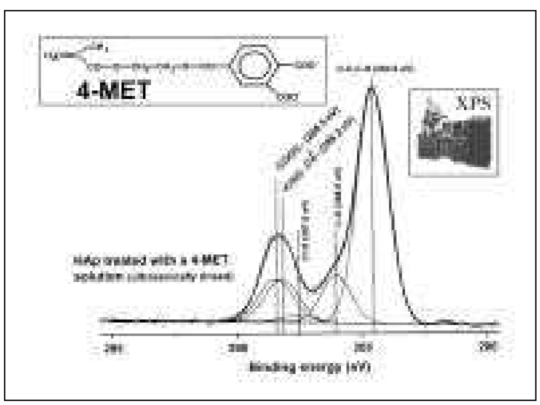


Figure 14. *XPS narrow-scan spectrum of the C 1s peak when 4-MET was applied on synthetic hydroxyapatite suggesting the formation of an ionic bond between the –COO^- of 4-MET with Ca^{2+} of hydroxyapatite.*

The bonding mechanism of "mild" self-etch adhesives to dentin is also based on hybridization, with the difference that only submicron hybrid layers are formed and resin-tag formation is less pronounced (Figure 13). Within such submicron hybrid layers, collagen fibrils are not completely deprived from hydroxyapatite (in contrast to total-etch adhesives, Figure 6). This residual hydroxyapatite may serve as a receptor for additional intermolecular interaction with specific carboxyl or phosphate groups of the functional monomers. For instance, the primary ionic bonding potential of the two carboxyl groups of a 4-MET (4-methacryloxyethyl trimellitic acid) based two-step self-etch adhesive (Unifil Bond, GC) with hydroxyapatite has been confirmed in a correlative XPS (X-Ray Photo-electron Spectrosopy) and TEM study (Van Meerbeek & others, 2000a) (Figure 14). If not through primary chemical bonding, we speculate that such monomers will at least be able to more intimately interact with hydroxyapatite-coated collagen than with collagen that due to the rather aggressive total-etch technique, almost completely lost its hydroxyapatite coating (Figure 6). Moreover, this two-fold bonding mechanism may be advantageous in terms of restoration longevity. It comprises a micro-mechanical bonding component that may, in particular, provide resistance to "acute" de-bonding stress (for instance, imposed during laboratory bond testing experiments which, however clinically, may be less relevant). The additional monomer/hydroxyapatite-around-collagen interaction on a molecular level may result in bonds that better resist hydrolytic degradation processes (through, for instance, nanoleakage as suggested by Sano & others, 1995a,b), and thus may help keep the restoration margins sealed for longer periods. It is also noteworthy that although these mild self-etch adhesives typically present with submicron hybrid layers, nevertheless, they are most often documented with bond strength and marginal sealing data equal to those obtained with total-etch adhesives (Blunck, 2000; Inoue

Table 5. *Plus-Minus Balance of "Self-Etch" Adhesives*

Plus	Minus
• Simultaneous demineralization and resin-infiltration	• Insufficient long-term clinical research
• No post-conditioning rinsing	• Adhesion potential to enamel needs yet to be clinically proven
• Not sensitive to diverse dentin-wetness conditions	
• Time-saving application procedure	
• Low technique-sensitivity	
• Possibility for "single-dose" packaging	
• Consistent and stable composition	
• Controlled solvent evaporation	
• Hygienic application (>< cross-infection)	
• Possibility for particle-filled adhesive ('shock-absorber')	
• Adequate monomer-collagen interaction	
• Effective dentin desensitizer	

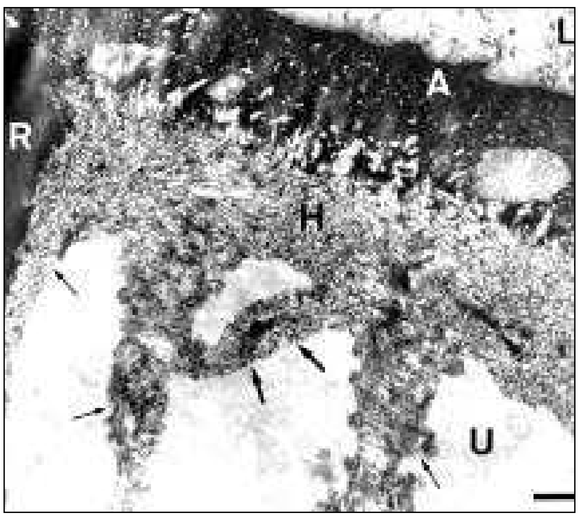


Figure 15. *TEM photomicrograph of a lab-demineralized and UA/LC positively stained section illustrating the acid-resistant hybrid layer (H) produced by the "strong" "one-step self-etching" adhesive Prompt L-Pop (ESPE). Note the "shag-carpet" appearance at the transition of the adhesive resin (A) to the hybrid layer (H), the "tubule wall hybridization" (thin arrows) and the formation of a micro-resin tag surrounded by "lateral tubule hybridization" thick arrows). L= Low-viscosity resin; R = Resin tag; U = Unaffected dentin (lab-demineralized); Bar* = 1 µm.

& others, 2000a,b). This suggests that such hydroxyapatite-containing hybrid layers apparently provide adequate bonding performance and that the thickness of the hybrid layer, itself, (or the amount of micro-mechanical interlocking) is probably of minor importance. However, little has been described regarding the distribution of minerals and/or the resins within such submicron hybrid layers of mild self-etch adhesives. Self-etch monomers should, while dissolving the smear layer, engage intact dentin. How far the resin must penetrate to obtain this goal remains unknown.

"Strong" self-etch adhesives have been documented with an interfacial ultra-morphology at dentin resembling that produced typically by total-etch adhesives (Figure 15). Consequently, the mechanism of bonding strong self-etch adhesives to dentin is more alike that of total-etch adhesives. This means that nearly all hydroxyapatite is removed from collagen and thus any chemical interaction between hydroxyapatite and functional monomers is excluded (Figure 6). These strong self-etch adhesives present with all typical hybridization features of total-etch adhesives (see above) along with the formation of abundant resin tags.

Clinically, self-etch systems not only simplify the bonding process by eliminating steps, but also eliminate some of the technique-sensitivity of total-etch systems (Gordan & others, 1998; Inoue & others, 2000b) (Table 5). Furthermore, the clinician is not preoccupied regarding the degree of moisture at the dentinal surface after etching, so the issue of "wet-bonding" is of no relevance for these kinds of adhesives. Finally, the risk on incomplete resin infiltration is eliminated by simultaneous infiltration of the exposed collagen fibril scaffold with resin up to the same depth of demineralization. The questionable self-etch potential on enamel is discussed below.

Glass Ionomer Adhesives

A third adhesion strategy differs from the former approaches (pursued by resin-based systems), as it involves a glass ionomer based interaction with the tooth substrate (Table 1 and Figure 1). Dilution of restorative materials by adding more resin has

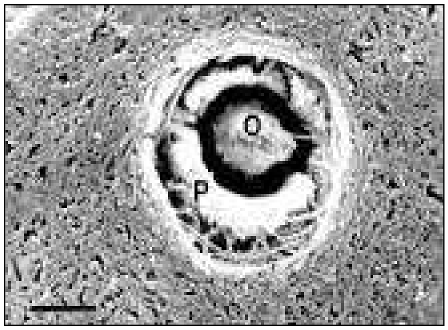


Figure 16. *Fe-SEM photomicrograph illustrating the effect of a 10-second application of 20% polyalkenoic acid (Cavity Conditioner, GC) to dentin. Note that although intertubular collagen was exposed, the fibrils were not completely denuded from hydroxyapatite. O = Odontoblast process; P= Peritubular dentin; Bar = 1 µm.*

resulted in the development of resin-modified glass ionomer adhesives that can bond resin composites to tooth tissue. From its origin, a two-fold mechanism of adhesion can be predicted. A short polyalkenoic acid pre-treatment cleans the tooth surface (Figure 16); it removes the smear layer and exposes surface collagen fibrils only up to about 0.5-1 µm depth; herein, resin interdiffuses with the establishment of a micro-mechanical bond following the principle

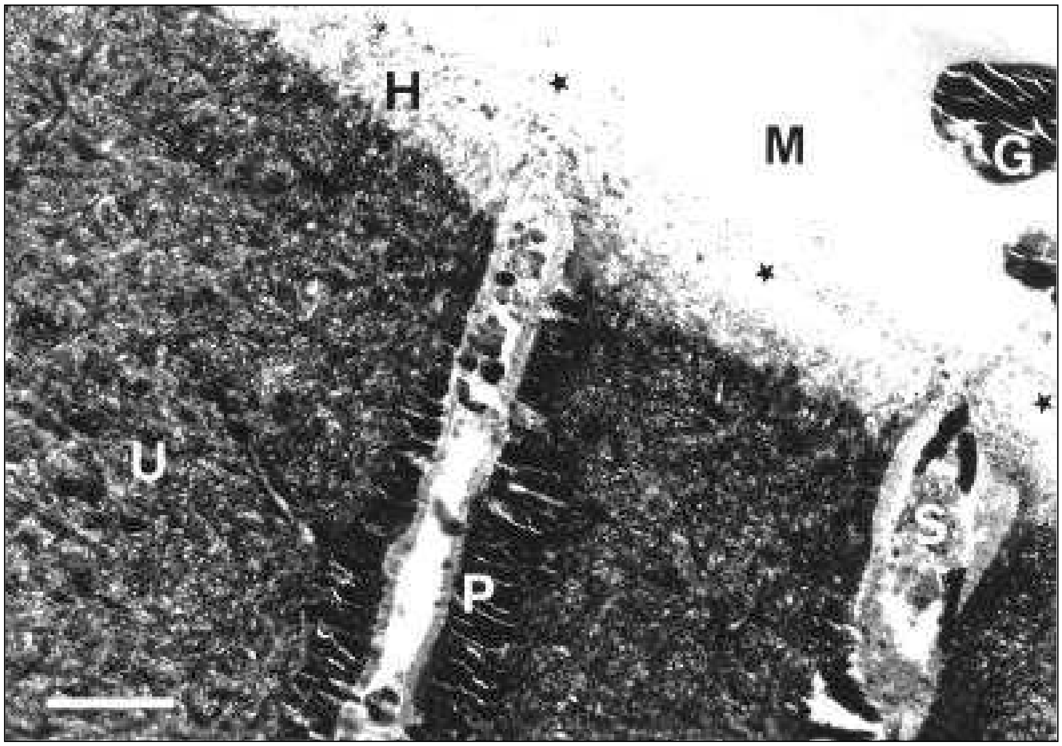


Figure 17. *TEM Photomicrograph of an unstained, non-demineralized section demonstrating the interface formed at dentin by a glass-ionomer adhesive (Fuji Bond LC, GC). The shallow hybrid layer (H) of about 0.5 µm results from the short (10 seconds) application of a 20% polyalkenoic acid, by which collagen fibrils are exposed, butnot completely denuded from hydroxyapatite (collagen is invisible on this image as the section was not positively stained). The hydroxyapatite crystals remaining around the collagen fibrils served as receptors for chemical bonding with the carboxyl groups of the polyalkenoic acid. On top of the hybrid layer, a 0.5-µm gray zone (asterisks) typically contains small black globules of yet unknown origin and is clearly demarcated from the glass ionomer matrix (M). This phase represents the morphological manifestation of a gelation reaction of the polyalkenoic acid with calcium that was extracted from the underlying dentin surface. G = fluoro-alumino-silicate glass filler surrounded by a silica hydrogel; P= Peritubular dentin; S = Smear occluding the tubule orifice; U = Unaffected intertubular dentin; Bar = 2 µm.*

of *hybridization* (Figure 17). The polyalkenoic acid pre-treatment is much less invasive than a traditional phosphoric-acid treatment in the way that the exposed collagen fibrils are not completely denuded from hydroxyapatite (Figure 16). Chemical bonding is additionally obtained by ionic interaction of the carboxyl groups of the polyalkenoic acid with calcium of hydroxyapatite that remained attached to the collagen fibrils (Yoshida & others, 2000) (Figure 18). As mentioned above, for mild self-etch adhesives, this supplementary chemical attachment may be beneficial particularly in terms of resistance to rapid hydrolytic degradation (Table 6). Consequently, the underlying mechanism of glass ionomer adhesives and "mild" self-etch adhesives may be similar.

Critical Steps in Clinical Bonding

Total Versus Self-Etching Enamel

Following a total-etch approach, both enamel and dentin are currently etched with phosphoric acid in a concentration between 30 and 40%. However, in the early '90s, lower concentrated (10-20%) phosphoric-acid etchants and phosphoric-acid alternatives, such as maleic, citric and nitric acid, were advocated in light of a *total-etch* technique that was not too aggressive to dentin. Consequently, dentin would certainly not be etched to a depth inaccessible for resin to penetrate up to the complete demineralization depth in a relatively short time. A few years after their introduction, clinical research has, however, learned that these *dentin-kind* total-etchants prepare enamel insufficiently (Swift & Cloe, 1993; Triolo & others, 1993; Van Meerbeek & others, 1994b,

Table 6. *Plus-Minus Balance of "Glass-Ionomer" Adhesives*

Plus	Minus
• Fast and simple application procedure (new liquid/liquid formulation under development)	• Adequate adhesion to enamel requires smear layer removal
• Viscous particle-filled adhesive ("shock-absorber")	• Insufficient long-term clinical research
• Cariostatic potential by release of fluoride	
• Two fold bonding mechanism:	
• Ionic bonding to hydroxyapatite	
• Micro-mechanical through hybridization	

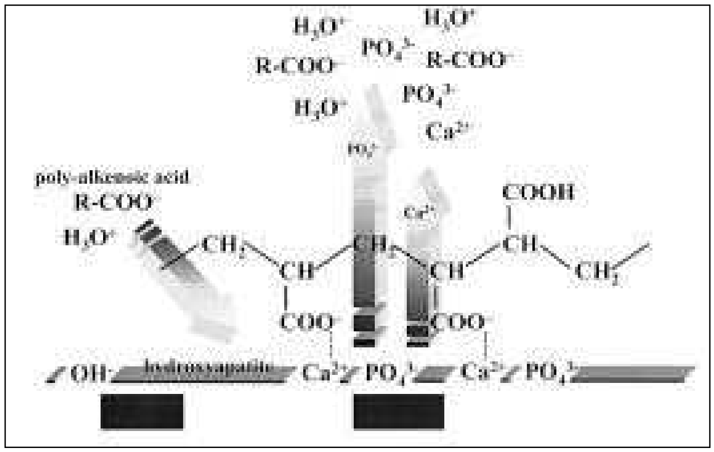


Figure 18. *Schematic presentation of the ion-exchange process and the formation of an ionic bond between the carboxyl groups of the polyalkenoic acid with calcium of hydroxyapatite.*

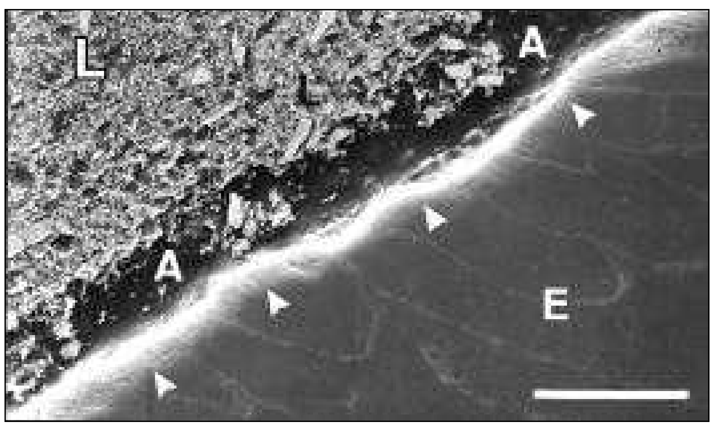


Figure 19. *Fe-SEM photomicro-graph of an argon-ion-bombarded resin-enamel interface as produced by a "strong" self-etching adhesive (experimental Vivadent). Note that the self-etching approach resulted in a clearly detectable effect (arrow-heads) at the enamel surface (E). No separation was observed between the adhesive resin (A) and enamel. The bonding mechanism is primarily based on the formation of micro-resin tags. L= Low-viscosity resin cured on top of the adhesive resin; Bar = 10 µm.*

1996). Enamel apparently requires more aggressive etching, such as that provided by conventional 30-40% phosphoric acid etchants; this not only to remove the smear layer, but also to produce a micro-retentive etch-pattern with high surface energy. When such 30-40% phosphoric acid etchants are used on dentin, over-etching can best be avoided by applying the acid first on enamel so that enamel is etched the longest (for at least 15 seconds) and successively dentin is etched for 15 seconds at maximum. Only sclerotic dentin surfaces can be etched longer without the risk of etching them too deeply. In fact, it is even advisable to etch this hyper-mineralized tissue longer to make it more receptive to bonding (Van Meerbeek & others, 1994a, 1998a; Tay & others, 2000). After etching, the conditioner and its byproducts should be thoroughly rinsed off prior to application of the primer and adhesive resin. For instance, not rinsing off the nitric acid conditioner, as was recommended by the manufacturer of ABC Enhanced (Chameleon), resulted in an incompletely resin-penetrated demineralized dentin surface layer or even any significant hybrid layer formation at all (Perdigão, 1995; Eick & others, 1995; Van Meerbeek & others, 1998a). Properly rinsing off the conditioner was sufficient to achieve adequate hybridization.

Concern is often raised regarding the bonding effectiveness of self-etch adhesives to enamel. Numerous recent laboratory studies provide data that suggests either equal or reduced enamel bonding effectiveness as compared to conventional phosphoric acid etching (Perdigão & others, 1997; Hayakawa, Kikutake & Nemoto, 1998; Yoshiyama & others, 1998; Hannig, Reinhardt & Bott, 1999; Hara & others, 1999; Kanemura, Sano & Tagami, 1999). Nevertheless, so far, no clinical evidence has been provided that this self-etch approach guarantees durable bonding to enamel. However, neither has a con-

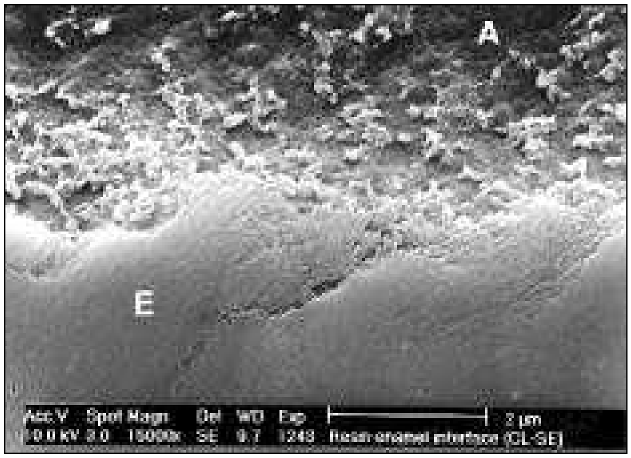


Figure 20. *Fe-SEM photomicrograph of an argon-ion-bombarded resin-enamel interface as produced by a* mild *self-etching adhesive (Clearfil SE Bond, Kuraray). Note that the self-etching approach resulted in a hardly detectable effect at the enamel surface (E). No separation was observed between the adhesive resin (A) and enamel. The bonding mechanism is primarily based on the formation of micro-resin tags. A= Silica-filled adhesive resin; Bar = 2 µm.*

trolled long-term clinical trial been published that concludes that self-etched enamel affects the clinical longevity of adhesive restorations. Fe-SEM (Field-emission Scanning Electron Microscopy) interfacial characterization of the resin-enamel interface clearly revealed that the interaction of self-etch adhesives again depends on the pH, and thus, the etching aggressiveness of the self-etching primer/adhesive. Whereas *strong* self-etch adhesives presented with the formation of "micro-tags" (Figure 19), the *mild* systems hardly showed any detectable interaction with dentin (Figure 20). Today, any correlation between morphologic findings and bonding effectiveness has not been provided, making the need for controlled clinical trials to test the *self-etch* against the *total-etch* approach towards enamel urgently needed. Until then, it remains clinically advisable to employ this simplified application technique first, only on enamel that has been previously coarsened by bur, second, by applying the self-etch primer during a sufficiently long time of at least 15 seconds and third, by actively applying it through rubbing the enamel surface with repeated applications of fresh material. Alternatively, a separate conventional etchant can be applied prior to the application of the self-etch primer.

Some of today's so-called "self-etch primers" are applied prior to the application of polyacid modified resin composites or *compomers* but hardly have a self-etching potential (Table 1). Nevertheless, manufacturers recommend bonding compomers into mixed enamel-dentin cavities using these one-step adhesives without any separate acid-etching step preceding their application. However, morphologic study of the resultant interface with dentin confirmed their limited etching action (Van Meerbeek & others, 1998a; Inoue & others, 2000b). A shallow, sub-micron interaction without substantial collagen fibril exposure was disclosed. Smear debris to keep the dentinal tubules plugged was observed, and at best was entrapped by resin, forming so-called resin-impregnated smear plugs. Consequently, these adhesives are certainly not aggressive enough to expose a highly retentive etch-pattern on the enamel surface. Moreover, recent clinical trials reported the occurrence of small to severe enamel margin chipping already after six months of clinical service, that if left untreated, rapidly could lead to marginal discoloration and even caries recurrence (Gladys, 1997; Gladys & others, 1998). These early enamel margin defects should be ascribed to ineffective etching of enamel using the weak self-etch primers only. These clinical results were confirmed *in vitro*, where the primers provided with compomers produced less effective bonding results on enamel (Cortes, García-Godoy & Boj, 1993; Fritz, Finger & Uno, 1996; Abate & others, 1997; Attin, Buchalla & Hellwig, 1996; Ferrari & others, 1998). Most likely, the clinical effectiveness of these polyacid modified composites could be substantially improved by supplementary acid-etching enamel prior to the primer application or by using adhesives with stronger self-etch potential.

Wet Versus Dry Bonding

After conditioning following a total-etch approach, the enamel and dentin surface should be properly treated to allow full penetration of adhesive monomers. On the enamel surface, a dry condition is theoretically preferred. On the dentin site, a certain amount of water is recommended to avoid collapse of the exposed dentin collagen scaffold, thereby, impeding effective penetration of adhesive monomers (Perdigão & others, 1995). Consequently, in most common cavities involving enamel and dentin, the clini-

Table 7. *Current Adhesives Categorized Following the Type of Solvent of the Primer or Combined Primer/ Adhesive Resin*

Acetone	Acetone-Water	Acetone-Ethanol	Ethanol	Ethanol-Water	Water
ABC Enhanced (Chameleon)	AQ Bond (Sun Medical	All-Bond 2 (BISCO)	Excite (Vivadent)	Gluma Comfort Bond (Kulzer)	Amalgambond Plus (Parkell)
EG Bond (Sun Medical)	Reactmer (Shofu)		Optibond Solo Plus (Kerr)	Optibond FL (Kerr)	ART Bond (Coltène)
Gluma One-Bond (Kulzer)	Tenure Quik (Den-Mat)		PQ1 (Ultradent)	Permaquik (Ultradent)	Clearfil SE Bond (Kuraray)
One Step (BISCO)				Quadrant Unibond (Cavex)	Denthesive II (Kulzer)
Permagen (Ultradent)				Scotchbond 1 (3M)	EBS (ESPE)
Prime&Bond NT (Dentsply)				Syntac Sprint (Vivadent)	FujiBond LC (GC)
Solid Bond (Kulzer)					One-coat Bond (Coltène)
Solist (DMG)					Prompt L-Pop 1,2 (ESPE)
Stae (SDI)					Scotchbond Multi-Purpose (3M)
Tenure Quik F (Den-Mat)					Syntac Single-Comp (Vivadent)

Table 8. *Basic Characteristics of the Three Solvents Commonly Used in Adhesives*

Acetone
Highly volatile, evaporates quickly
Excellent water-chaser
Strong drying agent (risk of overdrying dentin)
Storage and dispense problems
Ethanol (Water)
Excellent penetration capability
Good compromise in respect of evaporation
Good surface energy for wetting exposed collagen fibril network
Water
Good penetration capability
Enables self-etching capability of acid monomers
Evaporates slowly consequently more difficult to remove
Remaining water may hamper resin penetration/polymerization

cian should actually be able to balance over a short distance between wet and dry. Currently, two clinical methods exist to achieve adequate hybridization. The type of adhesive and, in particular, the kind of solvent of the primer (or of the primer/adhesive) determines which of the two methods can best be used. One way is to keep the substrate field dry and use adhesive systems that provide water-based primers (Table 7) to re-hydrate and thus re-expand the air-dried and consequently collapsed collagen network, allowing resin monomers to still interdiffuse efficiently (Van Meerbeek & others, 1998c). The other alternative is to keep the acid-etched dentin surface moist and to rely on the water-chasing capacity of acetone-based primers (Table 7). This clinical technique is commonly referred to as *wet-bonding* and has been introduced by Kanca (1992a,b,c) and Gwinnett (1992) in the early '90s.

It is fundamentally important to effective hybridization that the collagen fibril web, deprived of its mineral support following acid treatment, keep its spongy-like quality, allowing interdiffusion of resin monomers in the subsequent priming and bonding steps. Dehydration of the acid-conditioned dentin surface through air-drying is thought

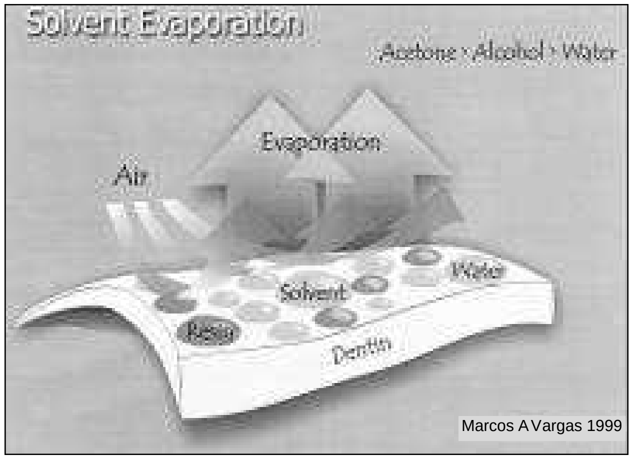


Figure 21. *Schematic presentation showing the principle of evaporation of the solvent during the priming step after it carried the active monomers through the channels within the exposed collagen fibril network.*

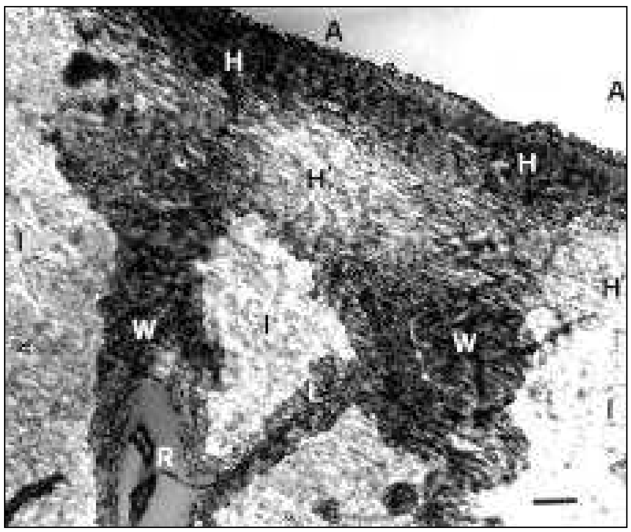


Figure 22. *TEM photomicrograph of the resin-dentin interface produced by Clearfil Liner Bond System (Kuraray) when applied to 35% phosphoric-acid etched dentin. Due to insufficient resin infiltration, a typical hybridoid zone (H') was formed underneath the top area of the hybrid layer (H) which was stained more electron dense as sign of adequate resin infiltration. A= Adhesive resin; I = Lab-demineralized intertubular dentin; L= Micro-resin tag in hybridized lateral tubule branch; R = Resin tag; W = Hybridized tubule wall; Bar = 1 µm.*

to induce surface tension stress, causing the exposed collagen network to collapse, shrink and form a compact coagulate that is impenetrable to resin (Pashley & others, 1993; Pashley & Carvalho, 1997). If some water remains inside the interfibrillar spaces, the loose quality of the collagen matrix is maintained and the interfibrillar spaces are left open (Perdigão, 1995; Kanca, 1992c; Perdigão & others, 1995, 1996a). It should, however, be emphasized that this wet-bonding technique can only guarantee efficient resin interdiffusion if all the remaining water on the dentin surface is completely eliminated and replaced by monomers during the subsequent priming step. In some of the currently available adhesive systems, hydrophilic primer monomers are therefore dissolved in volatile solvents, such as acetone and ethanol (Abate, Rodriguez & Macchi, 2000). These solvents may aid in displacement of the remaining water as well as carrying the polymerizable monomers into the opened dentin tubules and through the nano-spaces of the collagen web (Tay & others, 1996a; Tay, Gwinnett & Wei, 1996b, 1997). The primer solvents are then evaporated by gently air-drying, leaving the active primer monomers behind (Figure 21). The basic characteristics of the three solvents used in commercial adhesives are summarized in Table 8. When the water inside the collagen network is not completely displaced, the polymerization of resin inside the hybrid layer may be affected or, at least, the remaining water will compete for space with resin inside the demineralized dentin (Jacobsen & Söderhold, 1995). The risk that all moisture on the dentin surface is not completely replaced by hydrophilic primer monomers is clinically real and ultra-morphologically documented as overwetting phenomena for adhesive systems that provide water-free acetone-based primers (Tay & others, 1996a,b, 1997). In such overwet conditions, excessive water that was incompletely removed during priming, appeared to cause phase separation of the hydrophobic and hydrophilic monomer components, resulting in blister and globule formation at the resin-dentin interface. Such interface deficiencies undoubtedly weaken the resin-dentin bond and result in incompletely sealed tubules (Tay & others, 1996a,b). On the other hand, even gentle post-conditioning drying of the dentin surface for as short as three seconds prior to the application of a water-free, acetone-based primer has been shown to result in incomplete intertubular resin infiltration. Ineffective resin penetration due to collagen collapse has been ultra-morphologically observed as the formation of a so-called hybridoid zone (Figure 22). These hybridoid zones inside the hybrid layer do not appear electron dense on demineralized TEM sections. Consequently, this wet bonding technique appears rather technique-sensitive (Tay & others, 1995, 1996b; Finger & Balkenhol, 1999; Frankenberger, Kramer & Petschelt, 1999; Perdigão & others, 1999a), especially in terms of the precise amount of moisture that should be kept post-conditionally on the dentin surface. In other words, acid-etched dentin may not be kept too wet, but also may not be dried too long. A short air blast or blotting the excess water using a dry sponge or small piece of tissue paper has been recommended as most effective post-conditioning wet-bonding procedures.

This wet-bonding technique also has two other disadvantages of clinical importance. First, acetone quickly evaporates from the primer bottle, so that after the primer solution is dispensed in a dappen dish, the primer bottle should be immediately closed and the dispensed primer solution immediately applied to the etched surface. Despite careful handling, the composition of the primer solution may change after the bottle has been opened and closed several times due to quick evaporation of solvent out of the recipient. This will increase the ratio of monomers to the acetone solvent and will definitely have its effect on the eventual penetrability of monomers in the exposed collagen fibril network. To reduce such a rapid primer solvent volatilization, acetone-based adhesive formulations are also available today in pre-dosed single-patient-use capsules as with Prime&Bond NT Quix (Dentsply). In this way the capsules can be opened just prior to application of the “one-bottle” solution, giving the acetone little time to evaporate. A final clinical disadvantage of keeping the lesion wet after conditioning is that the clinician cannot check if the enamel surface turns white-frosted as clinical proof that enamel was efficiently etched.

On the contrary, adhesive systems that provide water-dissolved primers have been demonstrated to bond equally effective to dry or wet dentin (Van Meerbeek & others, 1998c). In that study, the hybridization effectiveness of two three-step total-etch adhesives, OptiBond Dual Cure (Kerr) and Scotchbond Multi-Purpose (3M), was examined by TEM. Neither substantial difference in the ultrastructure of the hybrid-layer nor signs of incomplete resin penetration or collagen collapse were detected when these water-based adhesives were applied following either a wet- or dry-bonding technique. Even excessive post-conditioning air-drying of the dentin surface for 15 seconds did not result in the formation of a hybridoid zone that would have clearly indicated that resin had ineffectively infiltrated the demineralized collagen network (Tay & others, 1996a). When both adhesives were bonded to wet dentin, no morphological evidence of overwetting phenomena was observed, either. This indicates that the two water-based primers were capable of sufficiently displacing the water that remained as part of the wet-bonding technique as well as the additional amount of water that was introduced with the primers themselves. A potential self-rewetting effect of the primer, which evidently provides sufficient water to re-expand the gently air-dried and collapsed collagen scaffold, has been advanced as a reasonable explanation for the ability of these systems to perform equally well in wet or dry conditions. In this regard, air drying of demineralized dentin has been described to reduce its volume by 65%, but the original dimensions can be regained after reimmersion in water (Carvalho & others, 1996).

In contrast to adhesive systems that provide acetone-based primers and show a restricted *window of opportunity* as far as a precise amount of water that should remain post-conditionally on the dentin surface for efficient bonding to be achieved, adhesive systems that provide water-based primers appear less technique-sensitive and bond equally well to varying degrees of surface dry and wetness. Bonding to dry dentin has the advantage of being the clinically accepted and utilized standard used by most clinicians. In addition, dry bonding permits the clinician to verify the frosted appearance of enamel following conditioning as proof of an adequate enamel acid-etch. In addition, dry bonding does not involve any risks for overwetting. Clinically, a standard dry-bonding procedure is recommended that involves gentle air drying of the dentin surface after conditioning for about five seconds or until the glossy wet surface turns dull and the acid-etched enamel surface appears white and frosted.

Alternatively, conditioned dentin may be air dried and remoistened with water or an antibacterial solution such as chlorhexidine (Gwinnett, 1992; Kanca, 1992a). In this regard, a recent study has shown that an aqueous HEMA (35%) solution (Aquaprep, BISCO) is effective for compensating the dryness induced on the dentin surface by air blasts from an air syringe after rinsing off the etchant (Perdigão & others, 1999b). The post-conditioning application of the re-wetting agent significantly improved the bonding effectiveness of some simplified adhesives.

Primer Application

Primers should be clinically applied with care to assure that resin effectively infiltrates the network of interfibrillar collagen channels. A primer application time of at least 15 seconds, as recommended by most manufacturers, should be respected to allow monomers to interdiffuse up to the complete depth of surface demineralization. When a dry-bonding technique is followed using self-rewetting water-based primers, this 15-second primer application time should allow the gently air dried and thus collapsed collagen scaffold to re-expand. Using a wet-bonding technique, the primer should be applied for sufficiently long time (at least 15 seconds) to displace all remaining surface moisture through concurrent evaporation of the primer solvent carrier. Moreover, water-free acetone-based primers, provided with three- and two-step (one-bottle) total-etch adhesives, should be applied copiously in multiple layers as per the manufacturer's instructions. After short and gentle air drying, the primed surface should appear glossy as a clinical control of an adequate primer application.

Instead of leaving the primer solution untouched on the dentin surface during the whole application time, an active rubbing application technique with moderate pressure using disposable brushes or sponge applicators may improve and accelerate the monomer interdiffusion process. In this way, primer monomers may be infused and aspirated in the network of interfibrillar collagen channels, producing the above-mentioned "shag carpet" (Figures 8 and 9).

Acid-etched enamel theoretically does not need separate primer application to achieve effective bonding when an unfilled or low-filled hydrophobic enamel-bonding agent is applied on air-dried enamel. On the other hand, primers can be applied on acid-etched enamel without harming the enamel bonding process. In case the cavity is kept moist following a wet-bonding technique, primers should, however, always be applied on acid-etched enamel to displace any residual surface moisture through concurrent evaporation of primer solvent. Eventually, the primer application should always be completed by short, gentle air drying to volatilize any remaining solvent excess prior to application of the adhesive resin.

Adhesive Resin Application

In the final step of the bonding process, the adhesive layer should also be appropriately placed. Spreading the adhesive resin over the surface to which it is bonded should be done preferentially by brush-thinning rather than by air-thinning. The adhesive should be copiously placed, then evenly spread using a brush tip that can optionally be repeatedly squeezed out between a paper tissue. In this way, the adhesive resin layer will reach an optimal thickness of about 100 µm (Moon & Chang, 1992). When placed in a sufficiently thick layer, the adhesive resin may, due to its relatively high

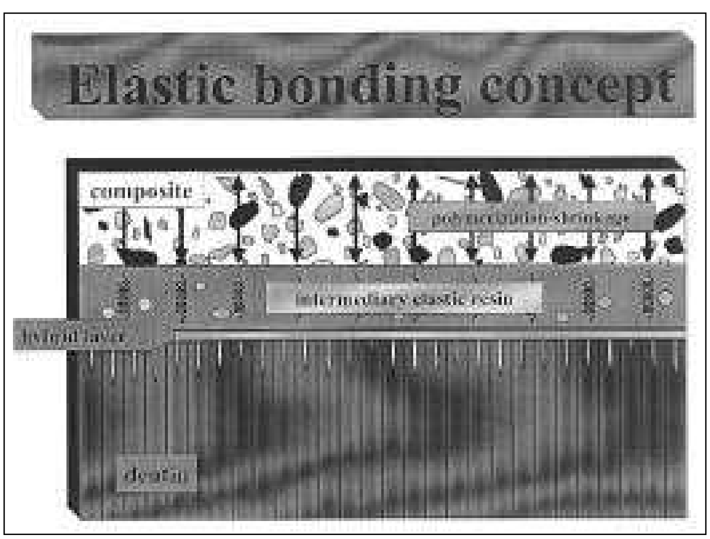


Figure 23. *Schematic presentation explaining the elastic bonding concept in which a relatively thick intermediary resin may compensate by elastic expansion for the polymerization shrinkage stress induced during contraction of the restorative composite.*

elasticity, act as a stress-relaxation buffer (Figure 23). This will absorb by elastic elongation, in part, the tensile stresses imposed by polymerization contraction of the resin composite subsequently placed over the adhesive resin (Kemp-Scholte, 1989; Kemp-Scholte & Davidson, 1990; Van Meerbeek & others, 1993b; Bayne & others, 1994; Rees, O'Dougherty & Pullin, 1999; Unterbrink & Liebenberg, 1999). In a recent study, the polymerization contraction stress generated during the placement of composite restorations was found to be significantly absorbed and relieved by the application of an increasing thickness of low-stiffness adhesive (Choi, Condon & Ferracane, 2000). Blowing the adhesive resin layer may reduce its thickness too much, decreasing its elastic buffer potential to relieve polymerization contraction stress. In support of this elastic bonding concept, dentin adhesive systems that provide a low-viscosity resin have been reported to produce higher bond strengths and less microleakage (Fortin & others, 1994; Inoue & others, 2000a,b). Likewise, microleakage was found to be reduced when a filled low-viscosity resin was used as an intermediate liner (Swift & others, 1996). Moreover, this elastic bonding concept can be regarded as an efficient means to not only counteract the polymerization contraction stress of the resin composite, but also to possibly aid in absorbing masticatory forces, tooth flexure effects and thermal cycling shocks which, all during clinical function, may jeopardize the integrity of the resin-tooth bond. Besides adhesives that provide low-viscosity particle-filled resins, thick adhesive layers are also placed with polyalkenoic acid-based adhesive systems, such as Scotchbond Multi-Purpose (3M) and Scotchbond 1 (3M), and with the more recently developed glass ionomer based adhesives, Fuji Bond LC (GC) and Reactmer (Shofu). Clinical evidence in support of this elastic bonding concept are the excellent clinical results that have been reported for Clearfil Liner Bond (Kuraray), Scotchbond Multi-Purpose (3M) and Optibond Dual Cure (Kerr) in several clinical trials (Van Meerbeek & others, 1994b, 1996; Bayne & others, 1994; Boghosian, 1996; Trevino & others, 1996; Peumans & others, 2000).

In theory, chemical and dual-cure adhesive systems that allow small flow-active porosities to be mixed in the resin layer and the polymerization to progress at a slower rate than solely light-cure adhesive resins may also contribute to this stress-relaxation mechanism (Perdigão & others, 1996b; Alster & others, 1992). For the same purpose, the use of adhesive lining and base cements underneath composite restorations should be considered as stress-absorbers. The use of an intermediate glass ionomer liner will reduce the total stiffness and increase the stress-absorption capacity of the restoration. Resin-modified glass ionomer cements are preferred over conventional glass ionomer cements because they can chemically co-polymerize with the restorative resin composite placed over the intermediate cement layer. This so-called "sandwich" technique has, for instance, been demonstrated to significantly reduce the loss rate of restorations placed with even an earlier generation adhesive, Scotchbond 2 (3M), when a resin-modified glass ionomer liner, Vitrebond (3M), was additionally applied as an intermediate liner (Powell, Johnson & Gordon, 1995). Also the so-called *flowable* composites are very popular for use as a stress-absorbing liner in the deepest parts of proximal boxes in posterior restorations (Prager, 1997; Bertolotti & Laamanen, 1999; Bouschlicher, Cobb & Boyer, 1999; Frankenberger & others, 1999; Murchison, Charlton & Moore, 1999; Unterbrink & Liebenberg, 1999).

For light-curing bonding agents, the adhesive resin should always be cured prior to the application of the restorative resin composite. In this way the adhesive resin is not displaced when the restorative resin composite is applied and adequate light intensity is provided to sufficiently cure the adhesive resin layer (Erickson, 1992). Pre-curing the adhesive resin will stabilize the resin-tooth bond and consequently activate the elastic stress-relaxation mechanism.

Because of oxygen inhibition, the top 15 µm of the adhesive resin will not polymerize (Rueggeberg & Margeson, 1990), but will provide sufficient double methacrylate bonds for co-polymerization with the subsequently applied restorative resin. Again, brush-thinning rather than air-thinning may prevent the film thickness from being reduced

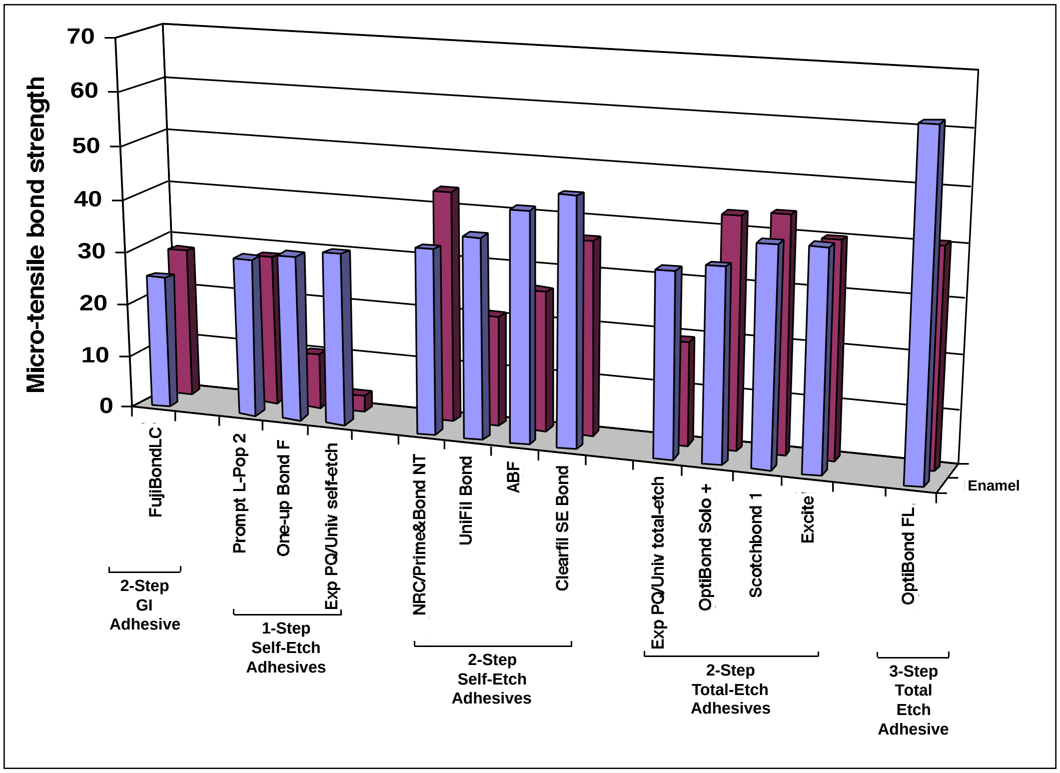


Figure 24. *Micro-tensile bond strength to enamel and dentin of 13 contemporary adhesives classified per adhesive approach.*

to an extent that the air-inhibited layer permeates the whole resin layer, reducing the stress-relaxation capacity and bond effectiveness.

Laboratory Bonding Effectiveness

The adhesive effectiveness of the self-etching adhesives to enamel and dentin was tested in terms of micro-tensile bond strength (µTBS) using a method introduced by Sano & others in 1994. This technique was selected as it enables more accurate measurements of tensile bond strength because the typical hourglass design of the specimens imposes the highest stress during testing to be built-up at the real interface.

The µTBS data clearly indicate that any kind of simplification either following a *one-bottle*, *self-etch* or *glass ionomer* approach leads to a significant drop in adhesive effectiveness to dentin (Figure 24). Apparently, the conventional *three-step* procedure allows a more accurate and less technique-sensitive application that is translated in higher tensile bond strength to dentin. This difference in effectiveness between conventional and simplified systems, however, may not be directly relevant in the early years of clinical service, but most likely may shorten the eventual longevity of adhesive restorations. Despite the high turnover of adhesives, there is a high need to re-evaluate long-term clinical trials since they only allow conclusions to be drawn on the longevity of adhesive restorations.

Aremarkable concern is the lack of consistency in µTBS recorded with two *strong* self-etching adhesives, Prompt L-Pop (ESPE) and NRC/Prime&Bond NT (Dentsply). The µTBS data mentioned for these two adhesives (Figure 24) did not significantly differ from the values recorded for the other self-etch adhesives. However, these data only represent the average bond strength of only 13 out of 17 (75%) Prompt L-Pop specimens, respectively, and 7 out of 14 (50%) NRC/Prime&Bond NT specimens. For both adhesives, the other specimens did not survive the specimen preparation method and failed prior to testing. Such inconsistent bonding performance is most likely caused by the high acidity of unpolymerized monomers remaining after light curing in a relatively high concentration at the oxygen-inhibited layer (Schiltz & others, 2000; Sanares & others, 2000). The unreacted acid groups have been hypothesized to attack the poly-

Figure 25A(right) 25B (below). *Clinical bonding effectiveness of 14 adhesive-composite combinations in terms of retention (%) in Class-V non-carious lesions. The figure at the base of each data bar represents the year when the study was started.*

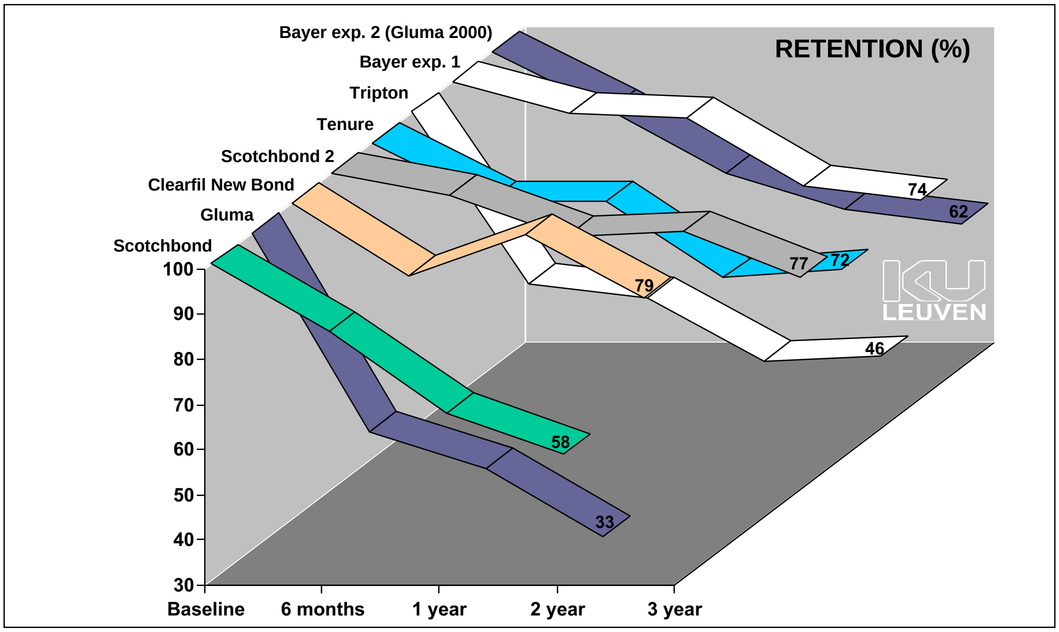
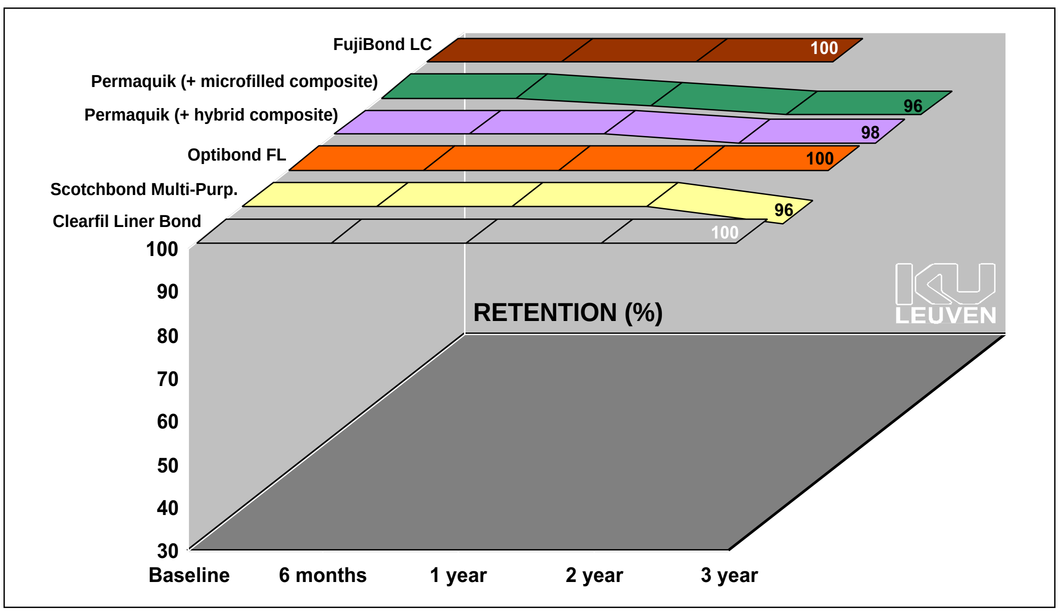


Figure 25B. *Clinical bonding effectiveness of 14 adhesive-composite combinations in terms of retention (%) in Class-V non-carious lesions. The figure at the base of each data bar represents the year when the study was started.*



merization initiation system of the composite material, especially in the case of prolonged contact of the acidic adhesive monomers with the uncured composite material. Lack of a sufficiently thick and uniform resin layer that stabilizes the hybrid layer may also have contributed to the lower bond strength values and relatively high number of pre-testing failures. More recent research has indeed shown that a sufficiently thick and separately light-cured adhesive (prior to application of the restorative composite), or the use of an additional intermediary low-viscosity resin reduced or even eliminated the occurrence of pre-testing failures (unpublished observations). This has been confirmed by other researchers (Perdigão & others, 2000). Further research is definitely needed to elucidate this inconsistency in bonding effectiveness recorded with these two specific adhesives.

In contrast to the µTBS data recorded to dentin, in general, the adhesives with simplified application procedures do not underscore against the conventional three-step total-etch control adhesive with regard to enamel-bonding effectiveness (Figure 24). This is certainly the case for three out of four "one-bottle" adhesives tested but also for the strong self-etch adhesive NRC/Prime&Bond NT and even the mild self-etch adhesive Clearfil SE Bond, of which the µTBS does not significantly differ from that of Optibond FL. Some pre-testing failures were recorded for the experimental PQ/Universal (three out of 10 specimens could be tested) when used following a self-etch approach, for One-up Bond F (six out of 11 were tested) and for Unifil Bond (10 out of 11 were tested). All adhesives in this study were bonded to enamel on which a 600-grit smear layer was prepared beforehand. In this respect, another study by Kanemura & others (1999) revealed that two other self-etch adhesives (Clearfil Liner Bond 2, Kuraray; Mac Bond 2, Tokuyama) scored µTBS data to ground enamel that were comparable to those measured for two one-bottle adhesives (One-Step, BISCO; Scotchbond 1, 3M) that involved a separate phosphoric-acid treatment. When the self-etch adhesives were directly bonded to unground, intact enamel, the resultant µTBS values, however, were significantly lower. Testing the marginal sealing potential and durability of the self-etching approach should obviously confirm these promising enamel performance data.

Clinical Bonding Effectiveness

At Leuven, the clinical effectiveness of adhesives has been routinely investigated in controlled two-to-three-year follow-up studies using the same experimental protocol for almost 20 years. The retention rates shown in Figures 25a and 25b clearly illustrate the significant progress made in adhesive performance when adhesives (Figure 25a) from prior to versus after 1990 (Figure 25b) were used to restore cervical Class-V non-carious lesions with their respective restorative composite material. In part, this must be attributed to the introduction in the early '90s of the *total-etch* technique by which phosphoric acid is now also applied to dentin. Earlier adhesives often showed many failures within the first six months when applied strictly to dentin without any selective phosphoric acid etching of adjacent enamel (Van Meerbeek & others, 1994b). When following the same protocol in more recent clinical trials (total-etch systems were applied selectively to dentin), almost any early de-bonding failures were recorded. This must be attributed to a great extent to the enamel immediately adjacent to dentin always being (unintentionally) etched and guaranteeing a durable bond to the enamel margin. Adequate bonding to enamel alone may keep such restorations longer in place.

Conclusions

A great diversity in adhesives that can basically be categorized *total-etch, self-etch* and *glass ionomer* adhesives exists. A clear trend exists towards simplified application procedures with a reduced number of application steps. However, simplification does not necessarily imply improved or even equal bonding effectiveness.

Conventional three-step total-etch adhesives remain the adhesives of choice for routine clinical use because of their least technique-sensitivity and their best laboratory and clinical effectiveness data. Today's major shortcomings are, amongst others, the relatively high technique-sensitivity of current systems and the apparent difficult-to-solve compromise to bond equally effective to enamel and dentin. Self-etch adhesives, either resin- or glass ionomer-based, may be most promising in overcoming these shortcomings. They do not require a rinse phase, which truly saves time and is less prone to manipulation errors. No discrepancy exists between demineralization and infiltration. They offer a twofold bonding mechanism based on micro-mechanical interlocking through hybridization to resist "acute" debonding stress and improved monomer-collagen interaction potentially by primary chemical bonding, which may be helpful to keep the bonds leakage-free in a long-term perspective.

An adhesive restoration, in conclusion, has many advantages over conventional non-adhesive restorative techniques except that it cannot yet be realized in a simple way.

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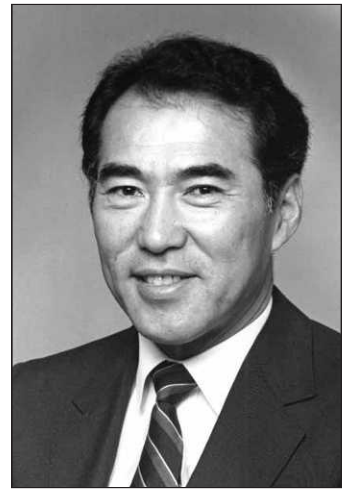

Recent Commercial Composite Formulations

M M Suzuki

M Mike Suzuki

Summary

Vastly improved bonding systems and the enhanced formulation of resin composites has resulted in their increased durability and reliability in a wide spectrum of restorative procedures.

The recent introduction of packable resin composites as posterior restorations has brought about easier handling characteristics; however, difficulties still exist in terms of providing positive proximal contact. Clinical performance of packable composite at the two-year recall revealed no significant difference from that of its predecessor.

Through clinical trials, several suggestions were made for the successful placement of resin composites in the posterior dentition.

Introduction

Increasing environmental concerns and public demands for tooth-colored materials have heralded patients to demand the replacement of traditional metallic restorations by more esthetic, biocompatible ceramics and resin composites (MacEntee & Mojon, 1991; Langan, Fan & Hoos, 1987; Christensen, 1995).

Of all the innovative esthetic materials available today, the direct placement of resin composite has assumed the current thrust in restorative dentistry. This has been facilitated by remarkable advances in their physical properties over the past 30 years, leading to significant improvements in their manipulative qualities and durability. Recent formulations of resin composites have shown that their wear rates are comparable to amalgams (Davidson & Suzuki, 1999; Mazer & Leinfelder, 1992; Wendt & Leinfelder, 1992; Dickinson, Gerbo & Leinfelder, 1993).

One of the principle advantages in the use of resin composites as restorative materials is their bondability to the adjacent enamel and dentin tooth structure (Suzuki, Jordan & Boksman, 1985). These have made resin bonding to tooth structure more predictable in a wide spectrum of dental treatments. Vastly improved bonding systems and the enhanced formulation of resin composites has resulted in their increased durability and predictability for restorations in posterior functional areas (Davidson & Suzuki, 1998; Suzuki & Davidson, 1998). For instance, seven-year recalls of 66 Z100 (3M Dental Products) resin composites in 30 patients has provided evidence regarding their excellent performance (Suzuki, 2000).

Figure 1. (left) Restoration placed on lower first molar with Z100 (3M Dental Products) after four years. Slight catch at the cavosurface margin (Bravo).

Figure 2. (right) Same restoration as Figure 1, at the seven-year recall stage. Pronounced chipping of the margin is visible at the mesio-buccal cusp area, however, excellent overall performance as a posterior restoration.

Figure 1 shows a typical four-year old resin composite restoration placed on a first molar with full occlusal function. Margins of this restoration were rated Bravo (explorer catches and crevices are visible but no dentin exposure). Among all the restorations at the seven-year recall, very limited additional wear was observed over four-year recalls, and the average cumulative occlusal wear from baseline was found to be about 50 µm over four years. Figure 2 shows the same restoration at the seven-year recall stage.

Packable Composite

The profession has had a long desire for esthetic direct filling materials comparable to silver amalgams in terms of durability, ease of handling and affordability.

The recent introduction of "packable" resin composite has been an interesting development toward this objective. Changes observed in this new family of resin composites, such as Filtek P60 (3M Dental Products), Prodigy Condensable (Kerr/Sybron), Pyramid (BISCO Dental Products), Solitaire II (Heraeus Kulzer, Inc) and Surefil (Dentsply/Caulk), include the following:

Increased Viscosity

Increased viscosity has been achieved by changes in the formulation of resin composite. Although there was already a high filler loading, additional increments greatly increased their viscosity. The use of high molecular weight resins also increases the overall viscosity of the composite (3M Technical Product Profile for Filtek P60, 1998).

As innovative filler configurations might hamper packing into the cavity, one product utilizes interlocking particle technology (Dentsply Caulk Technical Manual for Surefil). This apparently establishes synergistic linking with a unique inorganic filler system. The growing expectation of these innovations is to make composites sufficiently viscous to be placed in cavities using techniques analogous to those for the placement of amalgams. This is the expectation of so-called packable composites, although subsequent polishing and finishing has yet to match traditional standards. However, physical attachment to the cavity wall may be superior to traditional amalgams, provided the manufacturer's prescribed insertion techniques are precisely followed.

Lower Percentage of Polymerization Shrinkage

Previous concerns about resin composites stemmed from polymerization shrinkage. Improvements in this regard have been achieved by increasing the percent of filler loading, in addition to the use of higher molecular weight matrix resins, for example, urethane dimethacrylate and BisEMA (3M Technical Product Profile for Filtek P60, 1998).

As high molecular weight resins have fewer double bonds per unit weight, they create a lower degree of cross-linking, resulting in a relatively lower level of polymerization shrinkage. On the other hand, laboratory studies regarding the physical properties of some packable composites revealed no substantial differences from conventional composite materials (Ruddell & others, 1999; Bonilla, Mardirossian & Caputo, 1999; Leinfelder, Bayne & Swift, 1999).

Improved Manipulative Properties

Intraoral manipulation of the more viscous resin composites requires a new learning process in that these materials are generally less sticky than traditional composite systems. Such material stickiness has been reduced by slightly altering the filler content and the use of varied matrix monomers. As sticky materials tend to incorporate more air bubbles during placement, weaker composite restorations may be the net consequence. Whereas this may not cause serious problems for anterior restorations, it will greatly compromise their durability when placed in stress-bearing posterior regions.

Cavity Preparation

In the past, clinical studies involving biomaterials such as resin composites have been based on trial and error. Our earlier studies (Boksman, Jordan & Suzuki, 1984; Boksman, Jordan, Suzuki & Charles, 1986) utilized conventional cavity preparations for silver amalgams for the placement of resin composites. This attracted significant criticism largely because of the associated radical reduction of tooth substance.

Subsequent to GV Black's principles of cavity preparation, significant advances have been made in cavity design. Those traditional principles no longer apply to the placement of resin composites. Rather, cavity preparations have become extremely conservative in terms of outline form, since these materials are retentive due to bondability to the surrounding enamel and dentin tooth structure.

More conservative outline forms lead to less exposure of resin restorations to functional stresses as well as better marginal adaptation from less volumetric shrinkage on polymerizing the resin composite. It is also much faster and easier to place resin composites in smaller cavities, thereby saving operating time, in addition to improving their clinical success.

In cavity preparation involving proximal surfaces, pre-wedging with anatomically contoured wooden wedges is strongly recommended for the following reasons:

1. To allow slight separation of the teeth, which ultimately results in positive approximal contact by compensating for matrix thickness. In this regard, sectional precontoured metallic matrices are recommended for Class II cavities.
2. Pre-placed wooden wedges also protect the rubber dam septa and interproximal papilla from laceration during cavity preparation, although this may be aided by the topical application of haemostatic agents.
3. Wedges also guide the establishment of the gingival wall. For this most critical area of Class II restorations, it is important to maintain an enamel margin for better seal.
4. The same wedge can be used to stabilize the matrix during the placement of the resin composite, but care must be taken to ensure the removal after polymerization.

Use of Liners

For cavities of standard depths, the use of liners is not indicated in most instances. Deep cavities, particularly those with sclerotic dentin or altered dentin, for example, the replacement of a previous amalgam, a light cured glass ionomer lining cement is recommended at the interface for the following reasons:

1. Marginal leakage can be minimized because light cured ionomers show much better marginal seal to dentin than other restorative materials, thereby reducing the chance of post-operative sensitivities (Tjan & Dunn, 1990; Wibowo, Stockton & Suzuki, 1999). If these sensitivities do present, then consideration should be given to repetition of the careful placement of the restoration.
2. The strength of any bonding agent to altered dentin will be greatly compromised, so that there is a high prevalence for creating a gap at the interface on polymerization of the composite (Perdigão & others, 1994; Nakajima & others, 1995).

3. As there is a residual "flexibility" of glass ionomer liners after light curing, absorption of the contraction stresses of resin composite upon polymerization may result (Lacy, 1999; Kemp-Scholte & Davidson, 1990).
4. If future re-treatment of this cavity is necessary, it is nice to have an identifiable layer at the interface to preclude subsequent mechanical pulp exposure and associated need for endodontic treatment.
5. When applied as a thick layer, liners reduce the total volume of the resin composite required to fill the cavity, thereby minimizing the potential for polymerization contraction stresses (Lacy, 1999; Suzuki & Jordan, 1990; Tolidis, Nobecourt & Randall, 1998).
6. Antimicrobial properties of glass ionomer may contribute to the prevention of recurrent decay (DeSchepper, Thrasher & Thurmond, 1989; Shelburne, Gleason & Mitra, 1997).

After many years of clinical trials with posterior resin composites, the author regards the application of light cure glass ionomer cements (for example, Vitrebond, 3M Dental Products) as providing significant advantages in minimizing the post-operative sensitivity, and yet producing no other negative clinical consequence. This is a very simple technique to accomplish but adds one more step to the overall clinical procedure.

Use of flowable composite prior to the packable composite to facilitate better adaptation and marginal seal has been advocated; however, its effectiveness is still questionable (Wibowo, Stockton & Suzuki, 1999; Miranda & others, 1999). Further research is required in this endeavor.

Matrix

One of the major limitations with the use of directly-filled resin composite in Class II situations stems from difficulties in establishing an ideal proximal contour and contact.

Despite the recent introduction of high viscosity resins (packable composites), resin composites are still passive in nature and cannot be expected to distend during placement as amalgam.

Hence, a thin (38 µm), pre-contoured sectional metallic matrix is strongly recommended if spaces allow. Sectional matrices also permit maximum accessibility to the occlusal surface, thereby facilitating good anatomical sculpturing prior to light activation (polymerization). In the case of restricted proximal clearance, an ultra-thin dead soft matrix (25 µm) may be indicated, provided the contacting surfaces are burnished aggressively. The use of plastic matrices are convenient in terms of curing with lights, however, their relatively thicker consistency (75 µm) and lack of rigidity hampers the anatomical placement of resin composites.

Clinicians agree that circumferential bands are not suitable for the application of posterior composite as they frequently lead to inadequate proximal contacts on tightening. In fact, if the configuration of the cavity necessitates the use of circumferential bands, direct application of resin composite is probably not indicated as a final restoration, and should therefore be substituted by silver amalgam or some other form of indirect restorations.

Insertion

As stated earlier, resin composites are passive in nature and cannot be compressed into the cavity. Therefore, the proximal contour has to be provided by the matrix and held tight to the proximal tooth while the resin composite is being cured. The idea of making this process easier through the use of more viscous material has failed to match expectations. For this reason, bulk application of resin composite is very difficult to achieve; its incremental placement is highly recommended.

Figures 3 and 4 illustrate the placement of packable composite into a large cavity preparation. Careful attention is required for the proper restoration of proximal contour and contact as well as functional occlusal anatomy. The use of a proximal contact form-

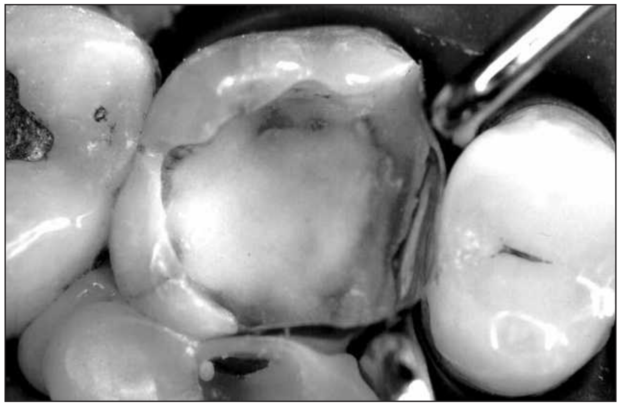

Figure 3. Large cavity preparation involving the replacement of cusps. Providing appropriate matrix for this situation is difficult.

Figure 4. Completed restoration, showing limitation in providing ideal anatomical contour.

Figure 5. Multiple surface restoration using Surefil (Dentsply/Caulk) on bicuspid and molar at baseline.

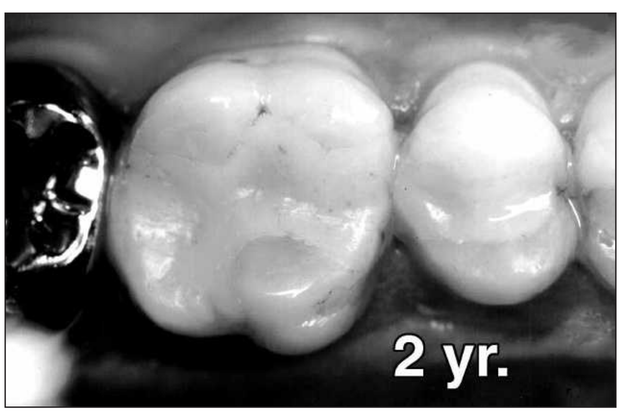

Figure 6. Same restorations as Figure 5, at two year recall stage. All margins are intact (Alpha) and show minimal occlusal wear.

ing instrument, for example, pyramid-shaped plastic light tips or pre-cured resin composite secured within a proximal box, have been advocated (Lacy, 1999) and each technique claims their effectiveness.

This is the most frustrating part of resin composite placement and the major and most frequent cause of restoration failure. In this context, indirect inlays and onlays are superior, although they are associated with other undesirable problems, such as the necessity to remove more sound tooth structure as well as added expenses for the patient. These preclude their routine use except in very large lesions involving cusp replacement.

Polishing the approximate surface of the adjacent tooth prior to the matrix placement results in superior contact relationships. In order for the restoration to be successful, efforts should be made to establish rolls on proximal embrasures, etc. Sharp edges left on marginal ridges often become the site of bulk fractures. The meticulous attention required for direct composite restorations often results with twice the chair-side time than that of silver amalgam. However, the resultant patient satisfaction is worth the additional effort.

Are packable composites better in this endeavor than the conventional composites? Despite acclaims for the introduction of high-density composites, many new resin composites have failed to match the operator's expectations in terms of establishing good proximal contour and contacts.

Clinical performance of packable composite Surefil (Dentsply/Caulk) at the two-year recall revealed no significant difference from that of its predecessor (Figures 5 and 6).

The parameter that really impresses many operators is their handling characteristics. They are definitely non-sticky and moldable. Easy release from the hand instrument lends itself to less frustration and time saving for the operator.

The future development of composite materials should include:

1. Contraction-free resin composites with low polymerization stress.
2. Resin composites capable of wetting the surrounding cavity walls.
3. Resin composites that are intraorally easy to use. This would reduce the multiple steps for insertion, each with the potential for error if the technique is not precisely followed.
4. Assurance of long-term durability.

Clearly, resin composites require considerable further development before they can be routinely recommended as an amalgam substitute.

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©Operative Dentistry Supplement 6, 2001, 153-176

Indirect Resin and Ceramic Systems

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Abstract

The esthetic component of dental care has become increasingly more important, while new tooth-colored materials are continually marketed. This article describes currently available indirect resin composites and all-ceramic systems. Mechanical properties of the materials and bonding of the restorations to tooth structure are discussed. A review of the clinical success of the different types of restorations is given, and finally, comparisons of the clinical success are made between new and clinically well-known types of restorations.

Introduction

Not that long ago the available methods for repairing teeth were limited. Consequently, the choices among materials and restorative techniques were generally easy and straightforward. Today's situation has dramatically changed. The esthetic aspect of dental care has become increasingly more important, and the research and development invested to address this aspect have brought numerous tooth-colored restorative materials onto the market. Consequently, dentists now have a multitude of materials and techniques at their disposal. Some types of restorations, such as gold inlays, are clinically well-documented. Other materials and techniques are new and promising but poorly documented. Having so many alternative choices has made selecting the "right" restorative material and technique far more complicated. Reality in the dental office is so complex today that it is almost impossible to define which treatment is optimal in a given situation. Hence, for every single tooth, the operator has to carefully consider several treatment options. Material and technique choices should be based on knowledge of material properties and the limitations of the materials and techniques.

Figure 1. Classification of esthetic restorative systems.

Figure 1 shows a basic classification of the esthetic restorative systems. This presentation focuses on the restorative systems for indirect use, that is, on resin composite inlay/onlay materials and on ceramic materials. The differences in chemical composition among the divergent types of materials will be highlighted, and the materials discussed from a technological viewpoint, that is, material comparisons, will be made on the basis of properties which may be determined in the laboratory. These properties include mechanical and physical and bonding capacity to tooth structure. It is critically important to be familiar with the fundamental composition of a material in order to understand its limitations and demands regarding factors such as cavity design, material handling and provision of retention. However, the ultimate arbiter of the performance of a dental material, in addition to general experience, is a controlled clinical trial. Therefore, laboratory testing results will be supplemented with results from clinical trials whenever they are available.

Resin Composites

Resin composites were introduced to the dental community in the mid-1960s (Bowen, 1962, 1965). Since their advent, composites have significantly developed. Today's most widely used composites are light-initiated, one-paste materials that generally encompass three main components: 1) a resin based on different, relatively hydrophobic dimethacrylate monomers (for example, BisGMA, UDMA and TEGDMA) and an initiator system, 2) an inorganic filler consisting of particulates such as glass, quartz and/or fused silica, and 3) a silane coupling agent chemically bonding the reinforcing filler to the resin matrix (Figure 2).

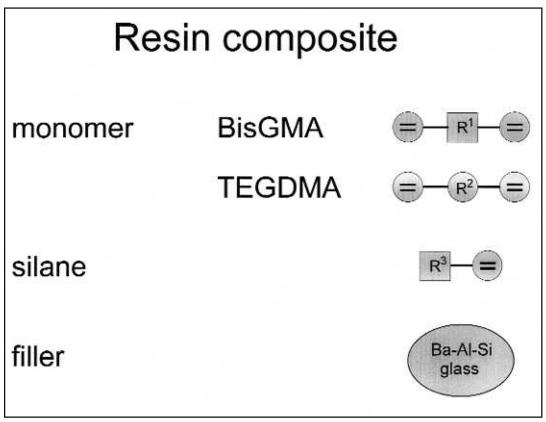

Figure 2. The three main components of resin composites.

Most of the inlay materials have a composition identical to that of a resin composite marketed by the same manufacturer for direct use. The inlay materials are often given a name partially identical to the direct material, for example, Herculite XRV and Estilux Posterior CVS. Other inlay materials have a composition similar to that of resin-based crown and bridge materials, for example, SR-Isosit.

The initiator system of resin composites comprises a diketone and an amine. Camphorquinone is the most commonly used diketone. Upon irradiation with blue light, camphorquinone absorbs radiation and decomposes to form free radicals. The radicals initiate polymerization, which continues under the formation of a highly cross-linked three-dimensional network (Figure 3). As polymerization proceeds, diffusion rates of free radicals and unreacted dimethacrylate molecules are drastically reduced, hampering complete conversion of methacrylate double bonds. Thus, as much as 25% to 50% of the methacrylate groups remain unreacted in the polymer (Asmussen, 1982a; Ruyter & Svendsen, 1978) in which they exert a plasticizing effect (Asmussen, 1982b).

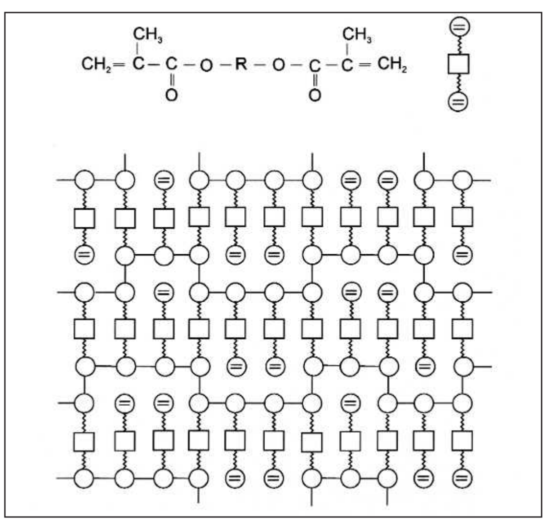

Figure 3. Simplified representation of a three-dimensional dimethacrylate network having 71% conversion of the methacrylate double bonds to crosslinks = : unreacted carbon-carbon double bond—: carbon-carbon single bond.

Composite Inlays

By giving the composite an additional or secondary cure extraorally, as is the case with the inlay technique, it has been hypothesized that the degree of conversion and a number of material properties would be improved. A further rationale for the introduction of the inlay technique addressed the negative effects of polymerization shrinkage (Mörmann, Ameye & Lutz, 1982; Lutz, Krejci & Mörmann, 1987; Burke & others, 1991). The inevitable shrinkage that accompanies polymerization has a detrimental effect on the marginal integrity of a direct composite restoration. By producing a composite inlay, only shrinkage of the relatively thin layer of resin cement used for bonding the inlay to the tooth may compromise the margins since shrinkage of the inlay itself takes place outside the cavity. Finally, the indirect technique often makes it easier to achieve proper contours and proximal contacts of the restorations. These advantages were thought to outbalance obvious disadvantages such as the inlay technique being more tooth-demanding, time-consuming and a more expensive treatment. However, the advantages were expected to increase longevity of the restoration, thereby saving tooth substance in the long-run and eliminating any cost gap.

Composite inlays may be produced by using a direct or an indirect technique. According to the direct technique, the dentist is in charge of the clinical and laboratory aspects of the treatment. This technique implies that the inlay is directly built up in the cavity, given an initial light cure, removed from the cavity, given an extraoral cure, finished, polished and finally bonded to the tooth.

Inlays can also be fabricated by an indirect technique. This normally infers that the dentist makes an impression of the prepared cavity and forwards it to a laboratory for pouring a model on which the inlay is fabricated. Following polymerization and polishing, the inlay is returned to the dental office for the final step of the procedure: bonding of the inlay to the cavity. According to a modification of the technique, the different steps can be done so quickly that the dentist can fabricate the inlay chairside while the patient waits. An impression of the prepared cavity is made in a fast-setting impression material, and the impression is also poured with a fast-setting material, such as a polyvinyl siloxane impression material. The inlay is built up on the model and given an initial and possibly a secondary cure before being polished and bonded to the cavity. Thus, as is the case with a direct inlay, the restoration is completed in one rather long visit with limited cost, since the laboratory phase has been avoided. Despite these advantages, “direct” and chairside composite inlays are not widely used. Compared to composite inlays fabricated at a dental laboratory, there could be several reasons for the limited use: the long visit required is very demanding on the patient and dentist and building up the inlay in the cavity does not give control of restoration contours as is the case when the work is done on a model. Furthermore, a dental technician’s time may be less expensive than a dentist’s chair time.

Composite inlays may be cured by a number of different methods. The simplest is to cure the composite by only using a conventional intra-oral light unit, as was the case with the EOS chairside system from Vivadent. However, most often the initial light curing at room or mouth temperature is supplemented by an additional curing in a light- and heat-curing device, such as Coltène DI 500 for the Brilliant inlay system. Finally, some inlay materials, for example SR-Isosit, are not light curable. These materials are cured during a one-step procedure at elevated temperature under pressure.

One of the first materials introduced for the inlay technique was SR-Isosit from Ivoclar. It was marketed as “Concept” in the US. SR-Isosit was a microfilled composite based on a crown-and-bridge material which was given a hydropneumatic heat cure in the Ivomat apparatus, that is, the polymerization took place in water at 120°C and a pressure of six bar for 10 minutes. The inner surfaces of the inlay were sandblasted with aluminum oxide to provide a rough and retentive surface.

Kulzer also launched a composite inlay system based on the hybrid composite Estilux posterior CVS. Following initial light cure, the inlay was given an additional cure either in a Dentacolor XS photocure unit or in a special Lightbox, an accessory of the conventional intra-oral light unit Translux.

Many more composites have been marketed or explored for inlay use. There is no reason to discuss every composite inlay system, since all posterior composites can, in fact, be used.

Effect of Additional Cure

Numerous *in vitro* studies have reported the effect of additional or secondary cure on the properties of composites. Table 1 shows the effect in percent on the degree of conversion of some materials reported in a number of different studies. All studies found a positive influence on the degree of conversion as a result of an additional cure. The degree of conversion increased by 6-44%. The effect of additional cure may vary among the different studies for several reasons: some materials respond better to additional cure than others, the additional cure varied from study to study and the studies utilized different procedures and methods for determining the degree of conversion. The fact that the degree of conversion was increased means that 1) dimethacrylate molecules diffuse and react even in a solid polymer and 2) greater flexibility of the chains in the polymer network, caused by the increased temperature, increases the mobility and thus the reactivity of pendent methacrylate groups. If the magnitude of the improvements reported are plotted against the degree of conversion obtained by conventional light cure only, a significant correlation between the two variables is found (Figure 4). Consequently, in cases where a high degree of conversion of the dimethacrylates is already obtained following the initial light cure, the chance that two unreacted double bonds will meet and react during an additional cure is less than if many double bonds were present.

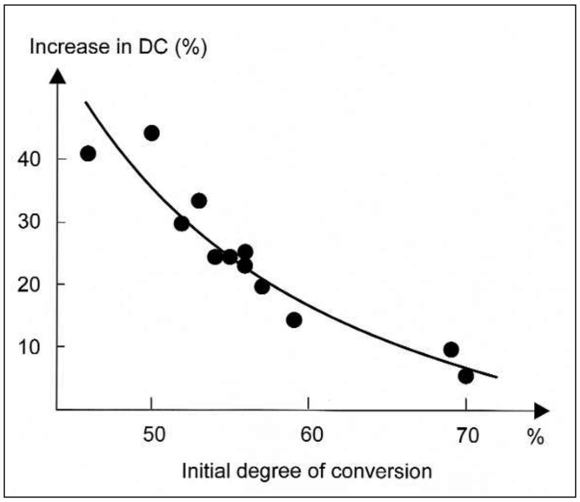

Figure 4. Correlation between degree of conversion of light-cured composite and increase in degree of conversion as a consequence of a secondary cure ($p<0.0005$).

Table 2 summarizes the improvements (in percent) of some physical properties following an additional cure reported in a number of different studies. It is evident that the results show no clear picture: additional cure improved the properties of some materials, while not for others. Obviously, the additional cures differed with respect to duration, temperature and more, which may account for a portion of the differences in responsiveness to additional cure. Also, there may be a difference in responsiveness from material to material. This is evident from the results shown in Table 3. The degree

Table 1. Reported Increases in Degree of Conversion as a Consequence of Secondary Cure

Composite	% Increase in DC	Researchers
Brilliant Enamel	6	Park & Lee, 1996
Brilliant	19	Kildal & Ruyter, 1994
Charisma	29	Kildal & Ruyter, 1994
Charisma	23	Peutzfeldt & Asmussen, 2000
EOS	14	Kildal & Ruyter, 1994
Estilux posterior CVS	24	Kildal & Ruyter, 1994
Herculite	33	Ferracane & Condon, 1992
Herculite XRV	44	Bagis & Rueggeberg, 1997
Heliomolar	41	Ferracane & Condon, 1992
Occlusin	10	Cook & Johansson, 1987
Prisma APH	25	Kildal & Ruyter, 1994
Z100	24	Peutzfeldt & Asmussen, 2000

Table 2. Reported Effects (in percent) on a Number of Properties of Secondary Cure of Different Resin Composites

Composite	Flexural Strength	Flexural Modulus	Diametral Tensile Strength	In Vitro Wear Resistance	Reseachers
Brilliant Dentin	4	20			Reinhardt, 1991
Brilliant Dentin	0	0	0		Peutzfeldt & Asmussen, 1991
Brilliant DI	53	62			Kullmann, 1988
Brilliant DI				40	de Gee & others, 1990
Charisma	26	34	11	30	Peutzfeldt & Asmussen, 2000
Charisma				46	Shinkai & others, 1994
Estilux posterior CVS	36	41	0		Peutzfeldt & Asmussen, 1991
Herculite	16				Ferracane & Condon, 1992
Herculite				32	Shinkai & others, 1994
Herculite				66	de Gee & others, 1990
Heliomolar	60				Ferracane & Condon, 1992
Heliomolar				0	Shinkai & others, 1994
Occlusin		4	13	73	Wendt, 1987
Occlusin	36		41		Cook & Johansson, 1987
Occlusin				25	de Gee & others, 1990
Z100	0	0	0	0	Peutzfeldt & Asmussen, 2000
Z100	10	20			Ferracane & others, 1995

Table 3. Effect (in percent) of Secondary Cure (1 hour at 110°C) on Five Properties of Z100 and Charisma

Composite	Degree in Conversion	Diametral Tensile Strength	Flexural Strength	Flexural Modulus	In Vitro Wear Resistance
Z100	24	0	0	0	0
Charisma	23	11	26	34	30

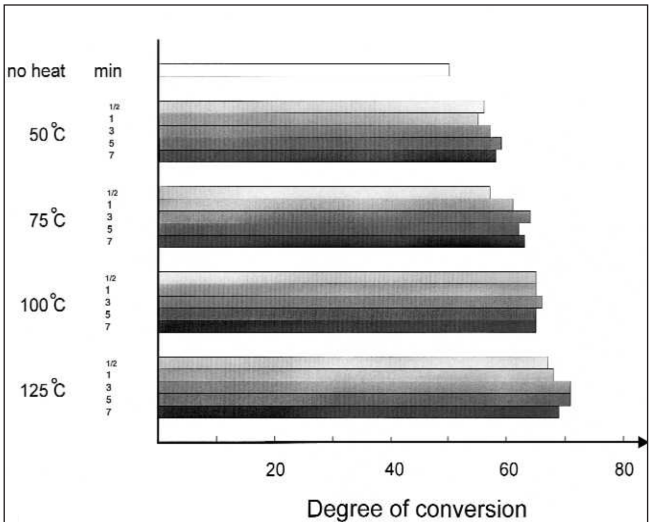

Figure 5. Effect of temperature and duration of the secondary cure on the degree of conversion (Bagis & Rueggeberg, 1997).

of conversion was significantly improved for Z100 as well as Charisma as a consequence of the additional cure. On the other hand, whereas the additional cure had a significant effect on the mechanical properties of Charisma, no effects were obtained for Z100. This difference in responsiveness to the additional cure corroborates with the findings of Shinkay, who determined *in vitro* wear of four different composites (Shinkai & others, 1994).

As previously mentioned, additional cure may consist of an additional light curing, heat

Table 4. Results of a Three-Year Follow-up of Class I and II Inlays (Occlusin) (Wendt & Leinfelder, 1992)

Type of Restoration	No of Restorations	Failures (%)	Comments
Inlay ÷ heat-treatment	30	0	No difference in wear
Inlay + heat-treatment	30	0	Improved marginal integrity of heat-treated inlays

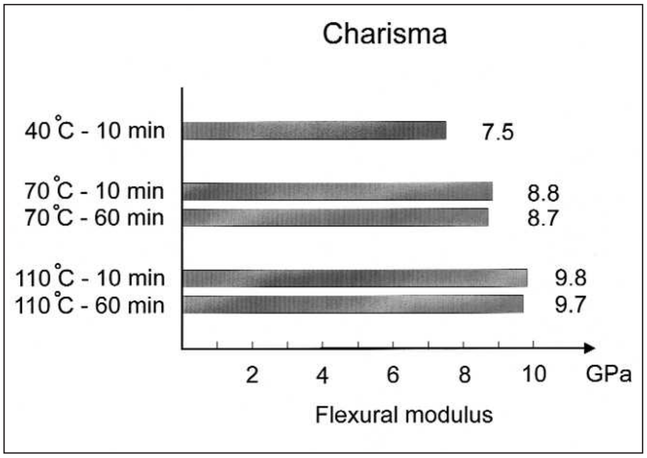

Figure 6. Effect of temperature and duration of the secondary cure on the flexural modulus of Charisma (Peutzfeldt & Asmussen, 2000).

treatment or combination of both. Because heat is also generated in light-curing devices (de Gee & others, 1990) it is not evident which treatment provides the highest effect. Results by Bagis & Rueggeberg, for example, emphasize the importance of temperature on the efficacy of the heat treatment (Figure 5) (Bagis & Rueggeberg, 1997). Thus, post-cure temperature had a much higher influence on the degree of conversion than post-cure duration (Bagis & Rueggeberg, 1997). This finding also prevailed in the study by Peutzfeldt & Asmussen (2000), for example, (Figure 6).

Wendt & Leinfelder (1992) evaluated *in vivo* the effect of an additional heat treatment of a resin composite (Occlusin) (Table 4). Direct inlays that had only been light cured or light cured and heat-treated were studied. After three years, heat-treated inlays displayed improved marginal integrity and surface characteristics compared to inlays that had only been light cured. However, heat treatment did not lead to improved wear resistance.

A few studies have indicated that the positive effect of an additional cure on physical properties may be only transient (de Gee & others, 1990; Ferracane, Hopkin & Condon, 1995). From the available data, this author concluded that supplementing conventional photo-cure with an additional cure will increase monomer conversion but not necessarily improve physical properties significantly, at least not in the long-term. The enhancement in the degree of conversion will not degrade with time, nor will resin composite that has only been light cured ever increase in conversion to become equivalent to additionally cured composite (Loza-Herrero & others, 1998). Increased conversion is an advantage whether or not it leads to long-term improvements in properties: an increased degree of conversion may imply fewer totally unreacted monomer components remaining in the composite. This means less leaching of free monomer from the composite into the patient's mouth, and thus improved biocompatibility of the restoration.

Bonding of Composite Inlays

Composite inlays are bonded to the tooth with a resin cement. Figure 7 shows that the cement has to bond to the tooth as well as the inlay. Bonding to enamel and dentin is obtained by acid etching and dentin bonding systems in a manner similar to that by which direct composite restorations are bonded to tooth structure. Adherence of the cement to the inlay may be provided by mechanical and/or chemical means. Regarding chemical means, adhesion is brought about by a copolymerization of the monomer of the resin cement with unreacted double bonds in the polymer at the surface of the inlay. Table 1 shows several studies that demonstrated secondary cure of resin inlays cause a significant reduction in the remaining double bonds of the material (Park & Lee, 1996; Kildal & Ruyter, 1994; Peutzfeldt & Asmussen, 2000; Ferracane & Condon, 1992; Bagis & Rueggeberg, 1997; Cook & Johannson, 1987). An inherent drawback of the increased

Table 5. The Effect of Secondary Cure of Z100 on Degree of Conversion and Bond Strength and Bond Energy Obtained Between Cured Z100 and Resin Cement (Asmussen & Peutzfeldt, 2000).

Secondary Cure	Degree of Conversion (%)	Bond Strength (MPa)	Bond Energy (J/m²)
None	[a]54 ± 3	[b]21 ± 1	[b]9 ± 2
110°C, 10 min	[b]64 ± 2	[a]17 ± 1	[a]5 ± 1

The cured composite had not been sandblasted. The different superscripts indicate significant differences between the mean values.

Table 6. The Effect of Sandblasting of Composite Inlays on the Bond Strength Between Composite Inlay and Resin Cement

Composite	Inlay Surface Treatment	Bond Strength (MPa)	Reseachers
Herculite XRV	None	6 ± 2	Stokes & others, 1993
	Sandblasting	13 ± 3	
Triad Inlay Composite	None	13 ± 5	Latta & Barkmeier, 1994
	Sandblasting	27 ± 6	
Brilliant	None	4 ± 3	Shortall & others, 1996
	Sandblasting	8 ± 1	
Z100	None	17 ± 1	Asmussen & Peutzfeldt, 2000
	Sandblasting	24 ± 2	

Table 7. The Effect of Etching with Hydrofluoric Acid (HF-etch) of Composite Inlays on the Bond Strength Between Composite Inlay and Resin Cement

Composite	Inlay Surface Treatment	Bond Strength (MPa)	Reseachers
Herculite XRV	Sandblasting	26 ± 10	Swift & others, 1992
	Sandblasting + HF-etch	18 ± 8	
Herculite XRV	None	6 ± 2	Stokes & others, 1993
	HF-etch	12 ± 2	
	Sandblasting	13 ± 3	
	Sandblasting + HF-etch	18 ± 4	
Triad Inlay Composite	None	13 ± 5	Latta & Barkmeier, 1994
	HF-etch	10 ± 1	
Herculite XRV	Sandblasting	10 ± 1	Shortall & others, 1996
	Sandblasting + HF-etch	7 ± 2	
Herculite XRV	Sandblasting	16 ± 3	Ejersbo & Peutzfeldt, 1994
	Sandblasting + HF-etch	11 ± 2	
Z100	Sandblasting	15 ± 2	Ejersbo & Peutzfeldt, 1994
	Sandblasting + HF-etch	15 ± 2	

conversion of the secondarily cured composite is fewer remaining double bonds available for copolymerization with the monomer of the resin cement and, thus, a compromised potential for bonding. When measuring bond strength between resin cement and three different composite inlay materials, Haller & others (1990) found the effect of the secondary cure to vary from material to material. However, in agreement with the results of Kullmann (1988); Asmussen & Peutzfeldt (2000) found the secondary cure to reduce bond strength and bond energy of non-sandblasted inlay materials (Table 5). Summing up the scarce data, it seems advisable to supplement the chemical adherence with some means of mechanical adherence.

Regarding mechanical adhesion, a number of studies have investigated the effect of various surface treatments on the adherence between resin cement and inlay material (Asmussen & Peutzfeldt (2000); Swift & others, 1992; Stokes, Tay & Pereira, 1993; Latta & Barkmeier, 1994; Ejersbo & Peutzfeldt, 1994; Shortall, Baylis & Wilson, 1996; Hummel & others, 1997). It has been found that sandblasting (50 µm aluminum oxide)

Table 8. The Effect of Silane Treatment of Composite Inlays on the Bond Strength Between Composite Inlay and Resin Cement

Composite	Inlay Surface Treatment	Bond Strength (MPa)	Reseachers
Herculite XRV	None	6 ± 2	Stokes & others, 1993
	Silane	13 ± 4	
	Sandblasting	13 ± 3	
	Sandblasting + silane	20 ± 4	
Herculite XRV	Sandblasting	26 ± 10	Swift & others, 1992
	Sandblasting + silane	28 ± 4	
Occlusin	None	9 ± 1	Heitmann & Asmussen, 1992
	Silane	17 ± 2	
Herculite XRV	Sandblasting	16 ± 3	Ejersbo & Peutzfeldt, 1994
	Sandblasting + silane	17 ± 1	
Z100	Sandblasting	15 ± 2	Ejersbo & Peutzfeldt, 1994
	Sandblasting + silane	16 ± 2	

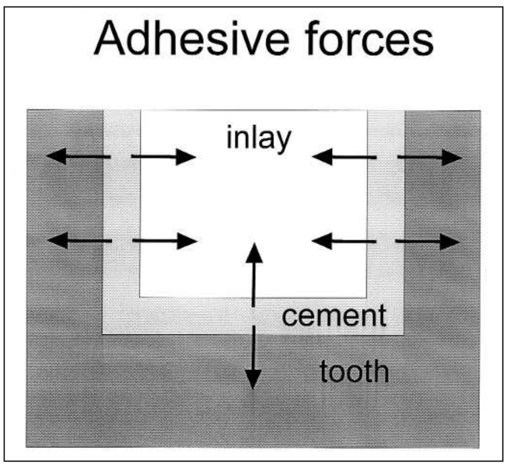

Figure 7. Bonding of an inlay to the tooth with a resin cement.

the inlay surface significantly improves the bond between resin cement and composite inlay (Asmussen & Peutzfeldt (2000); Stokes, Tay & Pereira, 1993; Latta & Barkmeier, 1994; Shortall, Baylis & Wilson, 1996) (Table 6). Hydrofluoric acid is commonly used to etch porcelain for indirect restorations. Since it also etches the filler particles in glass-filled hybrid and small-particle composites (Hummel & others, 1997) hydrofluoric acid has been suggested as a pretreatment in the aim of creating a more retentive internal surface of composite inlays prior to bonding. Table 7 shows studies that have reported contradictory results of the effect of hydrofluoric acid etching. The effect may depend on the composite and the hydrofluoric acid concentration. It seems that hydrofluoric acid treatment is too aggressive for some composites, such as Herculite XRV, and causes dissolution of the exposed glass particles. As hydrofluoric acid is a hazardous chemical that is best avoided, and as its effect is not convincing, etching of inlays with hydrofluoric acid cannot be recommended. Finally, priming with silane solution, also commonly used to enhance the bond strength of resin cement to porcelain, has also been studied as a means to enhance the bond to composite inlays (Swift & others, 1992; Stokes & others, 1993; Ejersbo & Peutzfeldt, 1994; Heitmann & Asmussen, 1992). Studies have found silane priming to have either a positive effect or no influence on bond strength (Table 8). Even if silane priming did not in all cases enhance short-term adherence, it may be that silanization inhibits degradation of the initial bond in the long run. To conclude, the safest and most effective treatment for promoting a bond between composite inlays and resin cement seems to be sandblasting followed by silane priming.

Clinical Studies of Composite Inlays

Composite inlays have been followed in numerous clinical trials. Unfortunately, most clinical evaluations are either short-term studies or studies that do not include a control material, such as a directly placed composite restoration, and thus, are of limited value. In a two-year follow-up of 43 direct composite restorations and 45 indirect inlays, 90% of the direct restorations and 93% of the indirect inlays were assessed as clinically

Table 9. Results of a Two-Year Follow-up of Directly Placed Composite Restorations and Composite Inlays (Scheibenbogen & others, 1999

Type of Restoration	No of Restorations	Failures (%)	Comments
Direct	43	7	Significantly better “anatomical form” of inlays
Inlay	45	4	

Table 10. Results of a Five-Year Follow-up of Class II Directly Placed Composite Restorations and Composite Inlays (Wassell, Walls & McCabe, 2000)

Type of Restoration	No of Restorations	Failures (%)	Comments
Direct (Brilliant Dentin)	57	8	No difference in wear
Inlay (Brilliant Dentin)	63	17	No advantage of inlays over direct composites

Table 11. Results of an 11-Year Follow-up of Class II Composite Inlays and Directly Placed Composite Restorations

Type of Restoration	No of Restorations	Failures (%)	Comments
Direct (Brilliant Dentin)	26	12	Reasons for failure:
Inlay (Brilliant Dentin)	24	17	1. fracture of restoration 2. secondary caries
Direct (Estilux post CVS)	25	20	No difference in failure rate
Inlay (Estilux post CVS)	26	12	between inlays and direct
Inlay (SR-Isosit)	27	22	composites

Table 12. Results of an 11-year Follow-up of Class II Composite Inlays and Directly Placed Composite Restorations

Type of Restoration	No of Restorations	Failures (%)	Comments
Direct (Fulfil)	33	27	No difference in failure rate
Inlay (Brilliant)	96	18	between inlays and direct composites Improved marginal integrity of inlays

acceptable or excellent (Table 9) (Scheibenbogen-Fuchsbrunner & others, 1999). Wassell, Walls & McCabe, (2000) have followed Brilliant Dentine inlays (directly fabricated) and direct restorations for five years (Table 10) (Wassell & others, 2000). The overall failure rate of 17% for inlays and 8% for direct restorations did not differ with statistical significance. The authors concluded that at five years, inlays showed no advantage over the directly placed restorations and that the former had a trend towards a higher failure rate. Recently, two 11-year follow-up studies have been published. Pallesen & Qvist (2000) have reported the results of their study on composite inlays (indirectly fabricated) and direct restorations (Table 11). There was no statistically significant difference between the failure rates of inlays versus direct restorations, neither when each composite system was compared separately, nor when all inlays and all direct restorations, respectively, had been pooled. In the latter case, the failure rate was 16% for direct restorations and 17% for inlays. The most frequent modes of failure for both types of restorations were fracture of the restoration followed by secondary caries. Finally, van Dijken (2000) reported an 18% failure rate for Brilliant DI inlays (directly fabricated) and a 27% failure rate for Fulfil directly placed restorations (Table 12). The difference was not statistically significant. It was noted that the inlays were characterized by improved marginal adaptation and low incidence of secondary caries compared with directly placed restorations. Compared to the results of previous clinical studies, the reported 11-year survival rates of inlays and direct restorations were thought to be acceptable. However, the studies did not indicate that inlays perform much better than directly placed restorations. There seems to be a trend towards improved marginal integrity of inlays, which favors inlays for large restorations and for those which approximally extend beneath the cemento-enamel junction.

As the data presented demonstrates, there is no unambiguous evidence of composite inlays showing better performance than directly-placed resin composite. Together with the need for increased tooth structure removal, this may explain why composite inlays made of conventional resin composite, produced directly or indirectly, never have become popular among clinicians.

New Resin Composites for Indirect Use

Within the last five years, a number of resin composites have been marketed with extended indications for indirect restorations compared with conventional resin composites: Artglass (Heraeus Kulzer), Belleglass HP (Belle de St Claire/Kerr) and Targis (Ivoclar). Although formulations and techniques differ, all three are polymer-based materials that promise reduced wear of opposing teeth, faster and easier fabrication and easy repairability compared to porcelain/ceramic restorations.

Artglass, introduced in 1995 as a "polyglass," contains 70 wt-% filler and 30 wt-% organic resin. The filler mainly consists of barium-aluminosilicate glass with a mean particle size of 0.7 µm but also has a moderate amount of colloidal silica. Artglass is unique because in addition to conventional bi-functional monomers, the resin matrix contains new multifunctional methacrylate monomers. The company claims that the content of multifunctional monomers generate a polymer characterized by a higher degree of conversion and a higher level of cross-linking when Artglass is cured with high intensity, xenon strobe-light (UniXS). Artglass was marketed for use as either metal-free, all-polymer restorations (veneers, inlays/onlays, crowns) or as metal-supported restorations (crowns and bridges, Maryland bridges and implant supported restorations). In the latter case, Artglass is bonded to the metal structure by use of the Kevloc system, which implies application of an acrylonitrile copolymer primer and a urethane resin to the sandblasted metal surface before placing and curing Artglass.

Belleglass HP was introduced in 1996 by Belle de St Claire. The resin matrix is based on conventional resin composite monomers: urethane and aliphatic dimethacrylates. The material has a 78 wt-% content of barium glass with a mean particle size of 0.6 µm (dentin materials) or a 74 wt-% content of borosilicate glass (enamel materials). The uniqueness of Belleglass HP lies in the mechanism of curing: Belleglass HP is cured under pressure (approximately 5 bar) at an elevated temperature (140°C) in the presence of nitrogen. The elevated temperature is used to obtain an increased degree of conversion. Nitrogen is applied to exclude oxygen inhibition of the polymerization process and results in a higher degree of conversion of the resin matrix and thus improved physical properties such as wear resistance. Furthermore, less entrapped air is thought to improve the translucency of the restorative material. Belleglass is marketed for use without metal reinforcement as inlays/onlays, veneers and ante-

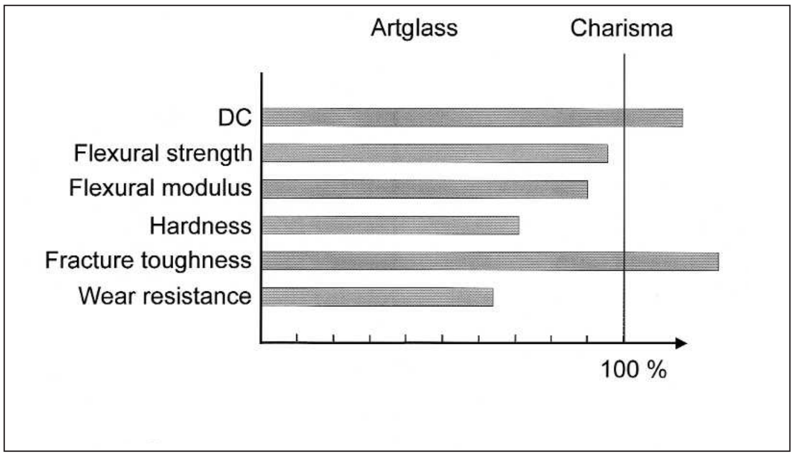

Figure 8. A relative comparison of Artglass with Charisma based on Freiberg & Ferracane, 1998. Each of the properties of Charisma is set at 100%. DC = degree of conversion.

Table 13. Flexural Strength and Fracture Toughness of Resin Composites for Indirect Use (Dyer & Sorensen, 1998).

Material	Flexural Strength (MPa)	Fracture Toughness ($MN \cdot m^{-3/2}$)
Concept	130 ± 18	2.3 ± 0.2
Artglass$_{dentin}$	132 ± 14	1.4 ± 0.2
Targis$_{dentin}$	135 ± 14	1.9 ± 0.2
Belleglass	150 ± 16	2.0 ± 0.1

rior crowns, and with metal reinforcement as veneering material, or with a fiber-reinforced framework as bridge material.

In 1996, Ivoclar launched Targis, a so-called ceromer (ceramic optimized polymer). Targis contains approximately 77 wt-% filler (57 vol-%) and 23 wt-% organic resin. The filler part is trimodal and consists of barium glass with a mean particle size of 1 µm, spheroid silica filler with a mean particle size of 0.25 µm as well as colloidal silica (grain size 0.015-0.050 µm). The resin matrix consists of conventional monomers. Superior properties of Targis are claimed to result from an "optimized chemical composition" and an "optimized curing process." The final curing takes place in a Targis Power light-curing unit at approximately 97°C for 25 minutes. Targis is marketed for veneers and inlays/onlays without a framework, for inlays/onlays, crowns and bridges (3 units) with a fiber-reinforced-composite (Vectris) framework and for crowns and bridges, including implant restorations, on a metal framework.

Figure 8 and Tables 13-18 show the results of *in vitro* and *in vivo* studies of these three relatively new resin composite systems. Freiberg & Ferracane (1998) have compared Artglass with Charisma, and Figure 8 shows the results obtained when both materials were cured with the UniXS unit. As claimed by the manufacturer, Artglass displayed an increased degree of conversion, increased fracture toughness, lower ridigity and lower hardness. However, the wear resistance by abrasion and attrition of Artglass was significantly lower than that of Charisma, probably as a result of the lower modulus and hardness of the former. Consequently, the claims by Artglass to have improved wear characteristics had to be refuted. The authors conclude that Artglass may not be indicated for extended clinical use in stress-bearing applications. Dyer & Sorensen (1998) have reported on the flexural strength and fracture toughness of a number of indirect resin composite systems. Table 13 compares Artglass, BelleGlass and Targis with Concept, a material representing the first generation of indirect composites. There were only minor differences in flexural strength, although Belleglass had a higher strength than Concept. Concept had the highest fracture toughness and Artglass the lowest. Knobloch & others (1999) have determined the degree of conversion and two-body abrasive wear of the same four materials as in the above mentioned study. Table 14 shows significant differences in both variables. Not one of the three new composite systems showed as high a polymer conversion nor as low a wear as Concept. Measuring wear in a three-body wear simulator, Sorensen & others (1998) found the results presented in Table 15 for the same four materials. For all types of wear, Concept performed the best and Artglass the worst.

In a multicenter clinical trial, 60 crowns each of Targis, Artglass and Belleglass (Christensen & others, 1999) were placed (Table 16). After one year of service, wear of all three materials was higher than previously placed Brilliant DI and Concept inlays. Artglass crowns, cemented with Denthesive II dentin bonding agent, showed a high frequency of debonding from the preparation (42%). Targis showed a high incidence of debonding from the substructure (28%). All Artglass restorations were without a substructure and therefore showed no prob-

Table 14. Degree of Conversion and Wear of Resin Composites for Indirect Use (Knobloch & others, 1999).

Material	Degree of Conversion (%)	2-body Wear (µm/revolution)
Concept	82	0.13
Belleglass	74	0.35
Artglass	54	0.46
Targis	48	0.46

Table 15. In Vitro Abrasion and Attrition of Resin Composites for Indirect Use and the Corresponding Enamel Wear (Sorensen & Dyer, 1998)

Material	Abrasion (µm)	Attrition (µm)	Enamel Wear (mm^2)
Concept	3 ± 1	22 ± 17	2 ± 1
Belleglass	10 ± 8	32 ± 7	4 ± 1
Targis	23 ± 8	54 ± 19	4 ± 1
Artglass	30 ± 9	92 ± 29	8 ± 1

Table 16. Results of a One-year Follow-up of Resin Composites for Indirect Use (Christensen & others)

Characteristic	60 Crowns of Each of Targis, Artglass and Belleglass
Wear	Belleglass ≤ Artglass < Targis Higher than 1ST generation materials
Debond from Preparation	Artglass 42% (Denthesive II)
Debond from Substructure	Targis 28% (OBS! Artglass was used without substructure)
Post-op Sensitivity	High for all systems
Occlusal Pitting	Higher than 1ST generation materials for all three systems
Wear of Antagonists	No problem

Table 17. Results of a 2-year Follow-up of 40 Artglass Inlays, Onlays and Crowns

Failures (%)	Reason for Failure
20	Debonding of restoration (10%) Fracture of Artglass restoration (5%) Pulpal damage (5%)

Table 18. Results of a Pilot Clinical Study of Artglass Veneered to Cast Gold Substructures by Use of Kevloc. 49 Restorations Had Served for 8-16 Months (Depew & Sorensen, 1998)

Failures (%)	Reason for Failure
35	Complete debonding of veneer (70%) Bulk fracture/delamination between dentin and incisal layers of Artglass (30%)

lems in this area. Post-operative sensitivity and occlusal pitting were high for all three systems. Wear of antagonists was not a problem with any of the materials. However, Artglass opposing itself caused substantial wear on both crowns. Also, *in vivo*, a two-year follow-up of 40 Artglass inlays, onlays and crowns without a substructure has been completed (Pallesen, personal communication). The overall failure rate of the Artglass restorations after two years was 20%, which Pallesen deems unacceptable even when considering that the Artglass restorations replaced direct composite restorations that had failed (Table 17). Causes of failure included: Debonding 10%, fracture 5% and pulpal implications 5%.

As previously mentioned, Artglass is also marketed as a veneer material bonded to metals by use of the Kevloc system. A pilot clinical study of 49 veneers bonded to cast gold substructures showed a failure rate of 35% after 8-16 months (Depew & Sorensen, 1998) (Table 18). This failure rate made the authors conclude that Artglass veneered to cast gold substructures is unreliable for clinical practice.

Based on the studies cited above, future long-term clinical studies may expect to find the so-called second generation of indirect resin composite systems discussed performing as well (or as poorly) as the "first generation" systems.

Ceramics

Porcelain and ceramic materials are strong alternatives to indirect resin composites. Ceramic materials have another constellation of advantages and disadvantages compared to resin composites. The main concerns of dental ceramics are their susceptibility to brittle, catastrophic fracture, and their ability to cause abrasive wear of opposing teeth. However, their high esthetic quality, biocompatibility and durability continue to make ceramics popular restorative materials.

The use of porcelain in dentistry began in the 18TH century with denture bases and denture teeth. So-called jacket crowns have been used since 1903, and in the early 1960s, the first successful porcelain-fused-to-metal system was introduced. This technique compensates for the relatively low tensile strength and brittleness of porcelain and thus increases the fracture resistance of the restoration. However, the metal base can compromise the esthetics of porcelain, which has motivated the development of all-ceramic systems with sufficient strength and precision of fit to compete with porcelain-fused-to-metal restorations. During processing and grinding of ceramic restorations, defects are introduced in the material. Porosities and cracks have been shown to be sites of fracture initiation in brittle materials. Thus, numerous all-ceramic systems have been introduced during the last 10 years, all which attempt to reduce the formation of defects and crack propagation while increasing strength. This presentation describes the different types of all-ceramic systems.

Ceramics is a very broad term. A ceramic material may be defined as a compound of metallic and non-metallic elements, the formation of which requires high temperature. Dental ceramics contain a glassy matrix reinforced by various dispersed phases consisting of crystalline structures, such as leucite, alumina and mica. Porcelain is a specific type of ceramic characterized by it being white and transparent. The term glass-ceramic has been introduced to classify ceramics where one or more crystalline phases has been precipitated from a glassy phase. Thus, the crystals are a product of the glass and have not been added.

Sintered Ceramics

Sintered ceramics are normally based on potassium ($K_2O{\cdot}Al_2O_3{\cdot}6SiO_2$) and/or sodium feldspar ($Na_2O{\cdot}Al_2O_3{\cdot}6SiO_2$) and quartz ($SiO_2$) and are produced by melting a number of minerals at high temperature (1200-1250°C). After cooling, the mass is ground to powders of various shades and translucencies. The dental technician adds water to the powder to produce a slurry, which is built up in layers on a model to form a restoration. The restoration is now heated, whereby the surface of the powder particles melt and the particles sinter together.

As mentioned, conventional feldspathic porcelain is essentially a mixture of feldspar and quartz. By adding alumina (Al_2O_3) particles to the porcelain powder, a strengthening of the porcelain is obtained as the particles inhibit the propagation of cracks in the material. Unfortunately, the addition of alumina reduces the transparency of the porcelain. Consequently, for full-coverage crowns, alumina-reinforced porcelain is often used as a core, which is covered by conventional feldspathic porcelain with a smaller content of alumina.

Procera AllCeram is a special type of sintered ceramic based on aluminum oxide. The shape of the die is read by a scanning device that transmits its shape to a milling machine. The milling machine produces a refractory die that is 20% larger than the original die in order to compensate for the shrinkage of the dense-sintered powder. A coping is produced, which is then veneered with either a conventional, feldspathic porcelain or low-fusing Procera AllCeram porcelain. As conventional etching with hydrofluoric acid has no effect on alumina, other techniques must be used. The very high alumina content and density make Procera AllCeram one of the strongest current dental ceramics.

Conventional feldspathic porcelain often has a small, inherent content of leucite ($K_2O{\cdot}Al_2O_3{\cdot}4SiO_2$). The use of a relatively high proportion of potassium feldspar results in a porcelain with an increased leucite content. This is warranted in porcelains used for porcelain-fused-to-metal restorations in order to raise the coefficient of thermal expansion. An extra content of leucite reinforces some porcelains intended for all-ceramic restorations, for example, IPS Empress and Optec HSP. The leucite crystals contract more than the surrounding glass matrix during sintering. The result is formation of compression stress in the glass phase, which may reduce the stress at the tip of a propagating crack. Unfortunately, the high content of leucite seems to contribute to a relatively high *in vitro* wear of opposing teeth (Seghi, Rosenstiel & Bauer, 1991).

Recently, a number of low-fusing porcelains have been introduced, including Finesse, Duceram LFC and Procera AllCeram porcelain. As the name indicates, these porcelains sinter at temperatures lower than normally used for all-ceramic porcelains. This effect is obtained mainly by a decreased, or even non-existing content of leucite and/or finer leucite crystals, which results in porcelains with considerably less potential for abrading opposing teeth and restorations (Hacker, Wagner & Razzoog, 1996). Low-fusing porcelains may be used by themselves for veneers and inlays/onlays or together with another material for crowns. Thus, Finesse may be used to veneer Finesse All-Ceramic pressable cores and Duceram LFC may be used as a second layer on top of a base layer of

Duceram Plus (earlier Duceram Metal Ceramic). Procera AllCeram porcelain has been developed as a veneering material for Procera AllCeram cores.

Castable Ceramics

This group of materials differs from sintered ceramics in that they are supplied as solid ceramic ingots. The ingots are used for cores or full-contour restorations produced by a lost-wax and centrifugal-casting technique similar to that used to fabricate alloy castings.

Dicor was launched in the mid-1980s as the first dental, castable glass ceramic on the market. In the dental laboratory, the glass ceramic is initially cast. During cooling of the cast Dicor restoration, MgF_2 submicroscopic crystals are formed. These crystals function as nucleators in the following heat treatment, the so-called ceramming, which leads to a glass ceramic material with approximately 55% tetrasilic mica crystals of 1-3 µm. The cerammed Dicor restoration may be covered by layers of feldspathic shade porcelain. As mentioned earlier, the presence of crystals has a strengthening effect.

Pressable Ceramics

With another glass ceramic material, IPS Empress, ingots are heated and pressed into a refractory mold by use of the lost-wax technique. IPS Empress has a 30-40% volume of leucite crystals and, thus, an increased flexural strength (Dong & others, 1992). The final shade of the restoration is obtained by staining or veneering. A few years ago, IPS Empress 2 was introduced for the veneering technique. The core material is a glass ceramic containing lithium disilicate and lithium orthophosphate crystals, while the veneering material contains fluoroapatite crystals. A higher volume of the crystalline phase results in increased strength of IPS Empress 2 compared to the original IPS Empress.

Optec OPC is also a leucite-containing glass ceramic, which is processed by molding under pressure and heat. It can be used alone for veneers, inlays/onlays and crowns or as a core material veneered with a leucite-reinforced feldspathic porcelain. Compared to Optec HSP, Optec OPC claims to contain an increased volume of smaller leucite crystals.

Machinable Ceramics

These products are supplied as ceramic ingots in various shades and are used either in computer-aided design—computer-aided manufacturing (CAD-CAM) procedures or in copy-milling techniques.

In the CAD-CAM technique (Cerec), developed by Mörmann & Brandistini and made commercially available in 1988, the prepared cavity is mapped by a mini-camera and fed to a computer linked to a milling machine. The restoration is milled in 10-15 minutes from an ingot. The occlusal surface is then adjusted and polished, and the restoration is ready for cementation. This CAD-CAM technique is intended for use in the dental office and produces a ceramic inlay in a one-visit appointment. Three ceramic materials have been used: Cerec Vitablocs Mark I was the first to be used with the Cerec system. It is a feldspathic porcelain with a composition similar to that of porcelains used for porcelain-fused-to-metal restorations. Cerec Vitablocs Mark II is a feldspathic porcelain with a finer grain size and allegedly increased strength and decreased *in vitro* abrasive wear of opposing tooth structure. Dicor MCG is a glass ceramic with fluoromica crystals in a glass matrix. It has greater flexural strength than cast Dicor (Rosenblum & Schulman, 1997). The CAD-CAM technique has mainly been used for inlays/onlays, but a software program, which allows machining of full-coverage crowns, is currently being marketed.

In the Celay copy-milling technique, a resin composite restoration is made on a master die. The restoration is then traced with a contact digitizer that transfers the shape to the Celay milling device. The same type of ingots available for the CAD-CAM systems may be used for the Celay system.

Obviously, being made from ingots of uniform shade, machined restorations have less esthetic potential and are predominantly used for posterior restorations.

Infiltrated Ceramics

In-Ceram is a so-called infiltrated ceramic and is used as core material, which is later veneered with a feldspathic porcelain. First, a crystalline core is produced by sintering either aluminum oxide or spinel ($MgO\text{-}Al_2O_3$). Subsequently, the porous framework is infiltrated with molten lanthanum glass by capillary action. The glass infiltration reduces porosity, and aluminum oxide or spinel crystals inhibit crack propagation. Both factors explain why In-Ceram is currently one of the strongest ceramic materials on the market. The use of spinel improves the translucency of the core but reduces mechanical properties. As is the case with the Procera AllCeram system, the core of aluminum oxide or spinel cannot be etched with hydrofluoric acid, and the etching must be replaced by other techniques.

Mechanical Properties of Ceramic Materials

One of the most frequently determined mechanical properties for ceramic materials is flexural strength. As conventional feldspathic restorations are prone to fracture, development has gone in the direction of stronger and stronger ceramics. This is evident from Figure 9, which shows representative values of different types and brands of ceramic materials.

As previously mentioned, the process of fracture is associated with the propagation of a crack through the ceramic material. It is, therefore, of interest to study the resistance of different ceramic materials to the propagation of cracks. This is often done by determining the fracture toughness, or more precisely, the so-called critical stress intensity factor, K_{1c}. K_{1c} is a measure of the force needed for a crack to propagate from a well-defined notch. Figure 10 gives the values of fracture toughness of different types and brands of ceramics. It may be noted that the newer types of ceramic materials have improved with respect to the resistance towards crack propagation. In ceramic materials composed of dispersed crystals in a glassy phase, a propagating crack is hindered or stopped whenever it encounters a crystal. Thus, the highest effect is obtained in materials with a high content of crystals. In In-Ceram and Procera All Ceram, the resistance towards crack propagation is due to the contiguous phase of aluminum oxide.

Flexural strength

Ceramic material	MPa
Feldspathic	70
Low-fusing feldspathic	105
Alumina-reinforced	130
Dicor	150
IPS Empress	130
IPS Empress 2	350
In-Ceram	450
Procera AllCeram	600

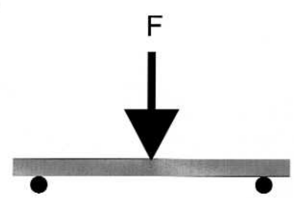

Figure 9. Representative values of flexural strength of different types and brands of ceramic materials.

Fracture toughness

Ceramic material	K_{1C} ($MN \cdot m^{-3/2}$)
Feldspathic	1.0
Low-fusing feldspathic	1.2
Alumina-reinforced	2.2
Dicor	1.6
IPS Empress	1.3
IPS Empress 2	3.2
In-Ceram	4.4
Procera AllCeram	4.4

Figure 10. Representative values of fracture toughness of different types and brands of ceramic materials.

Hardness

Ceramic material	Hv (GPa)
Feldspathic	5.5
Low-fusing feldspathic	6.2
Alumina-reinforced	5.4
Dicor	4.1
In-Ceram	9.8
Enamel	3.5
Gold-alloy	1.2

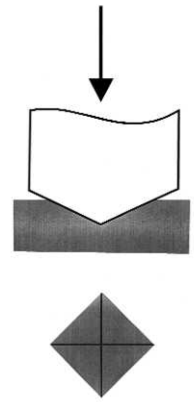

Figure 11. Representative values of Vickers hardness (Hv) of different types and brands of ceramic materials.

Wear of enamel

Ceramic material	Relative wear
Feldspathic	100
Alumina-reinforced	100
Optec HSP (leucite-reinforced)	130
IPS Empress	110
Dicor	80
Low-fusing AllCeram	25
Low-fusing Finesse	10

Figure 12. Relative wear exerted by different types and brands of ceramic materials. The wear exerted by feldspathic porcelain is set at 100%.

Abrasion of opposing teeth and restorative materials is one of the main disadvantages of conventional feldspathic porcelains, and hardness is a factor that influences abrasivity of ceramic materials. One method of determining hardness uses a Vickers diamond, which is forced into the ceramic surface with a well-defined force creating an impression. From the determined area of the created impression, the Vickers hardness is then calculated. Figure 11 shows all ceramic materials are harder than enamel and gold alloy.

Besides hardness, abrasion is also influenced by surface roughness of the ceramic material and by individual factors concerning occlusion, saliva and eating habits. Simulations of the functional chewing process may lead to the relative ranking of abrasivity of enamel presented in Figure 12. Conventional feldspathic porcelain may be up to 10 times more abrasive towards enamel than a gold alloy. While the leucite-reinforced ceramic Optec HSP has been found to have a very high abrasivity, the low-fusing porcelains, which are also low in leucite content, have been found to reduce abrasivity.

Bonding of Ceramic Restorations to the Tooth

Ceramic restorations, as with other restorations, may be bonded to the prepared tooth by an adherence that is mechanical and/or chemical in nature. Mechanical adherence relies on the degree of roughness of the bonded surfaces and may be obtained with any cement. Chemical adherence is best obtained by use of a resin cement. As mentioned above, a resin cement may be bonded to enamel and dentin by means of the acid-etch technique and dentin-bonding agents. The preferred procedure for bonding to a ceramic material depends on the material, as discussed below.

The bonding of a ceramic restoration to the tooth not only provides retention but also contributes to the strength and longevity of the restoration (Scherrer & others, 1994; Malament & Socransky, 1999). Thus, bonding of a ceramic restoration is an important step in the clinical procedure.

Hydrofluoric acid etches many ceramic materials to give a microroughness to the surfaces. With respect to morphology, the etch pattern of the ceramic is comparable to that of enamel etched by phosphoric acid (Al Edris & others, 1990). After penetration of the

Table 19. The Effect of Various Surface Treatments on the Bond Strength Between Ceramic Material and Resin Cement (Lacy & others, 1988)

Surface Treatment	Bond Strength (MPa)
None	7
Silane	15
HF-etch	10
HF-etch + silane	48

Table 20. The Effect of Various Surface Treatments on the Bond Strength Between In-Ceram and Resin Cement After Water Storage for 150 Days

Surface Treatment	Bond Strength (MPa)
Sandblasting +Twinlook	0
Sandblasting + Silane + Twinlook	3
Rocatec + Twinlook	50
Sandblasting + Panavia EX	41

Table 21. The Effect of Various Surface Treatments on the Bond Strength Between Procera AllCeram and Three Different Resin Cements (Kern & Thompson, 1995)

Surface Treatment	Bond Strength (MPa)		
	Porcelite	Panavia	Superbond
None	5	9	12
Silane	9	10	16
HF-etch + silane	3	2	1

Table 22. Failure Rates Reported in Clinical Studies of Sintered Ceramic Inlays (Asmussen, 1997)

System	Observation Time	No of Inlays	Failures (%)	Reseachers
Optec	3 yr	145	13	Molin & Karlsson, 1996
Mirage	2 yr	310	4	Jensen, 1988
Mirage	3 yr	50	18	Qualtrough & Wilson, 1996
Mirage	6 yr	59	12	van Dijken & others, 1998

monomer of the resin cement into the irregularities, a mechanical interlocking takes place, which bonds the resin cement to the ceramic. Several modifications of the hydrofluoric acid etching agent have been marketed. The concentration of hydrofluoric acid may vary, hydrofluoric acid may be used alone or in combination with other acids such as sulphuric acid, or hydrofluoric acid may be present in partly neutralized form as ammonium bifluoride. All types of etching agents have been shown to perform well, and existing data do not permit a distinction among the various modifications.

Silanization of surfaces of resin composites has been mentioned earlier. This treatment of the etched ceramic surface acts by giving a chemical component to the mechanical adherence provided by the etching. The silane is a bifunctional molecule that reacts with the ceramic surface through one end of the molecule, while the other end is a methacrylate group capable of co-polymerizing with the monomers of the resin cement. Table 19 gives results of measurements of bond strengths of a resin cement to a ceramic material after various surface treatments (Lacy & others, 1988). It has been found that a heat treatment of the silanated ceramic surface to about 100ºC gives significant increases in bond strength (Roulet, Söderholm & Longmate, 1995). Such a heat treatment is easily carried out by means of a hair dryer.

The ceramic material of a restoration belongs to one of several categories of ceramics. As mentioned above, etching with hydrofluoric acid is only an effective means of providing bonding for certain ceramic materials. Ceramic materials that have aluminum oxide as the main component (In-Ceram and Procera AllCeram) are not etched appreciably by hydrofluoric acid. In fact, etching of Procera AllCeram with hydrofluoric acid before the silanization has been found to result in reduced bond strength (Awliya & others, 1998; Asmussen, 1997). Several surface treatments have been proposed to give bonding with these materials. For In-Ceram, sandblasting in combination with an adhesive cement or Rocatec treatment (Kern & Thompson, 1995) was found to be the best surface treatment (Table 20). For Procera AllCeram, the best results were obtained with a combination of silanization and an adhesive resin cement (Asmussen, 1997) (Table 21).

Table 23. Failure Rates Reported in Clinical Studies of Cast or Pressed Ceramic Inlays

System	Observation Time	No of Inlays	Failures (%)	Reseachers
Dicor	4 - 83 m	123	10	Roulet, 1997
Dicor	4 yr	210	13	Noack & Roulet, 1994
Empress	4.5 yr	125	4	Fradeani & others, 1997
Empress	6 yr	163	7	Studer & others, 1998
Empress	6 yr	59	7	Frankenberger & others, 1999

Table 24. Failure Rates Reported in Clinical Studies of Milled Ceramic Inlays

System	Observation Time	No of Inlays	Failures (%)	Reseachers
Cerec	40-80 m	1011	4	Walther & Reiss, 1996
Cerec	4 yr	50	0	Heymann & others, 1996
Cerec	5 yr	115	3	Berg & Dérand, 1997
Cerec	8 yr	32	9	Pallesen & van Dijken, 2000

Table 25. Failure Rates Reported in Clinical Studies of Dicor Full-Coverage Crowns

Region	Observation Time	No of Crowns	Failures (%)	Reseachers
Anterior Posterior	3 yr	106	4 35*	Moffa & others, 1988
Anterior Posterior	3 yr	46 57	2 12	Richter & Aughtun, 1989
Posterior	4 yr	92	16	Kelsey & others, 1995
Ant + post	6 yr	98	16	Sjögren & others, 1999
Ant + post	14 yr	1444	13	Malament & Socransky, 1999

*zinc phosphate cement

Several studies have found that the use of particular resin-modified glass ionomer cements and also compomers in the cementation of ceramic full crowns, increases the risk of fracture of the crown. The reason is the relatively high hygroscopic expansion of these materials, which exerts an internal pressure of the crown large enough to fracture the crown (Sindel & others, 1999).

Longevity of Ceramic Restorations

There is no doubt that with the current ceramic materials it is possible to produce restorations with an initial high quality and high esthetic level. In order to be a viable alternative to direct resin, porcelain-fused-to-metal and cast gold restorations, the ceramic restorations have to last for 15, 20 or more years. Unfortunately, we are faced with the fact that most clinical studies are still short-term with an observation period of three years or less. Consequently, the longevity of ceramic restorations is not well documented.

Tables 22-24 summarize results from clinical studies of ceramic inlays/onlays. Sintered ceramic inlays behaved differently in divergent studies: after three years, failure rates of 13% and 18% were reported, while in another study, the failure rate after six years was "only" 12% (Molin & Karlsson, 1996; Jensen, 1988; Qualtrough & Wilson, 1996; van Dijken, Höglund-Åberg & Olofsson, 1998) (Table 22). Glass ceramic inlays (Dicor) showed failure rates of 13% and 10% after approximately five years (Roulet, 1997; Noack & Roulet, 1994). With a failure rate of 4% to 7% after five-to-six years, IPS Empress inlays seemed to do better than Dicor inlays (Fradeani, Aquilano & Bassein, 1997; Studer, Lehner & Schärer, 1998; Frankenberger, Rumi & Krämer, 1999) (Table 23). With regard to milled inlays (Cerec), failure rates similar to those of IPS Empress

Table 26. Failure Rates Reported in Clinical Studies of IPS Empress Full-Coverage Crowns

Region	Observation Time	No of Crowns	Failures (%)	Reseachers
Ant + post	3 yr	75	1	Sorensen & others, 1998
Ant + post	3.6 yr	110	14	Sjögren & others, 1999
Ant + post	6 yr	138	12	Lehner & others, 1998
Ant + post	5 yr	142	10	Studer & others, 1998

Table 27. Failure Rates Reported in Clinical Studies of In-Ceram and Procera AllCeram Full-Coverage Crowns

Material	Observation Time	No of Crowns	Failures (%)	Reseachers
In-Ceram	2.5 yr	61	8[i]	Pröbster, 1996
		34	0[ii]	
In-Ceram	22-44 m	63	2[iii]	Scotti & others, 1995
Procera AllCeram	5 yr	97	6[iv]	Odén & others, 1998

I: Posterior teeth and zinc phoshate cement
ii: Anterior teeth and glass ionomer cement
iii: Glass ionomer cement
iv: Zinc phosphate cement, glass ionomer cement, resin cement

Table 28. A comparison of the failure rates of various treatment alternatives for small-to-medium size defects in posterior teeth.

Restoration		Observation Time	No of Restorations	Failures (%)	Reseachers
Composite Inlays		2 yr	45	4	Scheibenbogen-Fuchsbrunner & others, 1999
		5 yr	63	17	Wassell & others, 2000
		11 yr	77	17	Pallesen & Qvist, 2000
		11 yr	96	18	van Dijken, 2000
Ceramic Inlays	Sintered	6 yr	59	12	Van Dijken & others, 1998
	Dicor	4 yr	210	13	Noack & Roulet, 1994
	Empress	6 yr	163	7	Studer & others, 1998
	Cerec	8 yr	32	9	Pallesen and van Dijken, 2000
Direct Composites		2 yr	43	7	Scheibenbogen-Fuchsbrunner & others, 1999
		5 yr	57	8	Wassell & others, 2000
		11 yr	51	16	Pallesen & Qvist, 2000
		11 yr	33	27	van Dijken, 2000
Gold Inlays		10 yr	2717	35	Fritz & others, 1992
		4 yr	25	8	Silvey & Myers, 1976

have been reported (Walther & Reiss, 1996; Heymann & others, 1996; Berg & Dérand, 1997); and Pallesen & van Dijken, 2000) (Table 24).

Tables 25-27 summarize results from clinical studies on full-coverage crowns. Table 25 shows that Dicor crowns behaved differently in the anterior region versus the posterior region. After three years, Moffa, Lugassi & Ellison (1988) found failure rates of 4% for anterior crowns, 12% for premolar crowns and 35% for molar crowns. The results of the study by Richter & Aughtun (1989) were not as drastic: a 2% failure rate of anterior crowns and a 12% failure rate of posterior crowns. After four and six years in mean, respectively, two studies reported failure rates of 16% (Kelsey & others, 1995; Sjögren, Lantto & Tillberg, 1999), and finally, Malament & Socransky (1999) estimated the failure rate of anterior and posterior Dicor crowns to be 13% after 14 years. Thus, the failure rates registered for anterior crowns seem somewhat lower than the failure rates for inlays, while only minor differences in failure rate are noted between inlays and poste-

Table 29. A Comparison of the Failure Rates of Various Full-coverage Crowns

Restoration		Observation Time	No of Restorations	Failures (%)	Reseachers
All-Ceramic	Dicor	6 yr	98	16	Sjögren & others, 1999
	Dicor	14 yr	1444	13	Malament & Socransky, 1999
	Empress	6 yr	138	12	Lehner & others, 1998
	AllCeram	5 yr	97	6	Odén & others, 1998
Porcelain-fused-to-metal		11 yr	estimated	5	Leempoel & others, 1999
		7 yr	2181	2	Coornaert & others, 1984
		11 yr	estimated	3	Leempoel & others, 1999
Gold		9 yr	390	8	Schlösser & others, 1993
		4 yr	49	2	Silvey & Myers, 1976

rior crowns. The 1% failure rate of IPS Empress crowns after three years observed by Sorensen & others (1998) is markedly lower than the rate observed by other investigators (Sjögren & others, 1999; Lehner, Studer & Schärer, 1998; Studer & others, 1998), and generally IPS Empress crowns seem to do worse than IPS Empress inlays (Table 26). In two relatively short-term studies of In-Ceram, the restorations showed very low failure rates when luted with glass ionomer cement (Pröbster, 1996; Scotti, Catapano & D'Elia, 1995), while caries had developed in association with 8% of the posterior crowns, which had been luted with zinc phosphate cement (Pröbster, 1996) (Table 27). A five-year follow-up of Procera AllCeram crowns showed a failure rate of 6% (Odén & others, 1998).

The primary mode of failure for all-ceramic restorations is fracture of the ceramic (Martin & Jedynakiewicz, 1999; Van Dijken, 1999). Long-term clinical studies of the newer types of ceramics, for example, In-Ceram and Procera AllCeram, are still very scarce. However, as these materials have improved with respect to strength, restorations based on these materials may be expected to show a lower incidence of fracture. Reports agree that premolar and especially molar restorations are associated with a higher incidence of fracture than anterior restorations. Whereas most all-ceramic materials may be estimated as having an acceptable success rate when used to restore anterior teeth, it seems advisable to choose as strong a ceramic material as possible for the restoration of posterior teeth.

Conclusions

In conclusion and despite all possible differences in the materials and methods of the studies cited, an attempt has been made to compare the various treatment options for medium size defects in premolars and molars (inlays) (Table 28) and for large defects in anterior and posterior teeth (crowns) (Table 29). Table 28 lists representative failure rates found for composite inlays, ceramic inlays, directly placed composite restorations and gold inlays. Compared with composite inlays, sintered inlays and Dicor have a similar failure rate, while Empress and Cerec inlays have a slightly lower failure rate. Generally, directly placed composite restorations have a failure rate similar to that of composite inlays. Finally, gold inlays do not seem to be associated with a much lower failure rate than the three other treatment alternatives. Consequently, when a choice has to be made among the four treatment options in question, longevity cannot be used as a selection criterion, and focus can be directed to several other aspects which may be important to the patient, for example, price, esthetics and number and duration of dental appointments.

Table 29 compares all-ceramic crowns with porcelain-fused-to-metal and gold crowns. With all precautions imaginable as to differences between the study conditions, there seems to be no difference among the failure rates between porcelain-fused-to-metal crowns and gold crowns. However, all-ceramic crowns appear to have a higher failure rate than the other two types of restorations. Therefore, longevity may currently be a relatively important selection criterion as regards full-coverage crowns.

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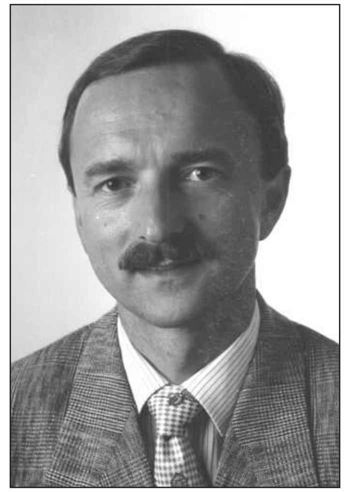

Various Forms of Glass Ionomers and Compomers

RA Hickel • M Folwaczny

Reinhard A Hickel

Abstract

In recent years conventional glass ionomers, resin-modified glass ionomers and polyacid-modified resin composites have attained increasing attention in clinical practice. Concerning the restoration of posterior teeth, these materials broadened the therapeutic armamentarium. Tooth-colored direct restorative materials have been advocated with the hope that these materials can substitute for amalgam as the material of choice for posterior restorations. The physical properties of these materials have been reported in numerous studies but little is known about their clinical long-term performance to date. A literature review regarding the longevity of these particular kinds of tooth-colored restorative materials in different clinical indications follows.

Introduction

Currently, different kinds of tooth-colored filling materials, composites, polyacid-modified resin composites, self-curing glass ionomers and resin-modified glass ionomer cements have reached acceptance in the treatment of carious lesions in primary and permanent dentition. However, each shows several advantages as well as some shortcomings.

Conventional glass ionomer cements are able to adhere physico-chemically to the surface of the cavity because they contain polyalkenoic acids and have a coefficient of thermal expansion which is almost equal to that of tooth substance (Fritz, Finger & Uno, 1996; Misra, 1993). In addition, the glass particles of these types of cement release fluoride after the filling hardens, thereby offering an anticariogenic effect along the cavity margins (Donly & others, 1999; Swartz, Phillips & Clark, 1984). Conventional glass ionomers reveal only moderate wear resistance, poor fracture toughness and rather rough surface conditions (Smales & Joyce 1978; Tyas, 1995). Furthermore, the esthetic results obtained with these materials are sometimes unsatisfactory due to their great optical opacity (Asmussen, 1983; Mathis & Ferracane, 1989; McCaghren & others, 1990).

The clinical use of conventional glass ionomers has recently been improved by the development of light curing and resin-modified glass ionomer cements, which have been suggested as an alternative to conventional glass ionomer restoratives. An additional light curing molecular system allows choosing the point of setting of these types of filling material within certain limits (Sidhu & Watson, 1995). Also, some physical properties of the resin-modified materials were improved compared to the conventional self-curing glass ionomers, whereas the advantages such as adhesion to dentin or fluoride release were maintained at least in part (Maneenut & Tyas, 1995; Mathis & Ferracane, 1989; Mitra, 1991; Momoi & McCabe, 1993; Sidhu, 1993; Uno, Finger & Fritz, 1996).

Another kind of material currently introduced, polyacid-modified resin composites or compomers, provided a new alternative in restorative dental therapy. Polyacid-modified resins are a subgroup of resin composites (Hickel, 1996). Following the initial formation, polyalcenoic acid was proposed to participate in a secondary acid base reaction (Gladys & others, 1997; Hickel & others, 1998). However, the significance of this reaction to the physical characteristics of the material and its clinical performance remains unknown. Polyacid-modified resin composite materials have to be applied with a dentin-bonding agent for sufficient adhesion onto the surfaces of the cavity (Cortes, García-Godoy & Boj, 1993; Fritz & others, 1996; Triana & others, 1994). In clinical use, this kind of material is easy to handle and the esthetic characteristics are quite satisfactory. The chemical and physical properties of compomers, especially their microhardness and compressive strength, are far more equal to the characteristics of resin composites than to that of glass ionomers (Uno & others, 1996; Attin, Vataschki & Hellwig, 1996).

Resin-composite materials show sufficient wear characteristics and good esthetic properties (Neo & others, 1996). Using the total acid-etch technique with a dentin bonding system, a strong bond to both dentin and enamel can be obtained (Duke, Robbins & Snyder, 1991). However, regarding the extensive shrinkage of resin composites during setting, the immediate occurrence of marginal openings may result (Powell, Gordon & Johnson, 1991). The risk for breakdown of the marginal seal appears to be strongly influenced by the size and shape of the cavity and the particular placement technique.

Primary Dentition

Amalgam has been the restorative material of choice for many years for the restoration of posterior teeth in the primary dentition. Although this particular material showed high success rates in permanent teeth, failure rate in the primary dentition has previously been reported as being high. Several clinical trials revealed failure rates for amalgam restorations placed in primary molars which ranged from 40% to almost 90% after a two-year period (Walls, Murray & McCabe, 1988; Qvist, Thylstrup & Mjör, 1986; Braff, 1975; Hickel & Voss, 1990). Barr-Agholme & others (1991) reported achieving significantly higher success rates for composite restorations compared to amalgam fillings, ranging from 88% for composite material and only 68% for amalgam fillings after two years. Accordingly, resin composites have been looked upon as a promising alternative to posterior amalgam. Contradictory results were, however, reported by Östlund, Möller & Koch (1992), who observed treatment failure after a three-year period only in 8% of the amalgam restorations but in 16% of the composite restorations. Varpio (1985) found considerably higher failure rates for composite restorations after six years; clinical acceptable restorations were reported only in 35% of the cases but at this time no sufficient dentin adhesives were available. When comparing the data derived from different studies, one has to bear in mind that the age of children at the time of restoration placement is one of the most important determinants for restoration longevity (Holland & others, 1986; Östlund & others, 1992; Barr-Agholme & others, 1991). Therefore, it does not appear appropriate to compare the results of previous studies unless the patients' age distribution is equal.

Obviously, one of the most prominent reasons for treatment failure in the restoration of primary teeth is the contamination of the cavity during restoration placement (Holland & others, 1986). Accordingly, their relative ease of handling has made glass ionomer cements interesting as an alternative to amalgam and resin composite materials due to the special needs in pediatric dentistry in working with children who are less compliant during dental procedures (Östlund & others, 1992). Moreover, since this particular kind of material releases fluoride over long periods, anticariogenic effects have been proposed and approved in many *in-vitro* investigations but only few clinical trials have addressed this problem. In fact, currently, only one study has proposed secondary caries

Table 1. *Longevity Studies of Posterior Restorations in Primary Dentition Using Glass Ionomer Materials and Compomers*

Reference	Period (Years)	Materials	Success Rate
Walls, 1988	2	Ketac fil amalgam	64% 60%
Hickel, 1990	3	Ketac silver amalgam	I:75% II:59% I:79% II:66%
Welbury, 1991	5	GI (Ketac fil) amalgam	67% 80%
Östlund, 1992	3	Chemfil Occlusin amalgam	40% 84% 92%
Qvist, 1995	1	Ketac fil Photac fil	86% 92%
Donly, 1996	2	3M-EXM155 amalgam	90% 85%
Kimura, 1996	1	Fuji II LC	88%
Peters, 1996	1	Dyract	97%
Roeters, 1996	2	Dyract	95%
Peters, 1996	3	Dyract	91%
Qvist, 1997	3	Ketac fil amalgam	63% 82%
Hse, 1997	1	Dyract Prisma TPH	98% 98%
Andersson-Wenckert, 1997	2	Dyract	100%
Frankenberger, 1997	2	Hi-Dense Ketac-Silver	72% 72%
Roeters, 1998	3	Dyract	91%
Marks, 1999	3	Dyract Tytin	94% 94%
Marks, 2000	1	Ketac molar Dyract	92% 90%
Welbury, 2000	3	Dyract Chemfil-Superior	90% 73%

as the foremost reason for treatment failure using glass ionomer materials (Mjör, 1996). The foremost problem in this regard may be that secondary caries is difficult to diagnose under clinical circumstances. Additionally, the results of many previous studies appear questionable (Hickel, Manhard & García Godoy, 2000; Mjör & Toffenetti, 2000; Randall & Wilson, 1998). Only one *in-vivo* study has been reported so far which clearly demonstrated histologically that glass ionomer restorations had considerably less demineralization along the cavity margins compared to amalgam restorations (Donly & others, 1999).

Although numerous studies on the clinical performance of glass ionomer restorations in permanent dentition have been reported, the results cannot be extrapolated on conditions in the primary dentition. Regarding the longevity of restorations, significant differences have been previously found between fillings placed on permanent teeth and those placed on deciduous teeth (Hickel, 1990). Unfortunately, concerning the treatment of the primary dentition, there have been an insufficient number of clinical trials conducted on glass ionomer restorations in Class III or Class V cavities to date. Therefore, available data on the clinical performance of glass ionomer materials in primary teeth were exclusively obtained in the restoration of Class I and Class II lesions (Table 1).

For restorations of primary molars with a conventional, self-curing glass ionomer material, Walls & others (1988) found similar clinical conditions at the two-year follow-up compared to posterior amalgam restorations. After five years in service, the conven-

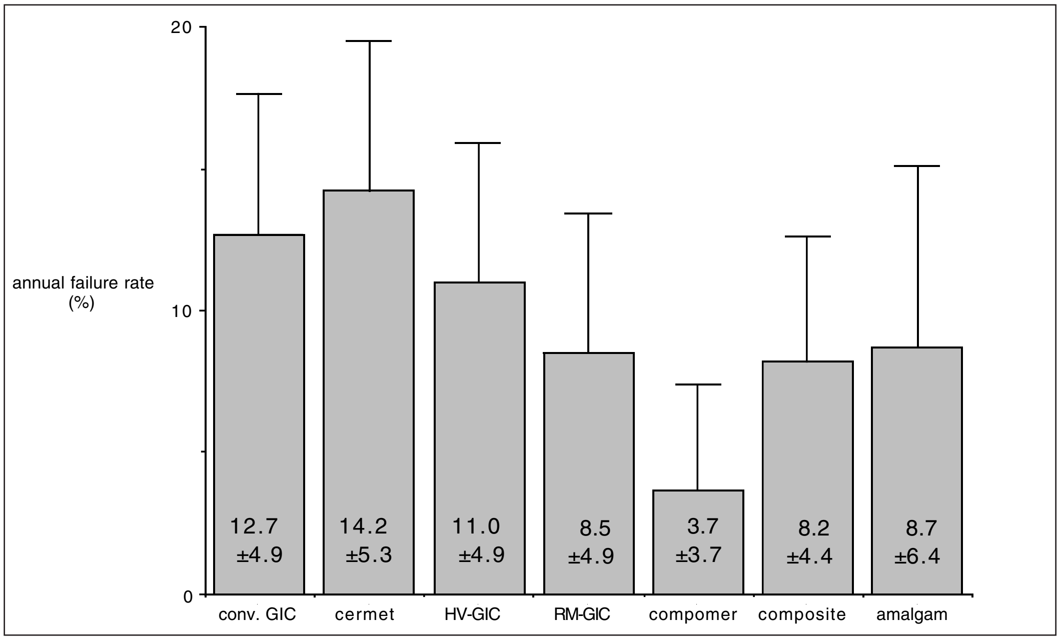

Figure 1. *Annual failure rate for different restorative materials in Class I/II cavities of primary molars (conv GIC: conventional glass ionomers; HV-GIC: highly viscous glass ionomers; RM-GIC: resin-modified glass ionomers). Bars indicate mean annual failure rate regarding all studies.*

tional glass ionomer restorations of the same study population were rated clinically acceptable only in 67% of the cases compared to 80% success for the posterior amalgam restorations (Welbury, Walls & Murray 1991). The authors' study included a metal-reinforced glass ionomer material and amalgam material and found similar clinical performance after two years (Hickel & Voss 1990). Although both materials placed in Class I and Class II lesions revealed similar success rates after 3.5 years, numerous glass ionomer restorations presented with fractures when used for restoration of Class II defects. Using the same material, Hung & Richardson (1990) observed a considerable number of fractures on Class II restorations even after one year. Accordingly, the use of metal-reinforced glass ionomer materials for restoration of Class II defects has been strongly denied. Considerable high-failure rates have been reported by Qvist & others (1997) also for a conventional glass ionomer restorative material when used in Class II lesions. Despite the particular type of lesion, Östlund & others (1992) reported a 60% failure rate for a conventional glass ionomer material, which was mainly caused due to fractures of the isthmus area of the restoration.

Improved clinical performance maintaining the anticariogenic effects at the same time compared to a conventional glass ionomer restorative were found for the recently introduced resin modified glass ionomer materials (Qvist, Teglers & Manscher, 1995). Using a resin modified glass ionomer material, Kimura & others (1996) observed treatment failure of 20% after one year. Similar success rates after two years for amalgam and resin-modified glass ionomer posterior restorations were shown in a previous study (Donly & Kanellis 1996). Probably due to improved elastic properties of the resin modified materials, Croll & Helpin, (1995) did not observe any fracture at 18 months in 250 Vitremer restorations placed in Class II cavities. Using the newly developed, highly viscous glass ionomer cements, the failure rate after two years was 28%, with a considerable number of Class II restorations showing fractures (Frankenberger, Sindel & Krämer, 1997).

The best clinical results for restoring primary teeth were obtained with the polyacid modified resin composites. Since its introduction, this particular kind of material became increasingly popular in pediatric dentistry as an alternative for conventional glass ionomer materials. Hse & Wei, (1997) observed 60 compomer restorations in primary teeth. Within the one-year study period, only one restoration failed. The success rates found in several clinical trials after three years reached more than 90% (Kimura & others, 1996; Roeters & others, 1998; Peters, Roeters & Frankenmolen, 1996; Marks & others 1999). Welbury & others (2000) reported a failure rate of 10% at 3.5 years for polyacid-modified resin composite restorations in primary molars, which was better than for amalgam as shown in an earlier study. However, due to their lower fluoride release, one can only speculate the anticariogenic properties of polyacid-modified resin composites. In fact, one study on the use of a compomer restorative in primary teeth reported treatment failure in 22% of the cases at two years (Andersson-Wenckert, Folkesson & van Dijken, 1997). The second highest reason for restoration failure in this study was secondary caries. On the other side, the higher water uptake and a favorable E-modulus leads to less stress on the bond of the restoration to the cavosurface compared to hybrid composites.

All groups of glass ionomers have some shortcomings, for example, low wear resistance or moisture sensitivity, which lead to limitations in clinical use. With regard to their superior clinical performance over three years, polyacid-modified resin composites are very promising alternatives for posterior restorations in the primary dentition (Figure 1).

Posterior Restoration in Permanent Dentition

Traditionally, amalgam is the material of choice for restoration of stress bearing posterior regions in the permanent dentition (Hickel & Klaiber, 1992). Hickel, (1990) proposed the median age for posterior amalgam restorations ranged from six to nine years, whereas Barbakov & others (1994) mentioned an average durability of four to eight years. The median age of posterior amalgam restorations in the permanent dentition, as reported by Mjör, Dahl & Moorhead (2000), was 11 years. Regarding amalgam restorations, the most common reason for treatment failure in almost all investigations was secondary caries and bulk fracture (Jokstad & Mjör, 1991). Obviously, the longevity of posterior amalgam restorations is strongly influenced by the particular cavity design. Additionally, the survival rates of posterior amalgam restorations appear to be associated with the age of the patient and individual caries activity (Jokstad & Mjör, 1991).

Bulk fracture, changes of anatomic form and marginal breakdown also comprise the most meaningful reasons for treatment failure regarding posterior glass ionomer restorations in the permanent dentition (Mjör, 1997; Hickel, 1996; Hickel & Manhart, 1999) (Figure 2). After a five-year period, Mjör & Jokstad (1993) found a failure rate of 45% for metal reinforced glass ionomer restorations, which was caused primarily by fracture of the restoration (Table 2). Failure due to fracture phenomena has been predominantly attributed to the low flexural strength of glass ionomer cements, leading to early fatigue under cyclic occlusal loading of the restoration. Again, the risk of fracture appears dependent on the cavity design. According to the results performed by Krämer & others, (1994) on metal-reinforced glass ionomer materials, especially restorations placed in Class II cavities, revealed a high portion of bulk fractures. In this study the survival rate at four years for restorations placed in Class I cavities was 90% and 72% for restorations in Class II lesions. Changes in anatomic form might be predominantly caused by low wear resistance of glass ionomer restorative materials (Mjör, 1997). Depending on the test procedure, the mean cumulative wear for conventional glass ionomer materials and metal-reinforced glass ionomer cements *in vitro* has been reported to be three-to-four times higher than that for resin composites (Kunzelmann, 1996; Schreyger, Kunzelmann & Hickel, 1994). Different wear machines simulate two-body wear (direct contact of antagonists, for example, Munich or Zürich) or three-body abrasion (which simulates demastication, for example, ACTA) and also focuses on different wear phenomena (for example, impact/fatigue or sliding wear). However, the absolute wear rates, as obtained under different experimental circumstances, cannot be compared. Only the ranking of wear appears to be independent of the particular laboratory conditions in some limits (Table 3a). According to Lutz & others (2000), the wear rates of some compomers equal hybrid and packable composites.

Significant differences regarding treatment failure of restorations placed in Class I and Class II cavities, respectively, were also assessed in a previous study which revealed a failure rate of 67% at three years for the Class II group, whereas in the Class I group it

Table 2. *Longevity Studies of Posterior Restorations in Permanent Dentition Using Glass Ionomer Materials and Compomers*

Reference	Period (Years)	Material	Success Rate
Hickel, 1988	3	Ketac silver (class I) Ketac silver (class II)	86% 33%
Smales, 1990	3	Ketac silver VisioMolar P 30 Dispersalloy	57% 94% 100% 100%
Setcos, 1991	4	Ketac silver Ful Fil	97% 100%
Lidums, 1993	2	Ketac silver Visio Molar Dispersalloy	53% 100% 100%
Mjör, 1993	5	Ketac silver P 10 Dispersalloy	57% 84% 93%
Frencken, 1994	1	Chemfil	82% 67%
Krämer, 1994	4 8	Ketac silver Ketac silver	82% 41%
Pilz, 1994	6	Ketac silver Visio Molar Amalgam	86% 82% 81%
Frencken, 1996	1	Fuji IX	98%
Kontou, 1999	1	Dyract AP Hytac	97% 97%
Huth, 2000	1	Hytac	95%
Hickel, 2000	2	Ionofil molar Dyract AP	95% 98%
Hickel, 2000	3	Dyract AP	94%

Figure 2. *Class II restorations in permanent dentition using resin-modified glass ionomer materials. Failure occured at one year due to bulk fracture.*

was only 14% (Hickel & others, 1988). In a study of 132 metal-reinforced glass ionomer restorations in Class I lesions, only 57% of the fillings were assessed as clinically acceptable at three years (Smales, Gerke & White, 1990). A considerable number of fillings failed due to surface cracking or crazing. After two years of treatment, failure was observed in 47% using a metal reinforced glass ionomer material for the treatment of 57 Class I lesions (Lidums, Wilkie & Smales, 1993). Setcos, Philips & Braun (1991) found that only one of 32 posterior metal-reinforced glass ionomer restorations had to be removed during a four-year period. At six years Pilz, Hetzer & Viergutz (1994) reported a cumulative success rate for metal-reinforced glass ionomer restorations of 86%. Considering a very small study population of eight Class I posterior restorations, Mount (1997) even reported a 100% success rate after 12 years. In contrast, in another study performed on 790 restorations, secondary caries contributed to 50% of treatment failures observed within a five-year period (Mjör, 1996).

Frencken, Makoni & Sithole (1998) used a newly developed high viscous glass ionomer material for restoration of 212 Class I cavities with the atraumatic restoration technique (ART) and found 98% of the fillings clinically acceptable after one year. The success rate after two years was 93% and at three years, 88.3% (Frencken & others, 1998). However, regarding the same study, 6 of 18 (33%) restorations placed for Class II cavi

Table 3. *Physical Properties of Different Polyacid-Modified Resin Composites. N Represents the Different Number of Products Investigated*

Table 3A: Wear rate as obtained in different studies (Data of "Zürich" from Lutz & others, 2000), Munich and ACTA from our wear lab data bank, partly published by Kunzelmann, 1996)

Wear-Simulator	**Zürich**		**Munich 1 Impact**		**Munich 2 Sliding**		**ACTA**	
Group	**n**	**Mean (µm)**	**n**	**Mean (µm)**	**n**	**Mean (10^6 µm)**	**n**	**Mean (µm)**
Conventional GIC			4	795 - 920	1	277	4	42 - 132
Resin Modified GIC	1	612	4	780 - 995			4	65 - 359
High Viscosity GIC			4	330 - 380	4	1600 - 4200	4	18 - 61
Metal Reinforced GIC	1	412	2	445 - 505	1	4520	2	30 - 73
Compomers	4	117 - 254	6	155 – 295	10	450 – 1600	6	36 – 51
Hybrid Composites	1	120	4	105 - 165	20	41 - 390	6	24 - 46
Packable Composites	4	112 - 163			6	64 - 220		
Amalgam	1	158					2	10 - 18

Table 3B, C. *Vickers-hardness and (c) flexural strength (own filling material data bank, publication in preparation). Note the wide range of physical properties of different products in the same group of materials.*

	Pr.	**Flexural Strength**		**Diametral Tensile Strength**	
Material Group	**n**	**Mean**	**Range**	**Mean**	**Range**
Compomers	8	96.6	81.5 – 131.6	33.9	25.4 – 48.9
Hybrid Composites	16	126.6	102.4 – 160.8	33.2	25.7 – 42.1
Packable Composites	8	113.9	82.3 – 136.3	33.4	22.9 – 46.8
Ormocers	2	104.3	88.2 – 119.3	35.2	26.9 – 43.4
Microfilled Composites	37	5.6	62.8 – 87.6	28.3	21.5 – 25.1

Table 3C.

	Pr	**Compressive Strength**		**Vickers Hardness**	
Material Group	**n**	**Mean**	**Range**	**Mean**	**Range**
Compomers	8	231	201 - 256	65.6	45.1 – 84.0
Hybrid Composites	16	260	218 - 286	65.2	50.4 – 107.4
Packable Composites	8	240	142 - 276	65.7	42.7 – 89.2
Ormocers	2	216	208 - 224	57.7	46.2 – 69.2
Microfilled Composites	3	258	231 - 290	33.3	23.8 – 45.3

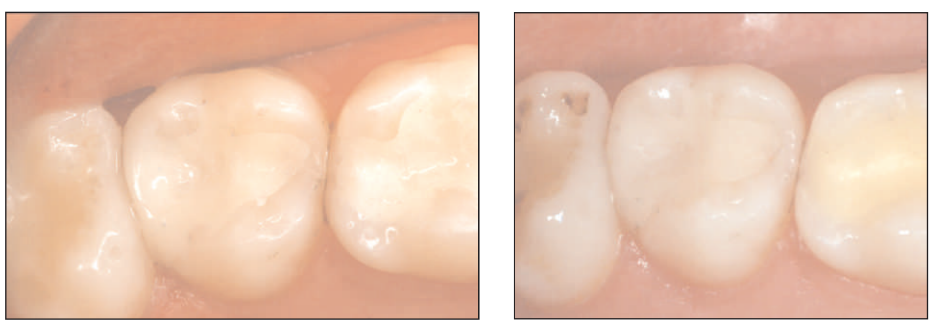

Figure 3. *Restoration of Class II lesions in permanent dentition using the highly viscous glass ionomer Ionofil-molar at baseline (a) [left] and after two years (b) [right].*

ties failed within the first year. According to a two-year study, 5% of the high viscous glass ionomer restorations failed, which was in majority caused due to bulk fractures (Hickel, 2000) (Figure 3). Generally, bulk fracture appears to represent the major reason for treatment failure also using high viscous glass ionomer materials despite their improved physical properties.

Regarding polyacid-modified resin composites, little data are currently available regarding their clinical performance in Class I and Class II lesions. Most studies yielded results of a six-month observation period (Benz & others, 1998). The success rate within this time frame ranged from 91% to 100%. The use of a polyacid-modified resin composite in posterior Class I and Class II cavities in the permanent dentition showed clinical success in 97% of the restorations after one year (Kontou, Frankenberger & Krämer, 1999; Huth & others, 2000). A study of compomers placed in Class I and II cavities revealed a 98% success rate after two years and 94% at three years (Hickel, 2000).

Considering the high risk for fracture of conventional glass ionomer materials and cermets, these restorative materials do not appear appropriate for the restoration of posterior permanent teeth. Although the more recently introduced high viscosity glass ionomer cements reveal improved *in-vitro* properties, only few data exist on their clinical long-term performance. Finally, polyacid-modified resin composites reached increasing attention in clinical use for restoration of posterior lesions of the permanent dentition in recent years. Especially, the ease of handling might have contributed to the high popularity of this kind of material (Lutz & others, 2000). Physical properties show a wide range, for example, regarding flexural strength and wear resistance (Table 3 B-C), but some products show comparable or even better results with conventional hybrid composites or packable composites. Some packable or hybrid composites show inferior physical data compared with the best compomers. Discussing the indication of different groups of filling materials (for example, compomers for posterior restorations in permanent teeth), one should be very careful with general recommendations. It is more reasonable to look into detail and specific products when recommending materials for particular indications.

Cervical Lesions

Due to esthetic reasons, glass ionomer cements represented the material of choice for the restoration of cervical lesions for many years. Chemical adhesion to the cavosurface and fluoride release might have additionally contributed to the widespread acceptance of glass ionomer materials in this field (Sidhu & Watson, 1995; Cortes, García-Godoy & Boj, 1993; García-Godoy & others, 1988). Treatment of this particular kind of lesion usually provides a special challenge to the clinician because of the lack of a retentive cavity shape. In addition, cavity margins are typically suited for both enamel as well as dentin or cementum. Several clinical studies approved the potential of conventional glass ionomer cements for the restoration of cervical abrasion lesions as well as for carious cervical lesions (Powell, Gordon & Johnson, 1991; Matis, Cochran & Carlson, 1996).

Various studies over one to six years showed success rates of cervical restorations using conventional glass ionomer materials which fall between 47% and 100% (Flynn 1982; Tyas & Beech, 1985; Reich 1992; Maneenut & Tyas, 1995; Powell, Johnson & Gordon, 1995) (Table 4). Observing the longest study period of 10 years, Matis & others (1996) found a cumulative success rate of 80% for glass ionomer restorations placed in non-carious cervical lesions.

However, the use of conventional glass ionomer materials for the restoration of cervical lesions has reached decreasing acceptance in recent years since the newly developed tooth-colored restorative materials, the resin-modified glass ionomer materials and the polyacid-modified resin composites have been introduced. The on-demand setting and better esthetics have especially made the newly developed tooth-colored materials more attractive as an alternative to the conventional glass ionomer materials (Brackett & others, 1999).

Using a resin-modified glass ionomer material, Neo & others (1996) obtained a clinically acceptable performance of cervical restorations in abrasion/erosion lesions after 18 months in 95% of the cases. However, within the same study, the conventional glass ionomer restorations revealed no failure.

Using two different resin-modified glass ionomer materials for the restoration of 59 carious cervical lesions, Abdalla & others (1997) observed no treatment failure at one and two years. Van Dijken (2000) obtained a failure rate of 7% at three years, restoring non-carious cervical lesions with resin-modified glass ionomer cement. Data from our studies on cervical restorations of non-carious lesions showed a 28% failure rate after five

Table 4. *Studies on Longevity of Glass Ionomer and Compomer Restorations in Carious and Non-Carious Cervical Lesions*

Reference	Period (Years)	Material	Success Rate
Flynn, 1982	6	Aspa Cervident	47% 59%
Tyas, 1985	2	Fuji Type II Cervident Scotchbond/Concept	92% 53% 88%
Hickel, 1988	2	Ketac silver	81%
Matis, 1991	5	Ketac fil Chelon fil Cervident	90% 87% 43%
Reich, 1992	4-6	Fuji II Ketac fil (sandwich-technique)	100% 94% 74%
Maneenut, 1995	1	Fuji II LC Photac fil Vitremer	100% 100% 100%
Barnes, 1995	1	Variglass Variglass APH	100% 100% 100%
Powell, 1995	3	Ketac fil Scotchbond2/Silux (sandwich-technique)	97% 76% 100%
Matis, 1996	10	Ketac fil Chelon fil Composit	80% 67% 17%
Neo, 1996	3	Ketac fil (sandwich-technique) Silux/Scotchbond	96% 96% 78%
Elderton, 1996	2	Dyract Dyract (without DBA) Chemfil	100% 18% 97%
Abdalla, 1997	2	Compoglass Dyract Fuji II LC Photac fil Vitremer	100% 100% 100% 94% 100%
Barnes, 1997	2	Dyract	100%
Folwaczny, 2000d	3	Tetric Dyract Fuji II LC Photac fil	96% 90% 94% 89%
Folwaczny, 2000a	5	Dyract Fuji II LC Photac fil	80% 75% 74%

years for a resin-modified glass ionomer material (Folwaczny & others, 2000a) (Figure 4). One of the most important reasons for restoration failure was the breakdown of the margins, both on enamel and cementum or dentin. In addition to the clinical observations, the quantitative determination of the restoration material along the restoration margins using a three-dimensional scanning device showed strong substance loss for the resin-modified glass ionomer cement over a three-year period (Folwaczny & others, 2000b). The marginal loss at resin-modified glass ionomer restorations was significantly stronger than that for a resin composite and a polyacid-modified resin composite. The second greatest reason for treatment failure in this study represented changes of anatomic form. Regarding the low wear resistance, loss of restoration material due to tooth brushing seemed to have caused the stronger changes in anatomic form.

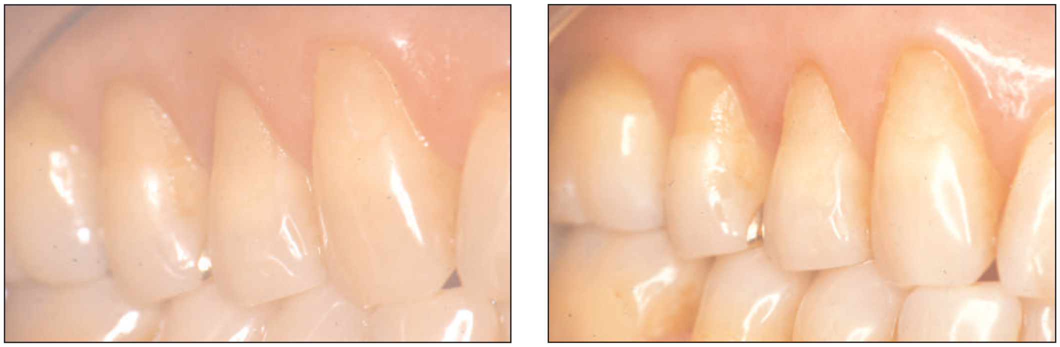

Figure 4. *Restoration of non-carious cervical lesions using a resin-modified glass ionomer material (Fuji II LC, GC Corp, Japan) at six months (a) and after five years (b).*

No restoration failure was obtained for polyacid-modified resin composites in two different investigations after one and two years in clinical service (Barnes & others, 1996; Elderton & others, 1996). Using this kind of material for cervical restorations yielded a slight failure rate of 3% after three years (Elderton & others, 1996). Abdalla & others (1997) achieved a 100% success rate for two different polyacid-modified resin composites after two years in carious cervical lesions. At two and three years the authors found a success rate of 89% for a polyacid-modified resin composite placed in carious and non-carious cervical lesions (Folwaczny & others, 1998; Folwaczny & others, 2000c; Folwaczny & others, 2000d). After three years in clinical service, Tyas (2000) observed failure in 5.5% of the compomer restorations placed in non-carious cervical lesions. Regarding cervical abrasion/erosion lesions, the polyacid-modified resin composite failed in 25% of the cases after five years (Folwaczny & others, 2000a). Loss of restoration was the most important reason for treatment failure. Probably, the lack of enamel etching during the placement of the polyacid-modified resin composite restorations has predominantly contributed to the high rate of retention failure in this study. It has to be pointed out that the adhesive system has probably more influence on retention or loss of cervical restorations than the restorative material, itself.

In general, conventional glass ionomer materials as well as their resin-modified counterparts yielded significantly poorer clinical long-term performance than the polyacid-modified resin composites and the resin composites (Folwaczny & others, 2000a; Folwaczny & others, 2000c; Folwaczny & others, 2000d). Placing the resin composite and compomers in cervical lesions under the use of the total etch technique and dentin bonding system can achieve predictable and satisfactory clinical results.

Conclusions

The newly developed glass ionomer materials and compomers have reached considerable clinical significance within recent years for various indications. For the restoration of posterior lesions in the primary dentition, the polyacid-modified resin composites are currently the material of choice, which in most studies was superior to other materials. Also for the treatment of carious and non-carious cervical lesions, compomers revealed the best clinical results, which were considerably superior to the conventional and resin-modified glass ionomer cements. Regarding the restoration of posterior Class I and Class II cavities, again compomers showed interesting results. However, for final recommendation, clinical studies of up to four years remain to be seen. Within the group of compomers, there is a wide range of physical properties, such as strength and wear. Some products (for example, Dyract) show even better results when compared with packable or hybrid composites and their clinical data are very promising.

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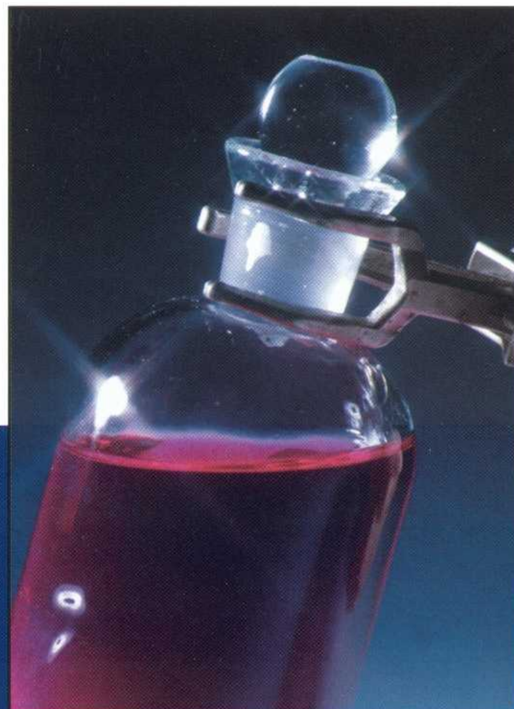
Future Materials and Biocompatibility

Future Materials and Biocompatibility



THEME 4

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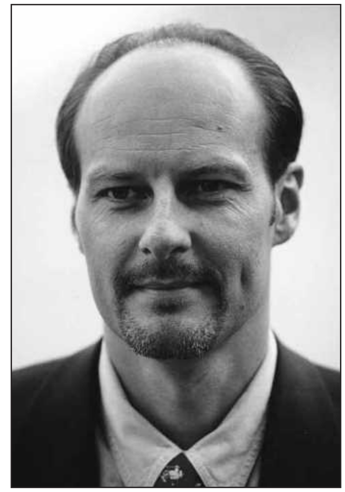
Theme 4

Adhesive Restorations in Posterior Teeth: Rationale for the Application of Direct Techniques

D Dietschi • I Krejci



Didier Dietschi

Abstract

Material properties as well as the clinician's ability to control the development of detrimental polymerization shrinkage stresses govern the behavior and quality of direct composite restorations in posterior teeth. In addition to the use of a strong adhesive, many other compensatory factors can help to achieve a good adaptation. Among the most important ones may be the application of a thick bonding resin layer or the application of a "soft" base-liner, the use of multilayer techniques and the application of the "selective" bonding concept. Understanding the principles of composite polymerization and stress development in the tooth-restoration complex is a prerequisite for achieving optimal results.

Introduction

Many dentists remain reluctant to use resin composites in posterior teeth, either because of their mediocre reputation in the past or because of the too many available layering techniques and confusing concepts which make their successful application doubtful. While catastrophic failures have rarely occurred, the insufficient wear resistance, poor mechanical properties and rapid marginal degradation of former composite generations were responsible for their rather short-term success. However, tremendous recent improvements in restorative composites and adhesive systems have generated a revolution in dentistry, placing adhesive restorations on the front stage and making resin composites an essential dental restorative material. Today, the successful use of these materials relies on their proper selection and on understanding their properties, in particular, their curing mechanism and application techniques. This paper reviews current knowledge about composite resin polymerization and proposes a rationale for the use of direct techniques in posterior teeth.

Managing Stress Development

While composite resin properties such as physico-chemical characteristics, wear resistance, radiopacity, handling and aesthetics can be regarded as clinically sufficient, composite polymerization shrinkage remains the material's ultimate drawback. Although it was significantly reduced in modern composite formulations (Bowen, Nemeto & Rapson, 1983; Davidson, de Gee & Feilzer, 1984; de Gee, Feilzer & Davidson, 1993; Stravidakis, Kakaboura & Krejci, 2000), it is still too high to allow direct techniques to be simply applied in large Class I and II restorations. Immediate and delayed composite polymerization shrinkage stresses and masticatory forces therefore are potentially

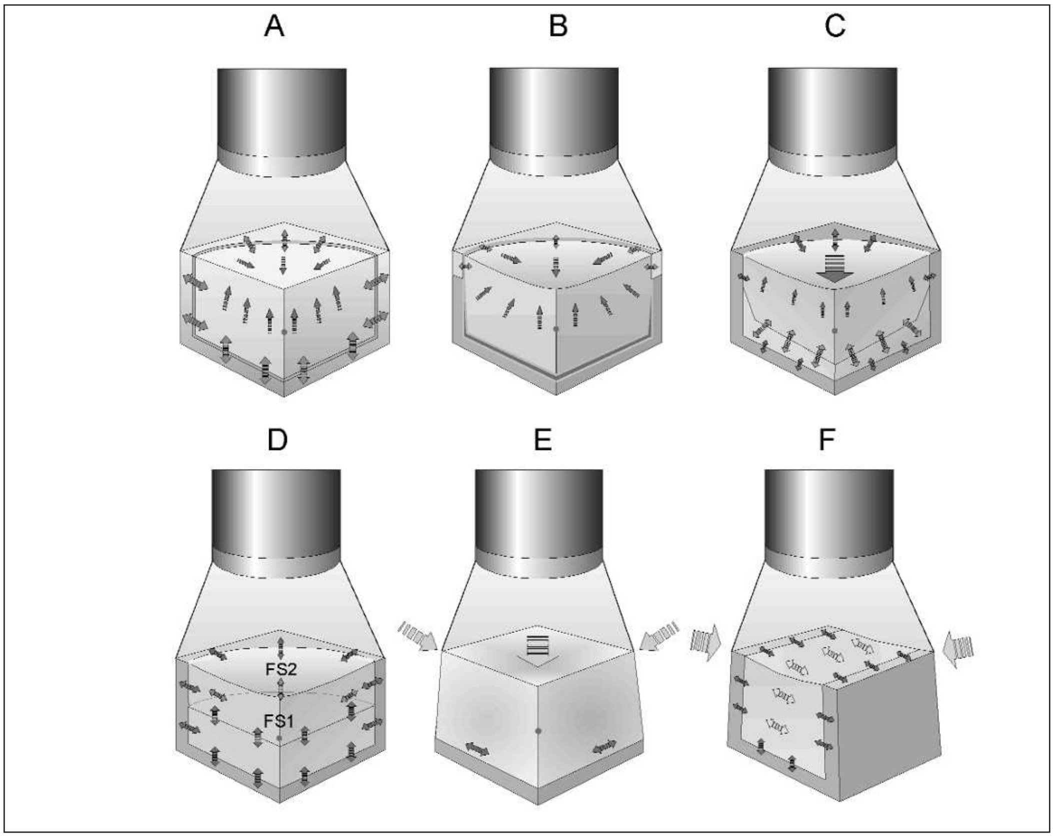


Figure 1. Means and phenomenon which allows stress compensation or reduction. A: thick bonding resin layer; B: Selective bonding concept; C: low elasticity module base-liner; D: multilayer technique; E: flow at the free surfaces; F: elastic deformation of tooth substrate and restorative material.

damaging to the internal and marginal adaptation. Apart from the restorative technique influence, these forces and their consequences are affected by several factors, such as:

- cavity volume;
- cavity configuration (Feilzer & others, 1987; Yoshikawa & others, 1999);
- extension of the cavity toward CEJ;
- enamel quality;
- dentin quality—location and depth; diameter, density and orientation of tubules; degree of tissue sclerosis; possible contamination (that is: by eugenol-based dental cements); decay...;
- bond strength of the adhesive; and
- material composition and structure.

Therefore, after having analyzed the conditions specific to the tooth being restored, the clinician's major challenge remains to balance stresses with adhesion and favor stress reduction or relief by all possible means. Stresses can actually be controlled or relieved by different means, not all of which are under the control of the operator.

1) Controlled stress reduction (Figure 1):

- application of a thick "elastic" bonding resin (first stress breaker layer) (Kemp-Scholte & Davidson, 1990a & b) (Figure 1A);
- use of the selective bonding technique (Lutz & others, 1986a,b; Krejci & Stavridakis, 2000) (Figure 1B);
- application of a "low elasticity module" base-lining (second stress breaker layer; Bindi, 1998) (Figure 1C); and
- use of a multilayer technique (optimizing of the configuration factor (Figure 1D).

2) Stress relief by other phenomenon (only partially or not under the control of the operator):
- deformation of the composite at the free surfaces, so called "flow" (Davidson & De Gee, 1984) (Figure 1E);
- elastic deformation of the restorative material (Figure 1F);
- elastic deformation of the tooth (Figure 1F); and
- water sorption.

Theories and Controversies Regarding Stress Development and Polymerization Vectors in Posterior Restorations

Understanding how stress develops during resin composite polymerization is of primary importance, as this information can bring definite solutions and concepts for controlling its negative effects. However, monitoring of stress kinetics and distribution within composite increments during the build-up of a restoration is a challenging task and has thus far been approached only by indirect observations (evaluation of the final restoration marginal seal or adaptation) or computer simulation (finite element analysis: Versluis & others, 1997, 1998). Although there is no universally accepted proof or model available, some basic rules seem to apply to direct light curing resin composite restorations. Actually, the stress magnitude and direction probably is governed by the following main factors:
- light intensity;
- light position;
- increment thickness;
- increment configuration (ratio free to bonded surface);
- composite reactivity (relative to initiator-catalyst amount);
- composite opacity and chroma; and
- filler composition, size, shape and amount.

Light Intensity and Direction

Within a thin increment (<1mm) of a low chroma and translucent composite material, the authors assume that the light produced by a powerful curing device (above 600mW/cm^2) kept close to the material surface will be attenuated but will remain at an intensity susceptible to generate an almost uniform distribution of polymerization stresses (Figure 2A) (Rueggeberg & Jordan, 1993; Rueggeberg & others, 1994a). Until research invalidates this hypothesis, the authors will develop their clinical concept accordingly. Since papers evaluating the influence of restoration quality on different curing concepts (high intensity versus low intensity; uniform versus step or ramp curing) presented conflicting results, one can conclude that the research failed to identify an optimal curing approach. This sustains the "uniform" stress distribution concept in

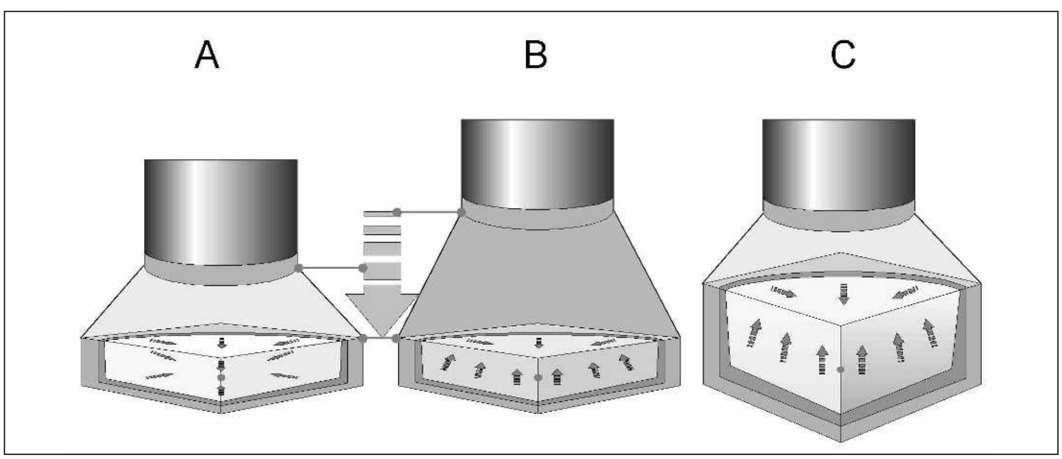


Figure 2. Expected polymerization vectors in thin (A&B) or thick layers (C), according to the light tip distance, the light intensity and increment thickness-chroma and opacity. "A" represents the light tip kept close to material surface–high light intensity– low composite chroma and opacity. "B" represents the light tip kept further to material surface–low light intensity–high composite chroma and opacity. "C" represents a thick increment (other parameters do not play any role).

thin layers (<1mm) or the fact that the curing protocol, besides practical considerations, probably has little, if no influence on restoration quality when a proper incremental technique is applied. The only well known rule remains that enough energy needs to be brought to the material to achieve an optimal conversion rate within a clinically reasonable irradiation time (up to 40 seconds).

Increment Thickness

The authors have to expect a different (non-uniform) distribution of polymerization stresses when curing large, thick increments (more than 2 mm of restorative material, especially with opaque and dark shades) or when light intensity is significantly reduced, for instance, when the bulb is deficient or in the case of light absorption by a restorative material or tooth substance (indirect curing) (Rueggeberg & others, 1993; Rueggeberg, Caughmam & Curtis, 1994; Rueggeberg & others, 1994; Myers & others, 1994; Rueggeberg & others, 1999) (Figures 2B&C).

Increment Configurtion

The ratio between the free and bonded surface determines the amount of stress relief by flow at the free surface (Feilzer & others, 1987). The rationale for applying multilayer techniques is to reduce the overall polymerization stress by increasing the number of increments and giving them an optimal geometry to augment the total free surface (Figure 2). Clinical experience and the largest number of studies support this theory. As a matter of fact, the application of a "bulk" technique should be indicated only for preventive restorations (minimal volume).

Composite Structure and Composition

The ratio resin-filler is another governing factor in determining polymerization shrinkage magnitude and physical performances. Therefore, choosing a material with a high filler content is a prerequisite for producing restorations of good quality in posterior teeth. In addition, an expired material will not only potentially change the curing kinetics but can also favor a premature restoration degradation because of an incomplete material polymerization. Composite structure seems less influential than the aforementioned parameters (Rueggeberg & others, 1993; Rueggeberg & others, 1994c).

Conditions to Achieve Optimal Results and Clinical Concept

Three situations need to be considered—the minimally invasive restoration—the medium size restoration—the large restoration (Dietschi & Spreafico, 1997). For the two "extreme" situations, a clear approach is mandated; a bulk technique for the minimal preparation (Simonsen, 1985) and a semi-direct or indirect inlay-onlay for a large volume and cusp replacement (Krejci & others, 1993; Dietschi & Herzfeld, 1998). Medium size restorations require a more discerning approach, as the best treatment option implies an optimal combination of the clinical effort and final restoration quality. Although layering techniques and base-liners have the potential to effectively reduce the damaging consequences of the aforementioned stresses, spontaneous post-polymerization shrinkage, which takes place during the following 5 to 10 days after light activation (Leung & others, 1983; Davidson, de Gee & Feilzer, 1984), still represents a major obstacle to the use of direct techniques in very large cavities with unfavorable configuration (such as two surface Class II or Class I restorations).

Thereafter, the following guidelines need to be taken into consideration:

1) Occlusal cavity, less then 1/3 of the bucco-lingual tooth width: horizontal-layering technique (Lutz & Kull, 1980).
2) Occlusal cavity, more than 1/3 of the bucco-lingual tooth width: oblique layering technique (Weaver & others, 1988).
3) Proximal cavity within the contact point area: horizontal-layering technique (Lutz & Kull, 1980).
4) Proximal cavity outside the contact point area: three-sited light curing method (Lutz & others, 1986a and b).

Table 1: Suggested Restorative Techniques According to Cavity Design, Cavity Size and Adhesive Concept (the clinician choose between TB or SB)

Cavity Design	Cavity Volume	Total Bonding			Selective Bonding		Technique	Layering
		DBA*	Thick DBA	Base-Lining	GI Base	DBA + Resin		
Class I Conventional	Minimal	+	+	-	-	-	Direct	Bulk
	Medium	(+)	+	(+)	-	+	Direct	Horizontal
	Large	(+)	+	+	+	+	Direct (Semidirect)	Vertical/ Oblique
Class I Adhesive	Minimal	+	+	-	-	-	Direct	Bulk
	Medium	(+)	+	(+)	-	+	Direct	Vertical/ Oblique
	Large	(+)	+	+	+	+	Direct	Vertical/ Oblique
Class II MO/OD	Minimal	+	+	-	-	-	Direct	(Bulk) Horizontal
	Medium	(+)	+	(+)	-	+	Direct	Horizontal
	Large	(+)	+	+	+	+	Direct (Semidirect-Indirect)	3 Sites + Vertical/ Oblique
Class II MOD	Minimal	+	+	-	-	-	Direct	(Bulk) Horizontal
	Medium	(+)	+	(+)	-	+	Direct	3 Sites + Vertical/ Oblique
	Large	(+)	+	+	+	+	Direct (Semidirect-Indirect)	3 Sites + Vertical/ Oblique
Cusp Coverage		(+)	+	+	(+)	+/-	(Direct) Semidirect-Indirect	(3 Sites + Vertical/ Oblique)

*= DBA, but without stress-breaker layer formation TB = Total Bonding SB = Selective Bonding

Polymerization stresses can further be absorbed by a lining or base made of a more "elastic" material such as a thick bonding resin layer (Davidson, 1994; Choi & others, 2000), a flowable composite (Olsburgh, 2000), a glass ionomer or compomer (Lutz & others, 1986a; Davidson, 1994; Friedl & others, 1997; Hannig & others, 1997; Bindi, 1998; Olsburgh, 2000). It is particularly useful to apply such a base-liner when applying a so-called "one-bottle" adhesive. Although most modern adhesive systems provide bond strength values in a similar range (May & others, 1997; Wakefield & others, 1998; Wilder & others, 1998; Tanumiharja & others, 2000), they do not necessarily provide the same quality of restoration adaptation. Actually, unlike thick-filled adhesives, "one-bottle" adhesives rely on the formation of a very thin adhesive layer (a few microns only) which has no potential of "stress absorption."

When applying the selective bonding concept, with the aim of determining the location of the separation, in case polymerization forces exceed a certain value, some specific adhesives are to be recommended (such as Syntac Classics; Vivadent and Fluorprotecter, Schaan-Liechtenstein) (Figure 1B). In larger cavities, a conventional glass ionomer base can be applied (Table I) which plays the same role and helps reduce the amount of composite material to be cured *in situ*.

Table I offers a guideline for selecting the adhesive system and concept, base-liner and restorative technique according to the clinical situation.

Conclusions—Clinical Relevance

To obtain the maximal quality and durability of direct posterior composite restorations, the clinician has to be aware of the following rules:

- limit the cavity size and extension where a direct technique is applied;
- evaluate all conditions which govern stress development and adhesion efficiency; and

- subsequently, use appropriate means (selection of the adhesive system and concept, application of a base-liner and use of a multilayer technique) to optimally reduce the negative consequences of polymerization stresses.

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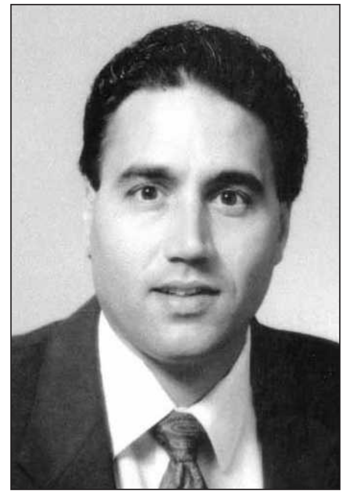

New Polymer Resins for Dental Restoratives

JL Ferracane

Jack L Ferracane

Introduction

Polymers are used in dentistry for many applications, including provisional restoratives, sealants, adhesives, impressions, dentures, dies and more. In recent years, the greatest emphasis in research has been on their use as restoratives. Resin-based composite restoratives are currently considered adequate for minimal stress-bearing clinical applications. However, enhancements in wear-resistance, biocompatibility and marginal sealing are still needed for posterior composites (ADA, 1998). Further research is encouraged to develop alternative matrix resins and polymerization initiators to produce materials with less polymerization shrinkage, less wear and fracture in sites of heavy occlusion, improved adhesion and easier placement techniques.

Numerous resin systems for dental applications have been synthesized, though few have been commercialized. Recent literature contains several reviews of the composition and properties of current dental resin-based restoratives (Bayne, Heymann & Swift, 1994; Ferracane, 1995; Leinfelder, 1997; Peutzfeldt, 1997a). This paper focuses on the ongoing work in new polymers and studies presented in the past three to four years, dividing them into the following topic areas: reduced polymerization shrinkage and shrinkage stress, enhanced degree of conversion and mechanical properties, fiber reinforcement, reduced hydrophilicity, anti-cariogenic activity, remineralizing activity and surface coatings.

Monomers for Reduced Shrinkage/Stress

The primary cause for failure of resin-based restoratives is secondary caries (Qvist, Qvist & Mjör, 1990; MacInnis, Ismail & Brogan, 1991; Mjör & Jokstad, 1993; Friedl, Hiller & Schmalz, 1995). This phenomenon is believed to be related to the difficulty in placing resin-based restorations that contract 2-4% by volume during polymerization (Feilzer, deGee & Davidson, 1988; deGee, Feilzer & Davidson, 1993; Choi & others, 2000). This contraction places the interface between the restoration and the tooth under stress (Feilzer, deGee & Davidson, 1987) and may result in marginal openings (Davidson, deGee & Feilzer, 1984). The magnitude of the stress depends on the overall contraction, the elastic modulus of the polymerizing composite, the polymerization rate and the ability of the resin to relieve the stress by flow.

It has become apparent that even with improved adhesives, leakage cannot routinely be prevented *in vitro* (Hilton, Schwartz & Ferracane, 1997; Hilton & Ferracane, 1999) or *in vivo* (Abdalla & Davidson, 1993; Ferrari & Davidson, 1996). Thus, alterations in the polymeric component are needed to minimize the deleterious effects of polymerization and render resin-based restoratives easier to use and less sensitive to technical parameters.

Several approaches are being pursued to reduce polymerization shrinkage in dental resins. Composites containing expanding monomers, such as spiroorthocarbonates (SOC), were introduced in the late 1970s but not successfully commercialized (Thompson, Williams & Bailey, 1979). More recently, Stansbury (1992) developed SOCs for use with dimethacrylate resins capable of free radical polymerization. In parallel work, others have synthesized SOCs and mixed them with epoxy (oxirane) resins capable of cationic polymerization (Byerley & others, 1992; Eick & others, 1992). The difficulty with these materials has been in producing sufficient ring opening expansion to offset the polymerization contraction without reducing the extent of cure. Recently, Krenkel & others (1999) showed that an experimental system containing an expanding monomer, a diepoxide monomer and a polyol (PTHF) had reduced polymerization contraction stress compared to a commercial bis-GMA/TEGDMA composite, Z100. Expanding SOC monomers can be added to these new systems. However, some evidence suggests that overall cure of the mixture with an SOC is less than that of dimethacrylate systems (Kaufman, Eick & Chappelow, 1999), and that this may explain some of the reduction in shrinkage and contraction stress. Chappelow & others (1997) have reported a reduced cure rate and reduced overall conversion of epoxy/SOC/polyol mixtures. However, this group has also shown that the photoreactivity of SOC-containing mixtures (tetraoxaspiro-undecane, TOSU) can be enhanced when a reaction promoter is added and the reduction in shrinkage stress is retained (Chappelow & others, 1999).

A recent publication reported on the properties of various epoxy-polyol mixtures, showing volumetric shrinkage as being nearly half that of bis-GMA/TEGDMA formulations while maintaining equivalent strength and stiffness (Tilbrook & others, 2000). Water sorption for these new resins was slightly higher than that of traditional dimethacrylates, owing to the hydrophilic nature of the polyols. It was concluded that the optimum properties were attained when the ratio of epoxide/polyol groups was between four and eight.

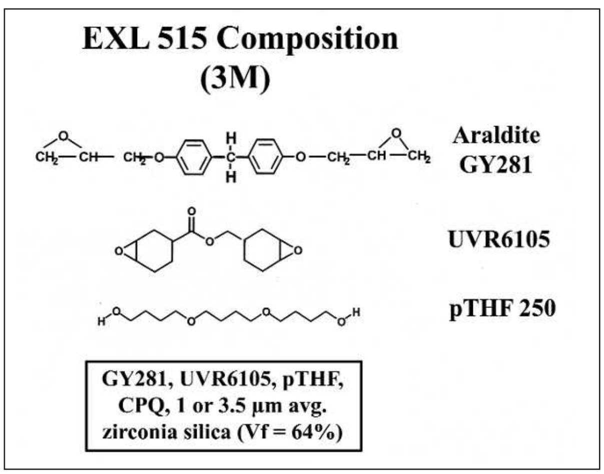

Figure 1. Chemical structure of experimental composite based on oxirane and polyol monomers.

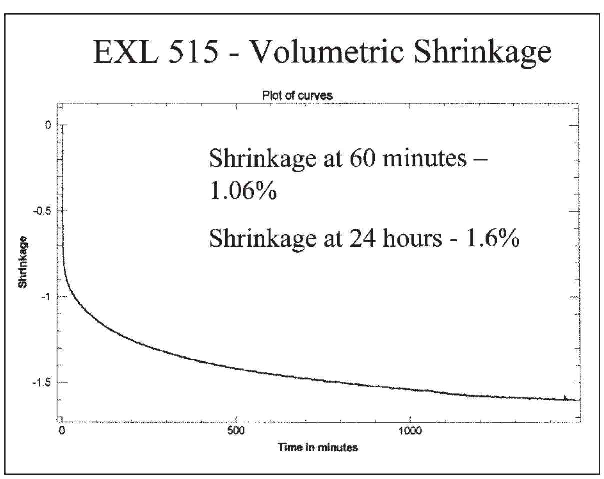

Figure 2. Volumetric contraction vs time for an oxirane/polyol composite tested in a mercury dilatometer (n=4).

ESPE has developed other epoxy-based systems for use in dental resins (US patents 6,075,068 and 6,084,004). These siloxane-based oxirane molecules are capable of cationic polymerization and produce composite materials with adequate properties for dental composites.

Recent work from 3M Dental Products has produced a prototype composite that is based on a mixture of two oxirane monomers and a small amount of a polyol (pTHF) set by a cationic-initiated, light-activated reaction (Figure 1). When filled with zirconia silica, this composite demonstrates mechanical properties that are similar to commercial posterior composites. Recent studies in our lab confirm the work

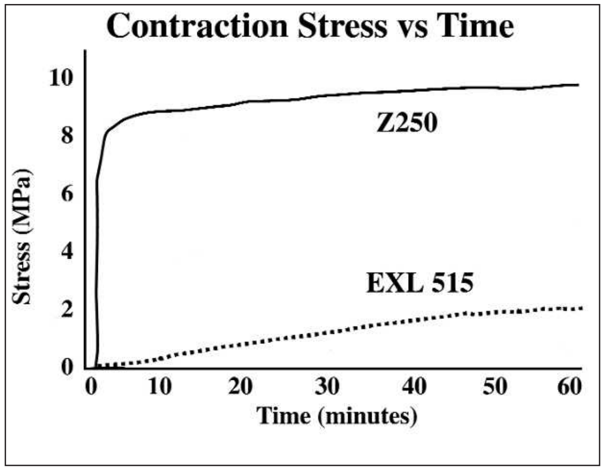

Figure 3. Polymerization contraction stresses generated by an oxirane/polyol composite and a conventional posterior composite (Z250) as measured in a servohydraulic testing machine more than 60 minutes.

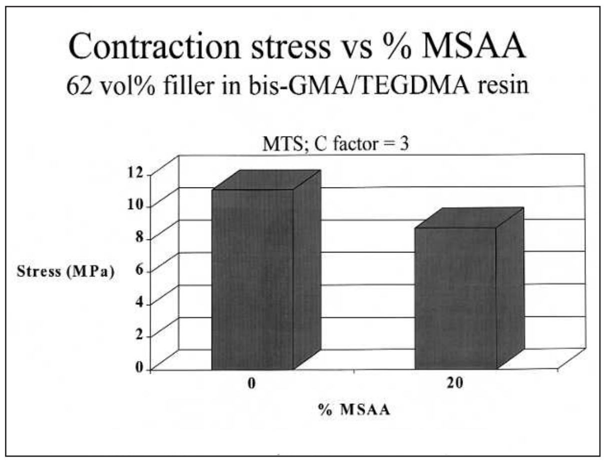

Figure 4. Contraction stress generated in composite with and without MSAA additive (Condon & Ferracane, 2000).

at 3M, showing this composite as having a volumetric shrinkage of approximately 1.0% at 60 minutes and 1.6% at 24 hours, which is essentially half that of other posterior composites (Figure 2). It is believed that low shrinkage results from expansion of the oxirane ring as it opens, which partially offsets the shrinkage associated with the formation of the covalent bond as monomers are linked during polymerization. More importantly, the material generates a contraction stress of less than 1.0 MPa at 10 minutes, which is significantly lower than that of Z250 (9 MPa) when tested under the same conditions (Condon & Ferracane, 2000) (Figure 3). The low stress is probably related to the slower curing rate, which allows time for molecular relaxations to relieve stress. Because the reaction is cationic, it is temperature dependent and the reaction rate and stress generation are slightly higher when tested at 37°C vs 27°C. Future modifications of this composite will lead to enhanced setting kinetics and improved wear characteristics, thus preparing it for clinical evaluation.

Several other avenues have recently been pursued to reduce contraction stress. Cyclopolymerizable di- and multi-functional oligomers synthesized through the reaction of acrylates and formaldehyde can produce resins with higher conversion and lower shrinkage than normal acrylates (Stansbury, Dickens & Lui, 1995). Radical ring opening of unsaturated spiroorthocarbonates or vinylcyclopropanes (VCP) has been tried as a means of reducing shrinkage in dental composites (Miyazaki & others, 1997). VCP monomers have been used to replace TEGMDA in a bis-GMA/UDMA resin and produced composites with two-thirds less shrinkage (Moszner & others, 1997). In other work, Lee (1999) reported on the use of 20 µm aggregates of polybutadiene rubber polymer adsorbed onto fumed silica (microfiller) and added to a bis-GMA/TEGDMA resin. The aggregates acted as a strain absorber and reduced shrinkage by as much as 25%. Liquid crystal monomers represent another approach to reducing polymerization contraction in dental resins. Rawls & others (1997) and Norling & others (1999) have described liquid crystal monomers, such as 1,4(4-(6-acryloyloxy-hexane-1-oxy)benzoyloxy)2-(t-butyl) benzene, that show volumetric shrinkage of 2% when mixed with 30 wt% of aerosol silica micro-filler (OX-50). Lower shrinkage is expected when composites are prepared with higher filler levels.

In other work, Culbertson, Tong & Wan (1997a,b) reported on the synthesis of a methacrylated derivative of styrene-allyl alcohol, MSAA. The aim of this multi-methacrylate comonomer was to produce composites with increased strength and cure. Recently, MSAA was used to replace 20% or more of the bis-GMA in a bis-GMA/TEGDMA resin composite formulation containing 62 vol% filler and shown to reduce polymerization contraction stress by 20% (Condon & Ferracane, 2000), presumably by facilitating molecular rearrangements to relieve stress (Figure 4).

Novel bismethacrylates have been developed by reacting various branching molecules at the hydroxy groups of the bis-GMA molecule (Holter, Frey & Mulhaupt, 1997). Though the initial resins produced in this way had low modulus, the use of branching molecules containing phenyl groups separated from the bis-GMA backbone by a flexible spacer produced resins having one-half the modulus of bis-GMA and only a third of the polymerization shrinkage.

Monomers for Enhanced DC and Properties

Other approaches to reduce shrinkage in dental resins have also been attempted, with the added benefit of producing resins with enhanced cure. Anseth & others (1996) described the use of monomers with high molecular weight, such as multi-ethylene glycol dimethacrylates. This work has also been described in US patent 5,730,601. Copolymers of diethylene glycol dimethacrylate and poly(ethylene glycol 600) dimethacrylate have achieved a degree of conversion near 95% to 100%, though this, in part, is due to the considerable reduction in available C=C, as the average molecular weight of the monomers increases. The large flexible monomers reduce elastic modulus due to the lower cross-linking density. However, when used in small quantities, up to 30wt% PEG600DMA in a DEGDMA resin, a significant increase in conversion is produced without a significant reduction in modulus. Such resin additions may also enhance the toughness of dental composites.

In other work, esterified multi-methacrylate oligomers of poly(isopropylidenediphenol) (BPA) have recently been synthesized and mixed with TEGDMA to produce resins with reduced polymerization shrinkage compared to bis-GMA (10-15% reduction) (Culbertson, Tong & Wan, 1997c,d; Tiba & Culbertson, 1999). There is evidence that the reduced shrinkage partly results from a reduced degree of conversion during light curing. However, these resins had higher compressive strength, were more rigid and had lower water sorption than bis-GMA. The increased rigidity is explained by their chemical structure, which consists of five phenyl rings connected by covalent bonds, and the lower water sorption is attributed to the lack of hydroxyl groups. One commercial composite (Solitaire, Heraeus) contains multi-functional methacrylate monomers originally developed for the indirect resin composite Artglass. Though Artglass demonstrated an enhanced degree of conversion and slightly greater toughness than conventional bis-GMA/TEGDMA composites, it also had lower hardness, elastic modulus and wear resistance (Freiberg & Ferracane, 1998). Solitaire has been shown to have inferior wear resistance and properties and greater polymerization contraction than bis-GMA or UDMA-based composites, probably because the multi-functional molecules plasticize the resin matrix (Ferracane & others, 1999; Choi & others, 2000).

Attempts to increase DC have involved the addition of monomethacryates to the resin formulation. Dickens, Stansbury & Floyd (1999) recently studied methods for improving the degree of cure of bis-GMA/TEGDMA resins through the addition of monomethacrylates, such as benzyl methacrylate and lauryl methacrylate. Differential scanning photocalorimetry showed that these low molecular weight mobile monomers enhanced DC presumably by lowering viscosity.

Peutzfeldt & Asmussen (1996a,b) and Peutzfeldt (1997b) reported on the addition of chain transfer agents, such as propanal (propionaldehyde) and diacetyl (2.3-butanedione), which become bound to the matrix and increase the degree of conversion and cross-linking of bis-GMA and UDMA resins from 80% to 90% to 98%. They previously demonstrated that the addition of limited amounts (up to 16 mole%) of the aldehyde or ketone to dental resins enhanced properties and wear resistance (Peutzfeldt & Asmussen, 1992a,b).

Another interesting area of study is the development of organic-inorganic hybrid molecules for dental composites. One such type of material has been termed ormocers. These materials are based on multifunctional urethane and thioether (meth)acrylate alkoxysilanes (Wolter, Storch & Ott, 1994). The alkoxy silanes are synthesized and through a sol-gel process undergo inorganic polycondensation of the silane groups to produce an inorganic gel network. The organic methacrylates of the gel can then undergo polymerization to produce a polymer network, thus achieving the formation of an inorganic/organic copolymer with properties that depend on the nature of the initial molecules. Additional ring structured silane precursor molecules have been developed that produce ormocers with low polymerization shrinkage (Wolter & Storch, 1994). When filled, they produce composites with adequate mechanical properties and shrinkage that are considered for dental use, and one such material (Definite, Degussa) has been marketed. Another type of organic-inorganic hybrid is organosilsesquioxane, which have the general formula $(RSiO_{1.5})_n$. These materials may serve as fillers for composites. They are composed of a rigid silicon-oxygen core with covalently linked methacrylate groups that are capable of bonding with typical dimethacrylate resins. These hybrids can be produced by the hydrolysis and condensation reaction of siloxane or silane molecules (Antonucci, Fowler & Stansbury, 1997). Cubic silsequioxanes have been synthesized by Zang & Laine (1997) and Gravel & Laine (1997).

A new organic/inorganic hybrid filler for dental composites has been produced by the sol-gel reaction of PMMA-co-3-(trimethoxysilyl) propylmethacrylate with TEOS in which the PMMA chains are covalently bonded to the silica network (Wei & Jin, 1997; Wei & others, 1998). These fillers demonstrated good wetting when mixed with bis-GMA/TEGDMA resins and produced composites with improved compressive strength due to enhanced filler/matrix bonding as confirmed by SEM.

Fiber Reinforcement

Fiber reinforcement of polymer resins has been available for many years but only recently has become very popular in dentistry for fixed prosthetics (Behr & others, 1999; Freilich & others, 2000). Silane-treated glass fibers are commonly used, as are plasma treated polyethylene, often in a woven form. Unlike glass fibers, which are commonly used due to their high modulus of elasticity, polyethylene fibers do not appreciably raise the stiffness of the structure. Instead, they act to strengthen and toughen composites for single and multiple unit restorations (Figure 5). Laboratory testing shows that these composite structures deform greatly during loading but do not crack in a brittle manner, such as unreinforced systems. The woven fibers are usually impregnated with a lightly-filled or heavily-filled resin, the latter being easier to accomplish by the manufacturer and supplied as such to the operator. Wetting of the fibers by the resin and homogeneous distribution of the resin between the fibers are critical to successful reinforcement for these materials.

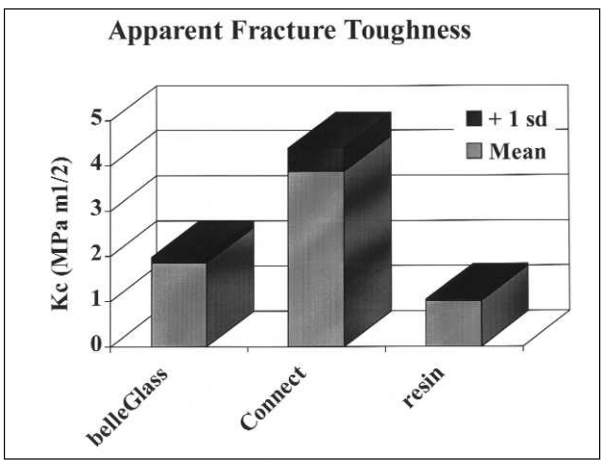

Figure 5. Apparent fracture toughness of hybrid composite (belleGlass) and woven polyethylene fiber reinforced composite (Connect).

Hydrophobic Monomers

Sankarapandian & others (1997a,b) studied the water sorption, hardness and glass transition of several bis-GMA analogues that substituted F and phenyl groups on the central carbon. Fluorine addition to the central methyl groups reduced sorption to less than 10% of bis-GMA, and the fluorinated polymers were more stable during water storage, showing less reduction in hardness. Kalachandra & others (1999) also reported that the increased flexibility of these resins contributed to a higher DC than occurs in bis-GMA during polymerization.

Fluorinated dimethacrylates based on bis-GMA and UDMA with lower water sorption than bis-GMA resins have been synthesized by Stansbury, Choi & Antonucci (1997).

Mixtures having adequate strength for dental composites are created when these resins are mixed with fillers treated with silane coupling agents, such as 10-methacryloxydecyltrimethoxysilane, that are more hydrophobic than the normal ϒ-methacryloxypropyltrimethoxysilane.

In similar work, fluorosubstituted TEGDMA (fTEGDMA) has been tried with limited success as a more hydrophobic diluent comonomer to be used with bis-EMA base monomer for composites (Uppituri & others 1999a,b). The water sorption of these composites is slightly reduced compared to those made from Bis-GMA, but they did not have improved resistance to ethanol solvents compared to non-fluorosubstituted formulations (Villarroel & others, 1999).

Other attempts to reduce water sorption of composites have included the synthesis of UDMA analogues containing either a phenoxymethyl group on the periphery or a bulky aliphatic group to replace the core segment of the UDMA (Khatri & Stansbury, 1999). The objective is to reduce the possibility for water to attack the urethane linkages through steric hindrance. These resins showed 10-30% reduction in water sorption compared to conventional UDMA, but also had lower flexure strength. Because of their low viscosity, these monomers are proposed as comonomers rather than base monomers for composites.

Anti-Cariogenic Materials

Imazato & others (1994) developed an antibacterial monomer, MDPB (methacrylyloxydodecylpyridinium bromide), to be added to dental resins. This methacrylated monomer can copolymerize, assuring that the anti-bacterial portion of the molecule becomes permanently affixed to the resin matrix. Composites containing MDPB have been shown to inhibit the growth of Streptococcus mutans (Imazato & others, 1994) and do not reduce the degree of cure or other tested properties (Imazato & McCabe, 1994). Recently, Imazato & others (1999) reported that the addition of 0.4-0.5% MDPB did not influence the water sorption of bis-GMA-based composites. The extent to which these monomers will effectively inhibit microorganism colonization of a composite margin covered with a pellicle intraorally is not known, but adhesives containing MDPB are currently being evaluated.

Recently, an antimicrobial material, Halo (Halo Scientific, Monterey, MA), was added at concentrations up to 1 wt% to a commercial composite and showed antibacterial behavior against *S mutans* and *A viscosus* that lasted for up to 10 weeks (Steinberg & others, 1999a,b). The anti-bacterial behavior of these composites was further evaluated over a two-week period using an agar diffusion assay. Zones of inhibition that increased in size with increased amounts of Halo were seen (Vaidyanathan & others, 1999a). In another study, the color stability of composites containing up to 1 wt% Halo exposed to accelerated UV aging for 24 hours was verified (Vaidyanathan & others, 1999b). In the absence of the ability to ensure an adequate marginal seal, resin composites and adhesives containing anti-bacterial agents may prove to be an important addition to restorative dentistry.

Bioactive Formulations

There is an intense desire to develop biomaterials that can effectively replace missing or decayed tooth structure through the process of remineralization. Fluoride applications are currently used to remineralize non-cavitated lesions. However, it is not currently possible to remineralize tooth structure after excavation of a substantial lesion. Calcium phosphate has been used as a filler to make composites that serve as bioactive liners and bases to enhance remineralization (Skrtic, Antonucci & Eanes, 1996; Park & others, 1998). Though these composites provide sustained release of calcium and phosphate ions, they have low strength and stability. In more recent work, Skrtic & others (2000) described bioactive polymeric composites based on amorphous calcium phosphate (ACP) but strengthened by hybridization of the fillers with glass forming elements. Bis-GMA, TEGDMA, HEMA resins containing zirconyl methacrylate as a dispersing agent for the ACP to which glass-forming elements, such as zirconyl chloride and tetraethoxysilane, were added during synthesis to improve the filler strength. Though these materials show improved properties and maintain remineralizing potential, still, they are not strong enough to be used as restorative materials without further modification.

Surface Coatings

A thin, clear polymeric material that could be coated onto the tooth to inhibit plaque formation and demineralization would be very beneficial. Mitra and others have developed such coatings (US Patent 5,866,639). These coatings are made from a copolymer of acrylic acid, an alkylmethacrylate, such as iso-butylmethacrylate and a polysiloxane. The copolymer is crosslinked via pendant silane groups using tetraethylorthosilicate. There are many possible formulations, and the properties and characteristics of one experimental material have been described in a series of studies. The material has been shown to provide protection against demineralization of bovine enamel *in vitro* (Kedrowski & others, 1998), inhibit plaque retention *in vivo* (Bohlig & others, 2000) and resist toothbrush abrasion (Rozzi & Mitra, 1999). Clinical trials continue with this experimental material from 3M.

Future Polymers

The future use of polymers in dentistry will undoubtedly expand, fueled by the investigations of dental manufacturers and researchers, as well as by discoveries made in other industries. One can envision polymer adhesives and sealants devoid of fillers but still possessing adequate radiopacity, stiffness, strength, wear resistance and esthetic characteristics. The literature already contains evidence of molecular additions (triphenylbismuth or other brominated or iodinated monomers) that enhance cure and radiopacify contemporary resin matrices (Davy & Labella, 1997; Farrell, Park & Rawls, 1999). There is a potential for the use of memory polymers that could serve as inlay/onlay materials that expand or contract to fit the prepared tooth as a result of intraoral heating. Such polymers are currently used in other applications. The development of lining, coating and restorative materials that are self-adhesive to dentin and enamel are also eagerly awaited. For example, oxirane (epoxide) chemistry, such as that currently being developed for dental composites, is used in many applications due to its adhesiveness to many substrates. Cationic initiated curing reactions on basic surfaces, such as apatite, are not trivial, but current evidence suggests that it can be accomplished in the near future and could potentially eliminate the need for an intermediate adhesive. Biodegradable polymer scaffolds are currently available for carrying drugs, cells and growth factors to tissue sites to repair or close defects. It is not difficult to fathom the use of these materials to aid in the reproduction of dentin or enamel structures as linings or complete restoratives for decayed teeth.

Summary

Subtle modifications in comonomer formulation of commercial materials have produced composites with enhanced handling properties and color stability. Attempts to produce resins with enhanced cure and properties have not resulted in significant advances because increasing cure through the use of low-viscosity or longer-chain comonomers usually results in plasticizing of the polymer matrix. Therefore, the major emphasis for research on new resins for composites has been in the area of reduced polymerization shrinkage and shrinkage stress. Promising work has been described on the use of expanding monomers, such as spiroorthocarbonates, as additives to methacrylate or epoxy-based resins and in the area of liquid crystal monomers. Perhaps the most significant advances have been with the oxirane formulations, and it is likely that commercial dental composites based on resins with minimal polymerization shrinkage will be forthcoming within the next few years. This development will generate a flurry of research on the properties, biocompatibility and clinical performance of these new materials to determine whether they are truly an improvement over current bis-GMA-based or UDMA-based materials. Recent work with remineralizing resin composites containing calcium phosphate ceramics is very interesting, but so far these materials only provide properties sufficient for use as lining materials under conventional composite restoratives. The use of resin matrices as a tool to engineer new tooth tissue is just beginning, and in the near future, the field can expect significant effort in this area.

Ackknowledgment

The author thanks Sharon Rozzi and Joe Oxman of 3M/ESPE for providing some of the information for this manuscript. Also, acknowledged is support fromNIH/NIDCR Grant DE07079 and Kerr SDS.

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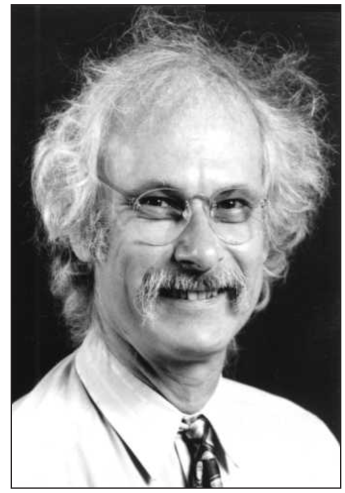
Future Ceramic Systems



J-F Roulet • R Janda

Jean-François Roulet

Introduction

Ceramics are everywhere in life; there is no way to think about a life without them. We eat from ceramic plates (feldspathic porcelain), cut with ceramic knifes (zirconium dioxide) and in the bathroom, we encounter lots of ceramics (feldspathic porcelain). Some of our watches have ceramic shells (zirconium dioxide), the chips in our computers are ceramic based, our cars have ceramic parts (aluminum oxide, zirconium dioxide), the milling of steel and other metals is done with ceramic tools, high-tension power lines use ceramics as insulators and nuclear power plants are unthinkable without ceramics serving as fuel structure elements or absorbents. Finally, there are some very special, but from a technological development standpoint, quite old-fashioned ceramics used for dentistry. Covering the whole ceramic world is far beyond the scope of this article; therefore, it will be restricted to dental ceramics. Yes, ceramics are somewhat outdated, but nevertheless, they are very interesting because in dentistry there is one major restriction: dental ceramics must be "white" and translucent, the same as teeth. This eliminates a number of high-performance ceramics, the so-called non-oxidic ceramics such as graphite, silicon carbide, silicon nitride, boron carbide or boron nitride (Salmang & Scholze, 1983).

How to Predict the Future

Actual technologies may trigger new developments in the changing demands of related fields. Some examples that underline this thought are listed below.

- The day cars were put on tires, it was foreseeable that the tire industry would become a big business since every improvement in the car's performance had to be followed by better tires.
- With the standard of living increasing in industrialized nations, the bicycle has faded out as a mode of transportation. However, health awareness and sports have created a revival in the once presumably doomed bicycle industry.
- As the power of computers increases and software becomes increasingly more complex, with the consequence of large and larger files, more storage space is needed, triggering the development of powerful mobile storage media (ZIP drives and writable CD-ROMs).
- The presence of the Internet, with all its possibilities, has created a new economy.

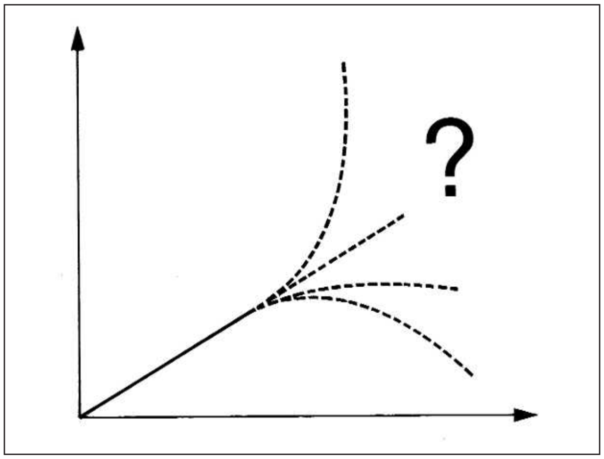


Figure 1. *Extrapolation: A linear relationship may be extrapolated.*

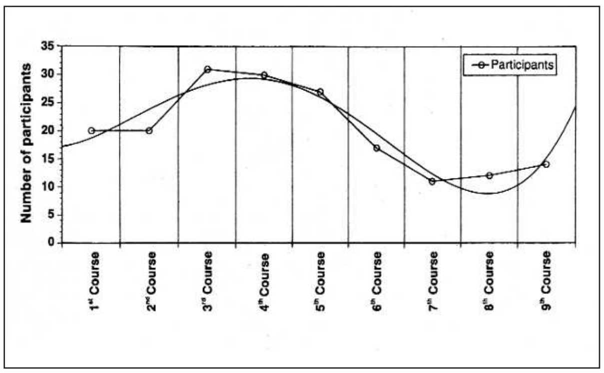


Figure 2. *Prediction of the future development of the number of participants in continuous education:*

Figure 2A. *A positive trend is calculated.*

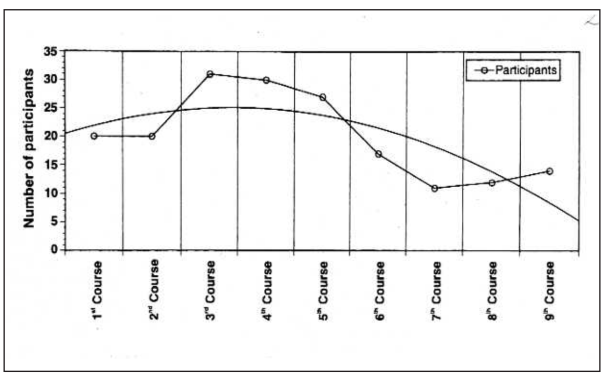


Figure 2B. *Based on the same data, a negative trend can be predicted.*

A good way to predict the future is by extrapolation. The simpler the process and the better the parameters governing it, the more reliable such a prediction is. An extrapolation from a number of votes during an election may lead to a precise prediction, while a weather report is very often prone to errors. In any case, extrapolation is dangerous. If the analysis of a process reveals a linear relation (Figure 1), it is very likely that it will continue to be linear. But how do we know this? It might be a relationship with a plateau or an exponential relationship, but our analysis was still in the initial, more or less linear phase of a more complex relationship. Despite very sophisticated analysis tools, such as polynomial regression, the method of choice can completely invert the result. A simple example is that our Department of Operative Dentistry has given many training courses on Cerec technology to a variety of participants. We tried to forecast, based on the number of participants, whether the courses should be continued or terminated. Unfortunately, based on the analysis technology, we got a highly positive, but also a highly negative trend (Figure 2).

Looking into the future may also be done through imagination and fantasy. Science fiction novels serve as the best example. However, the realization of such visions is highly dependent on the availability of the right technology. As Jules Verne wrote his story "Voyage to the Moon" in 1865, he thought in the technology of the 18th century and shot the manned spaceship to the moon with a huge, oversized canon. Today, we know this approach cannot work. Only with the proper technology, rocket propulsion, was it possible for human beings to visit the moon a little more than 100 years later.

Changes in the Future Dental World

Despite the fact that dental diseases are equal worldwide, dentistry varies considerably from nation to nation because the way dentistry it is practiced is dictated more by the system of health care and economics than from the disease *per se*. Therefore, it is almost impossible to give a global prognosis. However, it is foreseeable that there will not only be a split between the rich and the poor, nation-wise, but also within a nation and population-wise. In economically strong nations or populations, caries is declining, therefore, the demand for large restorations will also decline. However, only the younger populations have less caries, leaving a substantial part of the population with a greater demand for complex restorations. The rich people will probably be able to afford high-tech restorations such as inlays, crowns and bridges. Furthermore, this segment of the population has a high need for esthetics, giving ceramics a good chance for further development. On the other hand, economically weak nations or populations, which unfortunately are in the majority in this world, have to deal with problems other than healthy teeth and thus, must set priorities. For these people, the dental future is not so good since a pain-free situation must remain a minor goal. This means that dental treatment will mean simple restorations (ART = Atraumatic Restorative Technique) (Frencken & Holmgreen, 1999; Holmgreen & Frencken, 1999) or extractions. For this segment of the population, there is no future for ceramics since, if they ever become affordable, esthetics will be achieved with cheaper technologies such as resin technology, allowing for direct approaches.

Analysis of the Current Status of Ceramics and Potential for Future Developments

Today, different types of ceramics are available to manufacture ceramic restorations. While all these ceramics provide higher strengths than the conventional fused-to-metal ceramics (Figure 3), they can be subdivided as follows:

- silicon oxide (feldspathic) ceramics;
- aluminum oxide ceramics;
- aluminum oxide ceramics reinforced with zirconium oxide;
- zirconium oxide ceramics; and
- hybrid ceramics.

The number of ceramics that are sufficiently strong for posterior indications is very limited unless porcelain fused-to-metal is used, which is done with feldspathic ceramics. The strongest ceramic with white shade is yttrium stabilized tetragonal zirconium oxide (YTZP = Yttrium stabilized Tetragonal Zirconia Polycrystals).

A further differentiation is possible when considering how manufacturing depends on the respective ceramic (Table 1). Besides the techniques mentioned, there are other possible manufacturing techniques, such as sonoerosion, burnout and subsequent sintering, rapid prototyping (see below) and more that could be used in dentistry.

Silicon Oxide Ceramics

These ceramics can be processed according to the slurry and the press technique. However, regarding this ceramic type, slurry technique is not used much any more. For instance, Optec HSP (Jeneric/Pentron Inc, USA) is a ceramic processed on a refractory material (Vaidyanathan, Vaidyanathan & Prasad, 1989). The majority of silicon oxide ceramics is processed according to press techniques that have several advantages especially with regard to strength, homogeneity and fit. For instance, well-known ceramics of this type include Empress, Empress II (Ivoclar AG, Liechtenstein), Finesse All

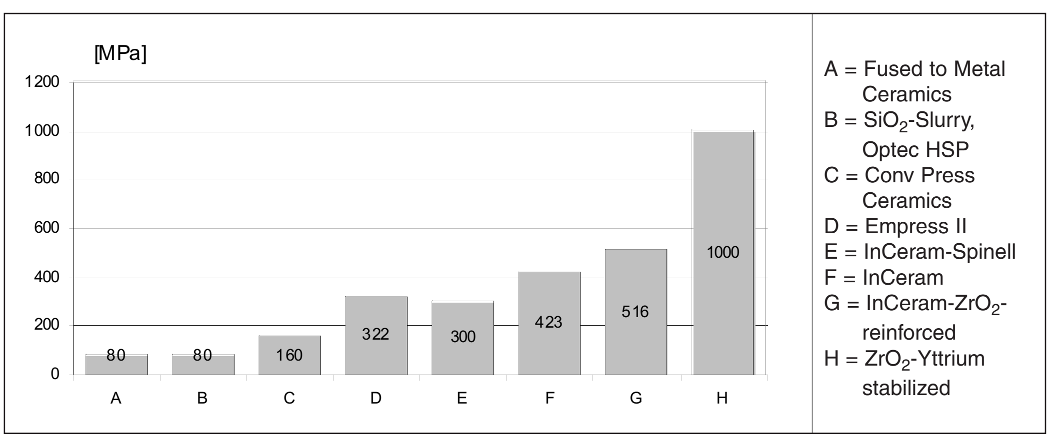


Figure 3. *Strength of different ceramics.*

Table 1. *Several Ceramics and Processing Techniques*

Processing	Type of Ceramic						
	SiO_2	Al_2O_3	Al_2O_3 glass modified	Al_2O_3 glass infiltritated	Al_2O_3 ZrO_2-reinforced	$MgAl_2O_4$ Spinell	ZrO_2 YTZP
Slurry technique	X	-----	-----	X	X	X	-----
Press technique	X	-----	-----	-----	-----	-----	-----
Machined	X	X	X	X	X	-----	X
Casting	X	-----	-----	-----	-----	-----	-----

Ceramic (Dentsply/Ceramco, USA), Carrara Press (Elephant, The Netherlands), Cergo (Degussa-Dental, Germany) and Optec OPC (Jeneric/Pentron Inc, USA). Silicon oxide ceramics are also machined, as is the case with the Cerec-System (Sirona AG, Germany, Cerec-Blocks: Vita, Germany). However, other machining systems such as Celay (Mikrona AG, Switzerland), DCS Precident System (DCS Dental AG, Switzerland) or DigiDent (Girrbach, Germany) can be used. Table 1 also lists casting as a processing technique. Between 1985 and 1995, this technique was extremely popular and successful. It is known under the trademark Dicor (Dentsply International Inc, USA). Dicor was the first acceptable all-ceramic system which provided very good esthetics as well. However, production has been stopped in the last years of the 20th century because the product has been replaced by ceramics providing higher strengths, improved processing and esthetic properties. Today the strongest known dental silicon oxide ceramic is Empress II, with a flexural strength of more than 300 MPa (Ludwig & Kubick, 1999).

Aluminum Oxide Ceramics

These ceramics are processed with the slurry technique or machined by CAD/CAM or other devices, such as copy milling (for example, Celay, Mikrona AG, Switzerland). Aluminum oxide ceramics are available in four different versions:

- Al_2O_3, sintered on a refractory die, then infiltrated with glass (InCeram, Vita, Germany) (Degrange, Sadoun & Heim, 1987).
- Al_2O_3/ZrO_2-reinforced, sintered on a refractory die, then infiltrated with glass (InCeram ZrO_2-reinforced, Vita, Germany).
- $MgAl_2O_4$-Spinell, sintered on a refractory die, then infiltrated with glass (Inceram-Spinell, Vita, Germany).
- Al_2O_3-glass modified (Cicero, Cicero Dental Systems BV, The Netherlands).
- pure Al_2O_3.

InCeram was the first aluminum oxide ceramic used in dentistry (Degrange & others, 1987). Although this material provides very high strength and an acceptable handling, it is very opaque, so its preferred indication is the posterior region. Since the processing technique is considered time-consuming, today, presintered InCeram aluminum oxide blocks that can be easily machined to produce a coping of a crown or bridge are offered, which only need to be glass-infiltrated and veneered. The copy milling machine Celay (Microna AG, Switzerland) and the CAD/CAM-machine Cerec (Sirona, Germany) are devices available for this process. InCeram-Spinell has been developed to provide a high strength ceramic with increased transparency. This material has lower strength but offers better esthetics, and its main indication is the anterior region. However, increasing strength is always a goal as a means of increasing patient safety. As a result of this research, the manufacturer developed zirconium oxide reinforced InCeram. This material is approximately 20% stronger than InCeram. Cicero is a further type of aluminum oxide ceramic modified with a special glass component and machined by a CAD/CAM-device, the Cicero System. However, pure aluminum oxide ceramic provides significantly higher strength than all other modifications that are glass-modified. This ceramic can only be machined with the DCS Precident System (DCS Dental AG, Switzerland) and DigiDent (Girrbach, Germany).

ZrO_2 is currently the strongest white shaded ceramic available and is more precisely known as YTZP-ceramic = Yttrium stabilized Tetragonal Zirconia Polycrystals ceramic. Only this type of ZrO_2-ceramic provides high performance. In the case of stress, the tetragonal crystal phase is transformed into the hexagonal crystal phase, stress is absorbed and no crack formation occurs. This material cannot be processed by simple technologies, as it is possible to install them in dental laboratories but only through rather sophisticated manufacturing processes. Therefore, special CAD/CAM-methods and devices have been developed for dental purposes. With regard to the devices, we must mention that the machining tools must be very strong and abrasion-resistant since ZrO_2-ceramic is an extremely abrasive product. Knowing this, not every grinding tool is appropriate. Currently, there are three rather successful CAD/CAM-processes known. They are DCS Precident System (DCS Dental AG, Switzerland), Procera All Ceram (Nobelpharma AB, Sweden) and DigiDent (Girrbach, Germany).

Hybrid Ceramics

Hybrid ceramics open simplified ways of application. Hahn (1995, 1997) proposed a new ceramic material that is a hybrid between organic and inorganic components. A precursor material consisting of 50% (vol) polyvinylsiloxane, 30% active filler (titanium 1 µm), 15% inert filler (aluminum oxide, 15 µm,) and 5% titaniumboride has been formulated. This mixture can be handled as a composite and cured. The precursors are stable and remain so during the following heat treatment: six hours at 1150°C in N_2 atmosphere followed by a few minutes in O_2 for surface treatment. Since the resulting ceramic is yellow, only copings are produced. They can be veneered with feldspathic ceramic, such as Vitadur.

Processing Techniques

Finally, not every product and processing technique is applicable for every indication. Table 2 provides an overview of product, processing technique and indication. When reading Table 2, the authors gave their best estimate based on the literature available. Table 2 is certainly not the "ultima ratio," especially considering that this area is highly dynamic. It should also be noted that only product examples are given and completeness is not claimed.

Regarding the processing technique, one should note that DCS Precident is the only system which is nearly material independent. It works with every ceramic, resin and metal. DigiDent works with every ceramic and metal.

Further Developments

What does the future hold for ceramics? One needs to first consider what indications call for the use of ceramics. The indication will define the requested material properties. The classical indications for all ceramics are certainly inlays, onlays, veneers, crowns and bridges. Ceramics could also be used for partial dentures with precision attachments (for example, telescopic attachments). Simple partial dentures with clasps are not pertinent to this discussion since these dentures belong to the so-called low-price segment of prosthetic work where ceramic application would be too expensive. However, all of the aforesaid reasonable indications request white materials because of esthetics. Regarding strength, longevity and shade aluminum and zirconium oxide ceramics best fulfill the requirements. There is no question that zirconium oxide ceramic is the ideal choice if strength and fatigue properties are of concern. When optimal esthetics are requested, as is the case for anterior restorations, materials with superior esthetic properties such as silicon oxide (feldspathic) ceramics, are the preferred materials. For this reason, aluminum and zirconium oxide ceramics are veneered with feldspathic ceramics. Material-wise, it is certainly possible to handle all aforesaid indications and fulfill all demands. It is more a question of how very hard and strong zirconium oxide ceramic, which is and will remain the number one ceramic for the next 15 years, can be processed in a dental laboratory. Therefore, future

Table 2. *Product, Processing Technique, Indication*

Product and Processing Technique	Indication						
	Veneer	Inlay	Crown	3-Unit Bridge Anterior	3-Unit Bridge Posterior	> 3-Unit Bridge Anterior	> 3-Unit Bridge Posterior
Optec HSP	X	X	X	-----	-----	-----	-----
Press Ceramics	X	X	X	-----	-----	-----	-----
Empress II	X	X	X	X	-----	-----	-----
InCeram-Spinell	-----	X	X	-----	-----	-----	-----
InCeram	-----	X esthetics?	X	X	-----	X	-----
InCeram-ZrO_2	-----	X esthetics?	X	X	X	X	?
Cicero	X	X	X	-----	-----	-----	?
Cerec	X esthetics?	X	X presintered InCeram	-----	-----	-----	-----
Celay	X esthetics?	X	X presintered InCeram	X presintered InCeram	-----	-----	-----
Procera	-----	-----	X	X	X	-----	-----
DCS Precident	X	X	X	X depends on material	X depends on material	X depends on material	X depends on material
DigiDent	X	X	X	X	X depends on material	X depends on material	X depends on material
pure Al_2O_3	-----	-----	X	X	X	X	?
ZrO_2 XYTZP)	-----	-----	X	X	X	X	X

development in all ceramics will be more a development of processing technique adapted to the possibilities of a dental lab than a material development. Since CAD/CAM processing is developing extremely fast regarding soft- and hardware, a steady stream of improvement can be expected in the future. The cost of the equipment, especially the milling machines, will determine if such equipment will be operated in dental laboratories or if more centralized approaches (for example, Procera) will dominate the market of the future. These authors predict that progress in electronic data transmission will promote the centralized approach. It has the advantage that the construction and milling steps can be achieved under industrial conditions. If such a "reconstruction factory" has a high turnover, the investment can be substantially higher than is usually possible for dental laboratories. If such factories produce only copings that are then veneered by the dental technician, which is probably best for high esthetic requirements, or if the complete restoration is produced by milling, techniques will depend on the market situation dictated by the patients' needs and the financial development (cost per item, insurance policy, and more).

Applying innovative manufacturing technologies used in the industry may also produce completely new ceramic technology. The better the ceramic, the more difficult milling gets. Furthermore, if precision is required, controlling the wear of the milling tools is a problem. One step away from these problems is milling of the precursors to

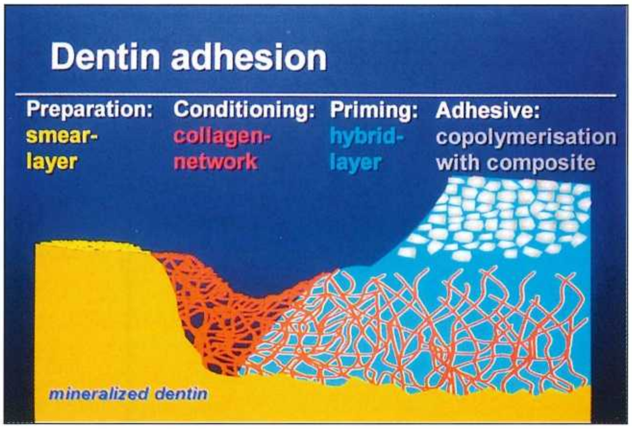


Figure 4. *Principle of bonding to dentin (Blunck, 2000).*

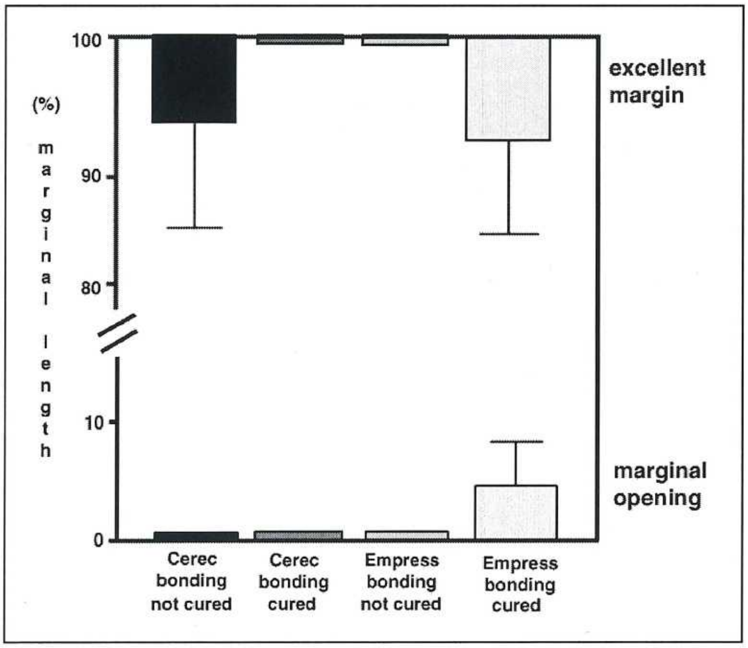


Figure 5. *Margin quality of ceramic inlays bonded to teeth with Etch & Prime.*

Figure 5A). Box plots show the enamel composite interface.

the ceramic (for example, InCeram blocks used with the Celay or the Cerec system), which are glass infiltrated after the milling process. CAD/CAM production of individualized pieces in ceramic is theoretically possible by adapting a technology used in the plastic industry. It is possible to produce thermoplastic items out of a liquid resin with focused lasers which produce locally sufficient heat to cure the resin. By scanning in a 3D mode through the liquid, the sample is produced. Using a ceramic-resin precursor, as used with the hybrid ceramics, it should be possible to produce resin-based restorations that are then converted into ceramics by a heat treatment. If this technology is taken one step further, it is theoretically possible to locally create such high temperatures with focused multiple lasers that ceramic dental restorations could be directly produced.

Adhesive Technique

There are many ways to use ceramics as dental restorations: many applications were only possible because of the adhesive technique that has broadened the indication for ceramic use. Therefore, a brief summary of these techniques is provided:

Almost 50 years ago, Buonocore published an article wherein he showed that it was possible to bond acrylic resins to enamel if the enamel was etched with phosphoric acid and rinsed prior to the application of the resin (Buonocore, 1955). This has paved the way for the first step in adhesive dentistry: the reliable bond to enamel. Bonding to dentin has proven to be more complex and difficult. Reliable materials and techniques were offered to dentists once it was realized that a permanent bond to dentin is also possible if a micro-mechanical bond is achieved (Nakabayashi, Kojima & Masuhara, 1982) (Figure 4). Two important components were changed in the treatment philosophy:

1. dentin must be etched, which does not harm the pulp; and
2. hydrophilic resins, which can penetrate into the etched dentin surface despite their moist condition, must be used (Perdigão & Lopes, 1999).

It is important that such resin-impregnated dentin layers be stabilized by polymerization before a composite resin is placed on top to prevent debonding at the interface due to polymerization shrinkage of the composite. This poses a problem for precise inlays and crowns since pooling of the bonding agent may prevent an exact relocation of the

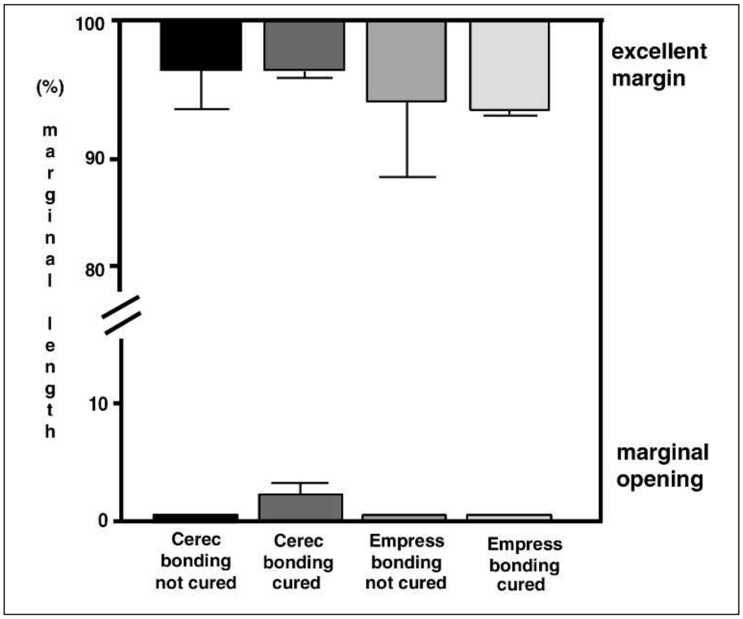


Figure 5B. *Box plots show the dentin composite interface (Clotten & others, 1998).*

inlay into the cavity. There are two ways out of this situation:

1. The dentin is sealed right after the cavity preparation, then the enamel finishing line is cleaned again to make sure that it is resin-free prior to the impression. In the next appointment, the cavity is carefully cleaned with pumice before the inlay is luted with an adhesive technique (Bertschinger & others, 1996).

2. The dentin must be sealed with an adhesive of very low viscosity that does not interfere with the inlay even if it is polymerized prior to insertion of the inlay. Clotten, Blunck & Roulet (1998) have demonstrated that with such a technique it is possible to obtain an excellent margin quality *in vitro* with ceramic inlays (Figure 5a,b).

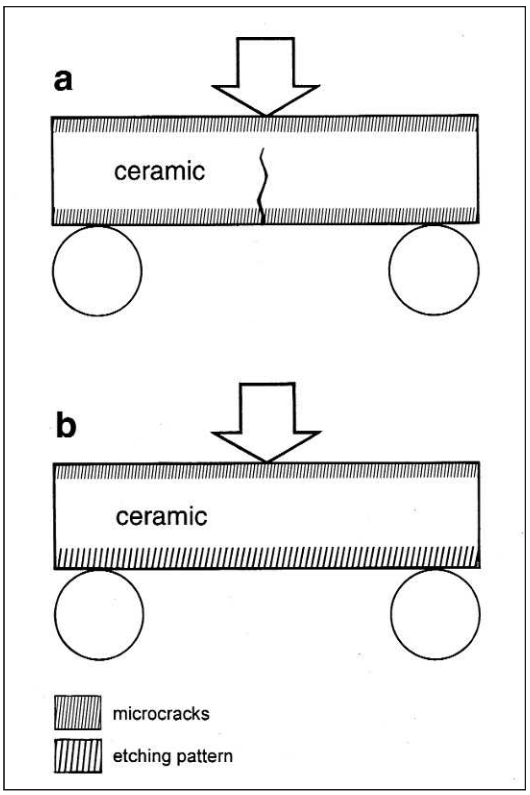


Figure 6. *Crack propagation in a ceramic beam.*

6A. If the beam is under load, the lower side is under tensile stress, where cracks are initiated.

6B. By etching the lower side of the beam the initial cracks are eliminated. Furthermore, the infiltrated composite, which is less brittle, decreases crack initiation.

An inlay or crown is frequently stressed similar to a beam in a three-point bending test. If loaded from the occlusal surface, the inner surface of the ceramic restoration is subjected to tensile stress. Ceramic is a brittle material and always contains micro-cracks at the surface due to finishing procedures. These micro-cracks can propagate under load (exception: YTZP-ceramics), including a moderate load after fatigue of the biomaterial with subsequent catastrophic failure (Figure 6A).

There are two ways out of this problem: (1) improve the mechanical characteristics of the ceramic material, which leads to high strength ceramics (see section 4), or (2) eliminate/prevent the crack propagation at the inner surface of the restorations. This is done with adhesive techniques. Feldspathic glass and lithium silicate ceramics contain a glass phase (Adair, 1984; Adair & Grossman, 1984; Craig, 1989) that can be etched with hydrofluoric acid (Calamia, 1983; Calamia & Simonsen, 1984; Calamia & others, 1985) or similar compounds (Adair & Grossman, 1984), exposing the crystallites contained in the ceramic to create micro-retentions. The etched surface can be wetted and penetrated by resins, which enable a strong micro-mechanical bond to the ceramic. Silanization of the surface increases wetability and bond strength (Pluddemann, 1970; Calamia & others, 1985). Since this surface treat-

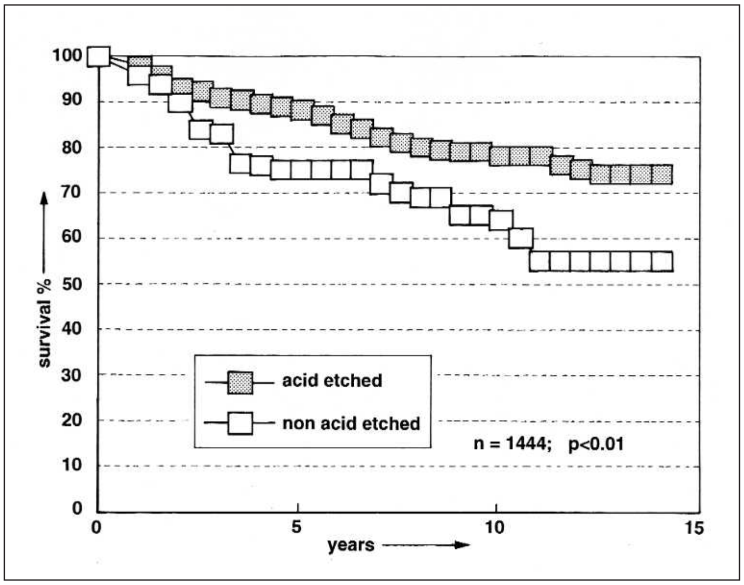


Figure 7. *Longevity of Dicor crowns (Kaplan-Meier statistics). Note that the bonded crowns show a superior longevity (Malament & Socransky, 1999a,b).*

ment is crucial for the clinical behavior, it is highly recommended that dentists perform conditioning of the ceramic's inner surface immediately prior to insertion of the restoration. Only with this approach can one exclude any surface contaminations that would jeopardize the bonding of the ceramic restoration to the tooth.

Ceramic Applications

The question is why are bonded ceramics more resistant to fractures? Theoretically, one can hypothesize that etching diminishes micro-cracks, and by penetrating the surface with a resin based material (composite) that is less brittle than ceramic, more stress at the inner surface is required to induce fractures (Figure 6B).

This hypothesis was supported by several publications based on laboratory data. Fracture strength of ceramic beams is improved if the lower surfaces were carefully polished to a high gloss (Fairhurst & others, 1992), strengthened (for example, by ion addition) (Anusavice, Shen & Lee, 1992; Anusavice & others, 1992) or by adhesively coating with composite resin (Rosenstiel & others, 1993). There has also been clinical evidence for this behavior. Analysis of the survival rate of 1,444 Dicor-complete crowns was performed using Kaplan Meier statistics by Malament & Socransky (1999a), and they reported significantly better results for acid etched and bonded restorations after 14 years (Figure 7).

The adhesive technique is a must as long as brittle, fracture prone ceramics are used because it successfully prevents fractures. However, it is more difficult and demanding for the dentist. Bonding to tooth structure requires efficient moisture control. Furthermore, removing excess luting material is usually difficult and time-consuming. If sufficient retention can be obtained in the classical way (friction) and high-strength ceramics are used, then traditional luting materials (zinc phosphate or glass ionomer cement) may be used. Therefore, it is important for the dentist to select the material and insertion technique prior to manufacturing the restoration. However, high-strength ceramics combined with reliable, efficient bonding techniques will open a new field of restorative techniques in dentistry.

The following briefly describes the different types of restorations and looks at possible future developments.

Veneers

Veneers are thin ceramic laminates that are bonded to the labial face of anterior teeth (Calamia, 1983, 1985, 1989a,b; Peumans & others, 1998). They may restore the strength of natural teeth up to 96% (Magne & Douglas, 1999a,b). Due to the high esthetic requirements, only transparent ceramics are suitable for the fabrication of veneers. Usually they are sintered on investment material dyes or platinum foils. Pressed or cast ceramics are also suitable, especially if the thickness of the veneer is not uniform. Finally, it is also possible to produce ceramic veneers by milling. However, it is more difficult to achieve good aesthetics because ceramic blocks for milling techniques are usually uniform in color. Such veneers must be characterized in a second operation, either with staining porcelains

Figure 8. *Ceramic veneers on teeth 11, 21, 22.*

or by applying intensive composite dyes at the ceramic inner surface during the luting process.

Since veneers usually must fulfill the highest esthetic requirements (Figure 8), transparent ceramics (feldspathic ceramics) are the materials of choice. Furthermore, veneers require the most artistic talent and knowledge and are highly individualistic in color, translucency and shape. We do not see any future alternative in their manufacture other than the use of the dental laboratory and ceramics which are sintered in layers. An analysis of the longevity data (Table 3) reveals that actual systems are reliable, provided the application technique is meticulously done.

Inlays

Ceramic inlays have a long tradition. Due to their esthetic appearance, they were first used at the beginning of the 19th Century (Qualtrough, Wilson & Smith, 1990). However, they have disappeared due to a high failure rate because of bulk fractures. The cementation technique was the reason for this. They were cemented with zinc phosphate cement and only after the introduction of adhesive techniques was it possible to successfully incorporate ceramic inlays (Roulet & Herder, 1991; Roulet, 1997a,b). They show an excellent margin morphology *in vitro* and *in vivo* (Geppert & Roulet, 1986; Herder, 1988), which can be obtained by many dentists (Hordt, 1990). Wear of the luting composite (Figure 9) is partially explained by (1) an oxygen inhibition layer (because composite was cured after removal of excesses and, therefore, under air) that can be minimized by applying a glycerin gel prior to polymerization (Bergmann, Noack & Roulet, 1991) (Figure 10) and (2) partially by the composition of the composite. Margin quality can be improved by using an ultrasonic insertion technique with highly-filled composite (Noack, Roulet & Bergmann, 1991, Roulet & others, 1991; Eidenbenz & others, 1993; Noack, Locke & Roulet, 1993). With ceramic inlays, it is possible to restore teeth in a natural way.

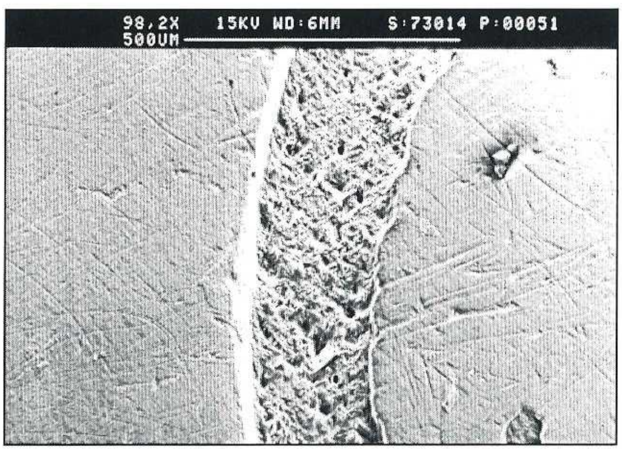


Figure 9. *Wear of luting composite.*

The stronger the better is not true for the inlay restoration. Silicon oxide ceramics have an excellent longevity record (Table 4) if bonded properly. Therefore, there is no need for further improvement. The future will show that onlays and partial ceramic crowns will behave even better than full ceramic crowns because the margins are situated in a far less critical area than crown margins and therefore bonding is less prone to errors. With this in mind, dentists will become much more flexible in the restoration of single teeth.

Ceramic Crowns

All ceramic crowns have a long tradition. As early as 1903, Land (quoted in O'Brien, 1989) developed the platinum foil technique to fire feldspathic ceramic crowns. These crowns were highly esthetic in appearance but prone to fractures due to their brittleness.

Table 3. *Longevity of Porcelain Laminate Veneers*

Authors	Material System	Method	Time (years)	Number of Restorations	Result
Calamia, 1989a	Porcelain not specified	USPHS	5	43 unprepared 72 chamfer	clinically satisfactory
Christensen, 1991	Cerinate	USPHS	3	165	excellent service overall
Karlsson, 1993	Dicor (38) Hi-ceram (81)	CDA+ Bleeding index	1.5	119	no restorations failed in service
Dunne, 1993	Porcelain not specified	clinical	5	315	83% problem free 11% failures
Nordbø, 1994	Ceramco		3	135 unprepared incisal	7 PLV chipped incisally
Pippin, 1995	Feldspathic Porcelain	Ryge modified	5	60	all PLV clinically acceptable
Walls, 1995	Porcelain not specified	clinical	5	46	2 (4.3%) complete failures 4(8.6%) partial failures
Shaini, 1997	Porcelain	Kaplan-Meier	6.5	372 (90% unprepared)	Failure in PLV bonded over restorations
Fradeani, 1998	Empress	USPHS modified	6	83	98.8% success (1 failure)
Friedman, 1998	Porcelain		15	3.500	7% failure: 1/3 leakage, 1/3 debonding, 1/3 fracture
Kihn, 1998	Ceramco Colorlogic	Ryge criteria modified	4	53	clinically acceptable
Meijering, 1998	Flexo Ceram	Kaplan-Meier	2.5	180	94% survival
Peumans, 1998	Feldspathic Porcelain		5	87	93% satisfactory 7% clinically unacceptable

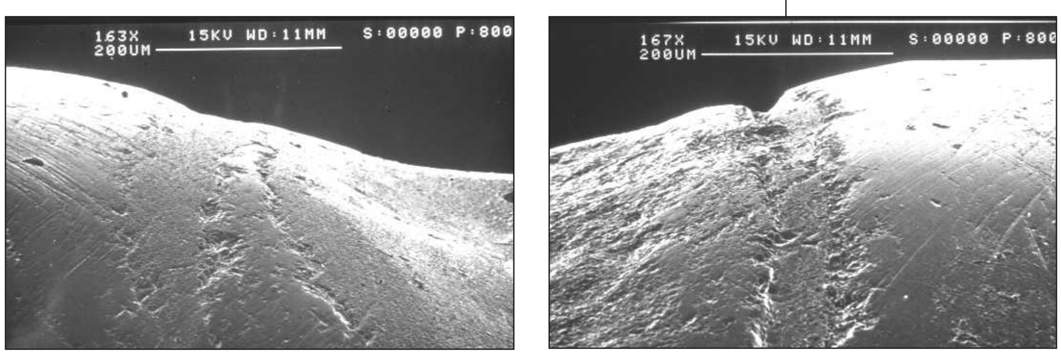


Figure 10. *Inlays luted with composite. Right after curing, the margins were brushed with a toothbrush and acetone, to remove uncured composite.*

10A (left) Composite was covered with glycerin gel before curing: The material is cured up to the surface.

10B (right) Composite cured under air: Note the substantial wear. (Bergmann, Noack & Roulet, 1991).

Therefore, they were only used in the anterior segment. The early ceramic materials were too weak and brittle to withstand occlusal and masticatory forces. McLean (McLean & Hughes 1965; McLean, 1983) performed the first successful attempt to produce high strength all ceramic crowns and introduced alumina-reinforced all ceramic crowns. These crowns consisted of an Al_2O_3 core that was veneered with feldspathic ceramic. They were successfully used in the anterior segment, where high esthetic requirements are present. Since porcelain fused-to-metal became a reliable and aesthet-

Table 4. *Longevity of Ceramic Inlays/Onlays (only studies with observation time >5 years)*

Year of Publication	Authors (First)	Duration of Observation (Years)	Class	Material	Number of Restorations	Survival Rate (%)	Annual Failure Rate (%)	Remarks
1992	Mörmann	5	II	Cerec	8	100	0	2 inlays fractured
1994	Walther	5	I and II	Cerec	1011	95	1	
1995	Otto	5	II	Cerec	100	98	0.4	
1996	Kanzler	6,5	II	Ceramco	280	85	2,3	
1997b	Roulet	6	I and II	Dicor	123	76	4	
1998	Felden	7	inl/onl	Dicor, Empress, Cerec, Ducera	287	94.2	0.8	
1998	Hayashi	6	I and II	G-Cera Cosmo-tech II	49	92	1.3	
1998a	Lehner	6	inl/onl	Empress	138/17	94.9	0.9	
1998	Reiss	7.5	I and II	Cerec	1011	91.6	1.1	
1998	Sjögren	5	II	Cerec	66	89	2.2	
1998	van Dijken	6	II	Mirage (resin cement)	58	88	2	
1998	van Dijken	6	II	Mirage (GIC)	57	74	4.3	
1999	Fuzzi	11	I and II	Microbond Nat Cer, Fortune	176	95	0.5	
1999b	Malament	11.3	inl/onl	Dicor	114	92	0.7	
2000	Reiss	10 12	I II	Cerec	1010	90 84.9	1.3 1.3	

ically acceptable restorative tool (Martignoni & Schönenberger, 1990), it took many years before new all-ceramic systems became available. It started in the 1980s with two completely different approaches: one created cores (Cerestore) which were definitely stronger than alumina cores. These cores had the advantage that the "green" ceramic produced with injection molding did not shrink upon firing. The raw ceramic contained aluminum oxide and magnesium oxide that, on firing, reacted to form magnesium aluminate spinell ($MgAl_2O_4$), which occupies a greater volume than the combination of magnesium oxide and aluminum oxide (Starling, Stephan & Stroud, 1981). These cores were veneered with modified conventional feldspathic ceramics. With this system, an exceptional margin quality was accomplished (Schaerer, Sato & Wohlwend, 1988). Unfortunately, over time, these ceramic restorations were also prone to fractures, probably due to fatigue (Linkowsky, 1988). The other approach was to use a castable glass ceramic that was produced using the lost-wax technique. In a first step, a selectively doed glass was cast. In a second step, the glass was cerammed with the intention of having tetra mica silica crystals grown within the glass phase, thus converting the glass into a ceramic (Adair, 1984; Adair & Grossman, 1984; Grossman, 1985, 1987). The final esthetic was performed by using staining porcelains on the surface of the quite transparent restorations.

A completely different approach is done with the Inceram ceramic (Degrange & others, 1987). High-strength cores may be produced by first producing a slightly porous coping with a slicker of pure Al_2O_3 with a particle size of 3-4 µm on a special dye. After the sintering process in a second step, the copings are infiltrated with a lanthanum glass, resulting in a very dense high-strength core. Finally, these cores are veneered with feldspathic ceramics (Vitadur).

Table 5. *Longevity of All Ceramic Crowns*

Year of Publication	Authors (First)	Duration of Observation	Type	Material	Number of Restorations	Survival Rate %	Annual Failure Rate (%)	Remarks
1965	McLean	7	Platinum bonded jacket		679	molar: 84.8 premolar 93.6 incisor: 97.9	molar: 2.2 premolar 0.9 incisor 0.3	non-adhesive glass ionomer
1985	Leempoel	11	jacket			75	2.3	non-adhesive
1994	Hankinson	5	feld-spathic	Optec HSP	158	91	1.8	adhesive
1995	Erpenstein	6	cast	Dicor	169	incisors: 80 molars: 72	molars: 3.3 molars: 4.6	
1996	Odén	5	milled	Procera	100	94.8	1	
1998b	Lehner	7	pressed	Empress	138	85.5	2.1	adhesive
1998	Studer	5	pressed	Empress	142	89.2	1.8	bonded
1999	Malament	14	cast	Dicor	1444	cemented: 50 bonded 76	cemented 3.6 bonded 1.7	
1999a	Sjögren	5	pressed	Empress	110	85	2.3	
1999b	Sjögren	6	cast	Dicor	96	86 molars: 70	2.3 molars: 5	

A modification of the Inceram technique to produce inlays (Sadoun, 1996) was proposed. With the so-called composite process, the inlays were made as direct inlays in the oral cavity with a special composite composed of vinylesters and $MgAl_2O_4$. These light cured preinlays are then removed from the cavities and post-cured. They are then subjected to two heat processes. In a first step between 250°C and 400°C, the organic components are destroyed and in a second step at a temperature of 1160°C, the spinell is sintered. Then the ceramic is infiltrated with glass as is done for the InCeram technique.

Pure aluminum oxide is also used to produce high-strength cores with CAD/CAM techniques (Procera). With this high-tech approach, the master dye is scanned in the dental laboratory and the data transmitted to a central manufacturing site. There, the dye is replicated in metal, but in a defined larger size to compensate for the shrinkage upon firing of the ceramic. Then a pure Al_2O_3 coping is pressed with high pressure on top of the metal dye and subsequently fired (Andersson & Odén, 1993). With this technique, a high precision is also obtained. As with the other systems, these high-strength cores are veneered with feldspathic porcelain.

If one looks at future developments for ceramic crowns, different situations must be considered. In the anterior segment, esthetics are usually of prime concern (if low-cost solutions are excluded). Therefore, full ceramic crowns will have a great future. Simple systems will be the winners. However, the manual and artistic skills of dental technicians will also highly determine future success. For posterior applications, besides (moderate) aesthetics, strength is most important. Simplified CAD/CAM techniques may be the winner. If systems such as the CEREC can be developed so that their use is so easy that after preparation and data acquisition the quick construction and manufacture can be delegated to dental auxiliaries, there is a good chance for universal use of such systems. "Semi-individualized" ceramic blocks with a layered ceramic (dentin core, enamel in the periphery) may improve aesthetics and allow chairside manufacture of the whole restoration in the dental office.

Table 5 reports the longevity of full ceramic crowns. One can see that most SiO_2-based ceramics serve quite well, with annual failure rates of approximately 2%, especially if they are bonded. The only long-term study with a Al_2O_3 Ceramic (Procera) had excellent results with an annual failure rate of 1% (Odén & others, 1996).

Ceramic Bridges

Currently, there are five types of ceramics suitable to manufacture bridges. They are:

- Empress II (Leistner, 1998; Sorensen & others, 1999; Pospiech & others, 1999; Riedel, 1999);
- InCeram (Kappert, 1996; Geis-Gerstorfer & Fäßler, 1999);
- InCeram zirconium oxide reinforced (Tinschert & others, 1999);
- Procera (zirconium oxide glass modified) (Luthardt & others, 1998; Braun, 1999;) and
- Pure zirconium oxide (Yttrium stabilized) (Geis-Gerstorfer & Fäßler, 1999).

However, not every one of the aforesaid ceramics is recommended for all types of bridgework (see Table 2). Empress II and Procera are only used for three-unit anterior bridges. InCeram and InCeram, zirconium oxide reinforced can be used for more than three-unit anterior bridges. InCeram, zirconium oxide reinforced might perhaps be used for smaller three-unit posterior bridges. Based on its mechanical and physical properties, one can conclude that the only ceramic which is highly likely to be suitable for posterior bridges is yttrium stabilized zirconium oxide ceramic.

However, clinicians must realize that these ceramics are so new in dentistry that there is no evidence base for their recommendation. The only data available are based on *in vitro* investigations (Rinke, Hülse & Chafizadeh, 1995; Ludwig & Kubick, 1999). Therefore, these recommendations must remain speculative until data based on controlled clinical studies are available. Of course, the clinical performance of all ceramic bridges especially in the posterior region is still a matter for discussion and needs to be investigated.

A Vision for Future Dental Ceramics

The ultimate restorative procedure would be the onsite production of a ceramic-like enamel substitute firmly bonded to the remaining tooth structure. In 1986, a hypothetical caries therapy was presented which involved the removal of the decayed tissue by rinsing with a caries-dissolving solution and filling the defect with an enamel precursor substance that could then be mineralized *in situ* following the mechanisms of enamel production by nature. If such a material could be hardened initially, it would even be possible to intraorally produce direct crowns that are later converted into a ceramic-like material. Taking this even further, imagine that molecular-biological techniques and gene technology can be used. Then it is conceivable that the genetic information to control the micro-organisms metabolism could be changed. By using viruses as a vehicle, one could, by a simple injection into a carious lesion, create micro-organisms that produce enamel instead of acids that destroy it (Roulet, 1988).

Conclusions

Ceramics have a great past in dentistry. Their biocompatibility and excellent esthetics have positioned them in the high-end segment of restorative dentistry. The future of ceramics is even greater since they offer great potential for improvement, especially in manufacturing technology. However, when esthetics are of prime concern, one will never be able to rely completely on machines for the production of restorations. In all these situations, the cooperation between the excellent dentist and the highly-skilled dental technician is unavoidable.

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Biocompatibility of Restorative Materials

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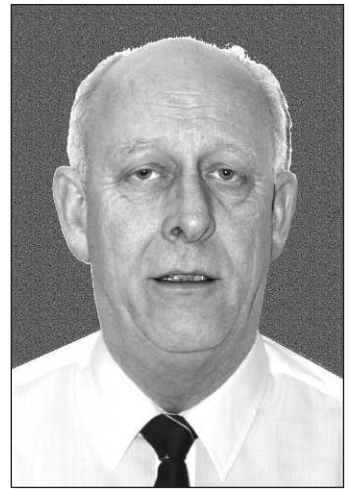


Arne Hensten-Pettersen

Biocompatibility Issues

Biocompatibility issues are a major concern in the selection of future restorative materials.

Risk analyses concerning possible adverse biological reactions of new materials start with literature surveys of biological reactions to materials of similar composition. Lack of relevant data may necessitate additional biocompatibility testing, which is often performed according to the methods referred to in ISO 7405 (1997) *Dentistry—Preclinical evaluation of biocompatibility of medical devices used in dentistry—Test methods for dental materials*. However, traditional, established preclinical tests are mainly suitable for evaluating local irritant effects to the tissues of the skin, oral mucosa and dental pulp tissues, and immune-mediated, delayed-type hypersensitivity reactions. Other clinical reactions, as reviewed below, may not be predictable by animal test methods. One reason is that the statistical power of predictive animal tests is not sufficient to cover events where the incidence is assumed to be low.

Risk management of residual risks not taken into account in the design of the materials is usually covered by detailed instructions for the intended use and handling. Precautionary statements about contraindications in patients and safe-handling procedures have become more common, as experience has shown that most materials may have some risks associated with their use. The Norwegian and Swedish Adverse Reaction Units for Dental Biomaterials have post-market surveillance systems for collating information about adverse reactions in patients and in the dental health team (Gjerdet & Askevold, 1998).

Adverse clinical reactions caused by new chemicals and the types of reaction elicited are usually first identified where the exposure is the highest, that is, in an occupational setting. The causes of occupation-related and patient reactions in dentistry are related to the dental materials and clinical applications used at any given time, and in the specific usage of the various specialties (Hensten-Pettersen & Jacobsen, 1990; 1991; Kallus & Mjör, 1991; Kanerva, Estlander & Jolanki, 1995, Kanerva & others, 2000; Moore, Burke & Felix, 2000; Wallenhammar & others, 2000).

Clinical Reaction Mechanisms

Reactions can be elicited by high local concentrations of irritant substances, or by small amounts capable of activating biological amplifying systems, such as the immune system.

The most commonly encountered problems are local inflammatory reactions due to toxic, irritant or allergenic components of dental materials. Unfortunately, many of the reports linking adverse clinical reactions to specific dental materials are inadequately documented.

The terminology of inflammatory reactions in the oral cavity may be descriptive, with terms such as "desquamative gingivitis; ulcerative gingivostomatitis" or constructed by indicating the suspected cause of the conditions, such as "denture stomatitis; stomatitis medicamentosa." The etiology may be suggested by the clinical appearance, but conclusive identification depends on data obtained through history-taking, as well as ruling out the possibility of diseases of similar appearance.

Dermatological literature often uses a terminology, albeit not always consistent, that indicates the *mechanisms* involved in the dermal reactions (Andersen & others, 1987). A modification is presented in the following parts.

Irritant Contact Dermatitis/Mucositis

Histopathological changes as well as the clinical appearance of the various types of dermatitis or mucositis are not type-specific and vary with the stage of the inflammatory response, that is, acute, subacute or chronic.

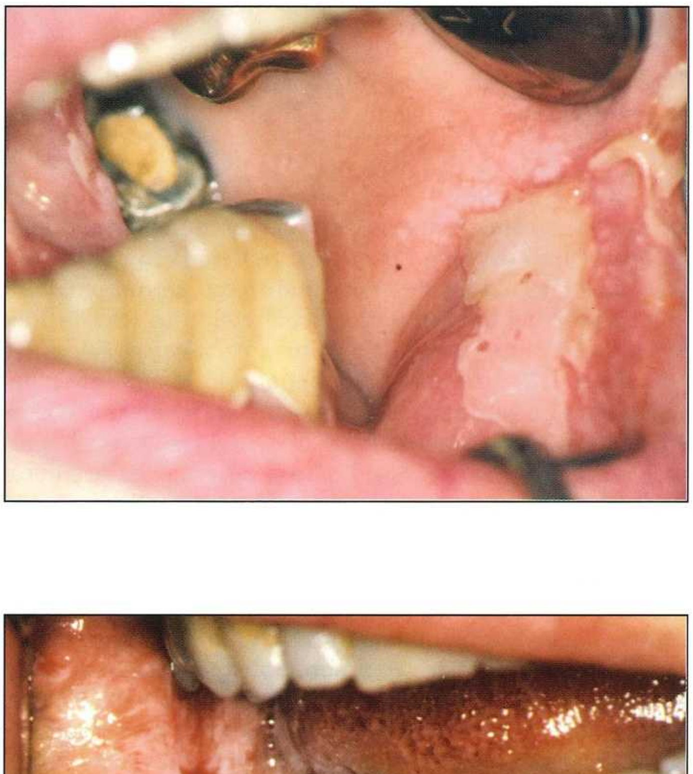


Figure 1. *Cumulative insult mucositis? Mucosal changes are still evident five days after student treatment at the Department of Prosthodontics in a dental school. The natural barrier function of the mucosa had deteriorated due to trauma related to (several) attempts at getting perfect impressions and (several) tryouts with* in situ *auto-polymerizing temporary crown and bridge materials. The use of local anesthetics with vasoconstrictors during the treatment may, in addition, have reduced the blood flow in the region, which in its turn, reduces the submucosal clearance of otherwise non-irritating substances from the area.*

Figure 2. *Oral contact lichenoid reaction of the buccal mucosa. A clear topographical relationship between the amalgam restorations and mucosal lesions may be indicative of a causal relationship.* Photo courtesy of Dr PO Lind, Oslo.

Acute toxic reaction is the dermal or mucosal inflammatory reaction to primary irritants. A primary irritant is capable of causing damage in everyone, if it is present in sufficient concentration for a sufficient time. It is a result of physical or chemical action due, for instance, to trauma, ionizing radiation, heat, bases, acids or other reactive chemicals. Depending on the concentration and exposure time, the reaction can vary from erythema to necrosis. The substances exert a direct cytotoxic effect on the cells in the superficial skin or mucosa, most often corresponding exactly with the site of application. In the oral cavity, the boundaries of the inflamed area may be more diffuse. This type of reaction is seen when phosphoric acid enamel etchants or bonding agents are inadvertently spilled onto the mucosa or skin and remain there for some time (Jacobsen, Åasenden & Hensten- Pettersen, 1991).

Cumulative insult dermatitis/mucositis develops by

Figure 3. *The lesion healed after exchange of the amalgam fillings with porcelain-fused-to-metal crowns. Some lesions may be related to contact allergy to constituents of the dental materials.* Photo courtesy of Dr PO Lind, Oslo.

repeated contact with low doses of primary irritants over extended time periods. The changes in skin or mucosa are localized to the contact area with the offending agent; they do not spread to other sites. It is caused by a gradual deterioration of the natural barriers. One special form of this may be seen in a dental school setting where the combination of several factors may cause a rapid deterioration (Figure 1). The diagnosis of cumulative insult dermatitis/mucositis is made by exclusion of other possibilities, based on the case history, clinical appearance of the lesion and negative patch tests. Examples of this type reaction are "denture stomatitis" and lichenoid reactions of the oral mucosa, with a clear positive topographical relationship between the mucosal changes and the dental materials in patients who have negative patch tests to the relevant constituents of the dental materials (Figures 2, 3).

Neurotoxic effects of chemicals may be associated with symptoms such as paresthesia. Dental technicians and orthopedic surgeons may have dermatitis associated with the use of methylmethacrylate monomer, often in the form of marked dryness and fissuring of the skin. A unique feature of irritant contact dermatitis caused by methylmethacrylate monomer is a paresthesia of the fingertips in the form of a burning sensation, tingling and slight numbness. This type of paresthesia has been observed in two orthodontists who became sensitized to the monomer in orthodontic bonding materials (Fisher, 1982). This might be due to a direct neurotoxic effect of the monomer (Seppäläinen & Rajaniemi, 1984).

Allergic Contact Dermatitis/Mucositis

Although allergic reactions are basically different from toxic reactions, their clinical manifestations can be similar or identical.

Most components of dental materials are of low molecular weight. By acting as haptens and combining with body proteins, they may form complete antigens capable of inducing sensitization of immune-competent cells. The risk of sensitization varies depending on the type and concentration of a substance and the type and condition of the contacting tissues. The basic mechanisms underlying induction, expression and regulation of allergic contact dermatitis are well-documented (Andersen & others, 1987). The actual contact site with the allergen will usually be the first place where clinical symptoms develop. However, sensitized individuals may develop a number of symptoms when exposed to the allergen systemically by ingestion, inhalation, infusion or transcutaneous or transmucosal absorption. The problems related to systemic allergic reactions are complex, as discussed in a recent report (McGivern & others, 2000).

Allergic reactions to just about any component of dental materials may occur in patients (Figures 4, 5) and in the dental professionals who handle the materials (Figure 6) (Hensten-Pettersen, 1986, 1989, 1992, 1998; Stenman & Bergman 1989; Dahl, Hensten-Pettersen & Lyberg, 1990; Kanerva & others, 1995, 2000; Bratel, Hakeberg & Jontell, 1996; Vamnes & others, 2000; Tsuruta & others, 2001).

Photo Induced Reactions

Phototoxicity is a dose-related response of all individuals to adequate simultaneous exposure to a chemical and radiation of the appropriate wavelength. It may be defined

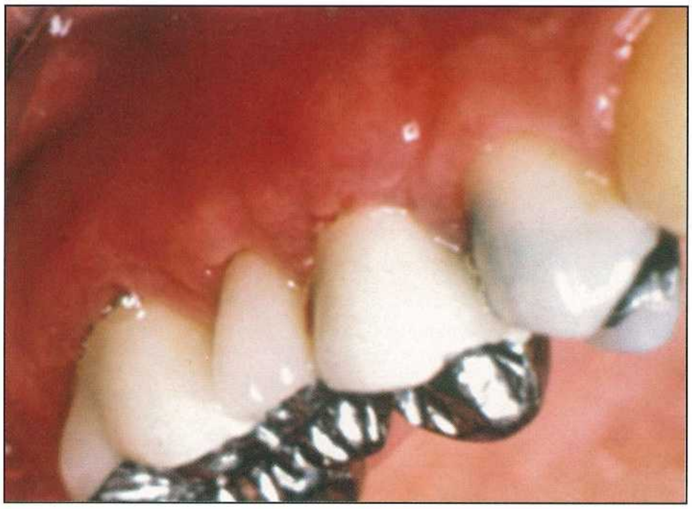


Figure 4. *Inflammatory changes of the mucosa in a 35 year-old female with nickel allergy in the vicinity of a cast restoration. The three-unit bridge was made of a base metal alloy containing 80% nickel. The bridge was exchanged with one based on a conventional gold alloy and the inflammation subsided within a short time. Photo courtesy of Dr J Swanson, Sacramento.*

as an increased reactivity of the skin to ultraviolet and/or visible radiation produced by a chemical agent on a non-immunological basis. Clinically, there are two main patterns of response: an immediate burning sensation, erythema and urticaria and a delayed reaction resembling sunburn which appears within hours or up to two days after exposure. Substances of dental interest which may have phototoxic properties are sulphonamides (present in some cavity liners), phenothiazines, griseofulvine and some tetracyclines.

Figure 5. *Inflammatory changes of the mucosa of the hard and soft palate in a 60 year-old female with chromium and cobalt allergy. The partial prosthesis was made of a cobalt-chromium alloy with a methylmethacrylate part. The inflammatory reactions cleared when the patient stopped using it.*

The patient also had positive patch test reactions to methylmethacrylate monomer and several other substances of dental relevance (nickel, mercury, formaldehyde and colophony). This limited the treatment options. A new, complete upper denture was made with a polycarbonate basis and porcelain teeth, which did not cause any inflammatory exacerbation.

Photoallergy is a reaction to a chemical and radiation in which an immune mechanism can be demonstrated. Minute quantities of chemical or radiation may be adequate to elicit a response. Photoallergic reactions may have an eczematous or polymorphic appearance and occur at lower concentrations of the agent than what is necessary for a phototoxic reaction. Examples of photoallergic compounds are eugenol, chlorhexidine, derivatives of para-amino benzoic acid, eosin (colorant in some lipsticks), sulphonamides and phenothiazines.

Phototoxic or photoallergic reactions have not been documented in the context of oral medicine but should be considered because of the extensive use of powerful light units in the curing of dental resin-based materials. The possibilities of photo-related reactions should also be taken into account when evaluating dermatoses in dental personnel. A generalized, intensely erythematous eruption of the face and submental area in a dental hygienist was attributed to a combination of long-term trimethoprim medication and exposure to stray light from a laboratory photocuring unit (Hudson, 1987).

Contact Urticaria

Many reports on adverse reactions to dental materials describe patients and personnel with urticarial reactions. Contact urticaria is a weal and flare response elicited by the application of various compounds to intact skin.

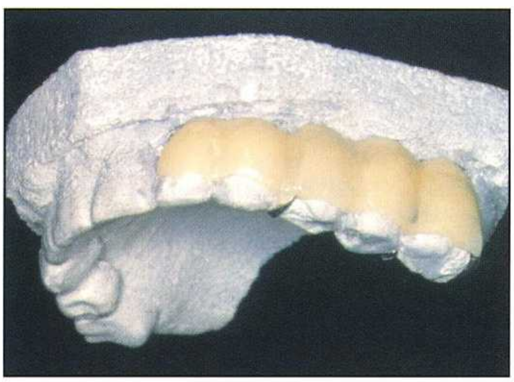
Immunologic contact urticaria is an IgE-mediated reaction resulting from mast cells releasing histamine. It may be localized or widespread and is sometimes associated with features of anaphylaxis. Such reactions have been observed after contact with surgical latex gloves, where both the powder and the latex may contain substances capable of eliciting urticarial reactions (Carrillo, & others, 1986; Wrangsjö, Wahlberg & Axelsson, 1988). Persistent generalized urticaria has been attributed to a resin-based orthodontic bonding agent (Tinkelman & Tinkelman, 1979) and a fissure sealant (Hallström, 1993).

Figure 6. *Occupational contact dermatitis in a female dental assistant. Note the shiny appearance of the fingertips due to a painful inflammation of the finger pulp. The sores became easily infected. She had positive patch test reactions to six different methacrylate monomers of dental relevance, especially constituents of bonding agents. The dermatitis healed during sick leave but returned after a few days at work. The extensive use of resin-based materials in the dental practice made it impossible for her to continue in the same job and she received a disability pension.*

Non-immunologic contact urticaria (NICU) is clinically indistinguishable from the other variety and occurs without previous sensitization in most exposed persons. The reaction remains localized and does not spread to become generalized urticaria, nor does it cause systemic symptoms. Its pathogenetic mechanisms are not clearly understood. NICU may be elicited by a number of compounds, notably benzoic acid—natural to many fruits—and added as a preservative (E 210) in salad dressings and other processed foods (Clemmensen & Hjorth, 1982); it also occurs as a degradation product of benzoylperoxide used in composites and denture base resins (Koda & others, 1990).

Requirements for Clinical Documentation

Assessment of possible adverse reactions to specific substances should be fully investigated. Detailed information about the composition of the various materials that patients and personnel are exposed to is a prerequisite for systematic evaluation of adverse events. It is essential to note details in patients' records regarding the materials employed. Elemental analysis is fairly easy to do with alloys by removing a small part of the restoration, but the analytical techniques for resin-based materials do not yet allow this.



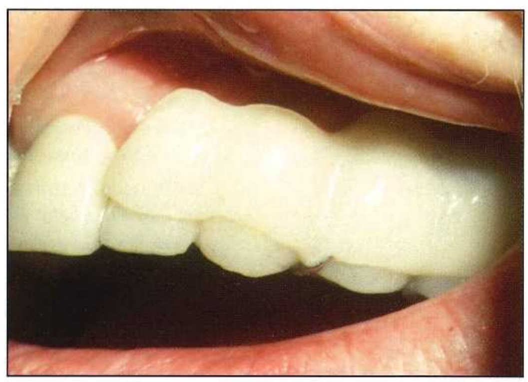


Figure 7 (left), Figure 8 (right). *Provocation testing. The 60 year-old female complained of intraoral reactions, primarily swelling of the tongue, after receiving a five-unit bridge with resin-based veneers. Patch testing showed a positive reaction to the catalyst of the veneer material. The bridge was replaced with a porcelain fused-to-metal one and the reactions subsided. The patient consented to a provocation test and a removable resin-based veneer was fabricated from the same material. The tongue swelling reappeared during the first night after placing the test piece on the new bridge. The provocation test was repeated twice, with the same result.*

The individual reaction mechanisms may vary greatly. Intraoral lesions may be topographically related to the restorations in question. Extraoral lesions are more difficult to associate with intraoral exposure, mostly due to a low level of suspicion on the part of the dentist, dermatologist and patient. In many instances, careful questioning may reveal a time-episode relationship between dental treatment procedures and ensuing extraoral reactions. However, this is only an indication. It does not necessarily imply any cause-effect relationship.

Good documentation requires an extensive investigation that includes:

1. establishing that the patient's history, sign and symptoms are consistent with the clinical reactions;
2. identifying the eliciting substance(s);

3. establishing the patient's ability to react;
4. demonstrating that the patient is symptom-free on removal of causative substance(s); and
5. eliciting a reaction by re-exposure (Figures 7, 8).

Preferably points 4 and 5 should be repeated. No published case reports satisfy these requirements. Several of the requirements may also come in conflict with practical and ethical considerations and may not be in the patient's interest.

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©Operative Dentistry Supplement 6, 2001, 237-241

Summary

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Carious Lesions: Management Alternatives

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The Conference was hosted by the Medical University of South Carolina's College of Dental Medicine, with Dr W Dan Sneed serving as Chairman. Eminent, internationally recognized speakers had been invited to lecture during the five half-day sessions of the conference. All sessions were followed by panel discussions facilitated by opinion leaders. The themes included two half-day sessions on non-restorative approaches and one half-day session on metallic restorative materials and historical standards, conservative dentistry through adhesion and non-metallic materials and systems, and future materials and biocompatibility.

Non-Restorative Approaches

The speakers emphasized the positive effects of various forms of fluoride treatment and the benefits achieved by different preventive programs. It is necessary to promote such programs to achieve optimal clinical outcomes. If this promotion is lacking or fails, a reduction in the disease level will not occur (Figure 1). Public health authorities, the insurance industry and individual clinicians all have responsibilities in this regard.

Despite the marked reduction in caries incidence in many industrialized countries, there is still a percentage of these populations (10-25%) that continue to suffer from high levels of dental disease and consume 70-80% of the dental treatment provided in public dental health programs. These groups must be identified and additional preventive programs considered, including antibacterial treatment specially directed towards streptococcus mutans and lactobacilli. Even with the benefits of fluoride prevention, there are those who may profit from short-term antibacterial treatment, such as 0.12 percent chlorhexidine rinses after tooth brushing in the evening for up to two weeks. Such treatment should be based on and monitored by risk assessment and bacteriological tests, as appropriate. Problems with approaches such as this include a lack of remuneration guidelines for

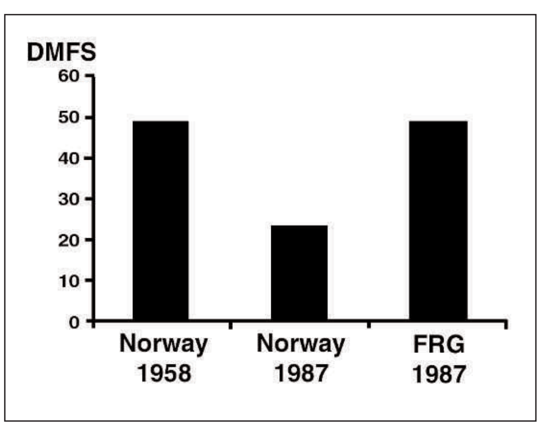

Figure 1. DMFS values for young adults in Norway 1958 and 1987 and in the Federal Republic of Germany (FRG) 1987. The decline in DMFS in Norway from 1958 to 1987 is considered an effect of a public campaign favoring the use of fluorides in different forms. Such a campaign had not been initiated in the FRG (but it has since been introduced in Germany).

monitoring lesions and the indifferent attitude among clinicians towards non-interventive approaches to the management of caries.

Alternative preventive techniques, less dependent on patient co-operation, other than those based on oral hygiene regimens, were outlined. Bacterial replacement therapy has the goal of replacing cariogenic microorganisms by genetically altered variants. These altered bacteria shall maintain all their characteristic properties except the cariogenic potentials, such as acid production under appropriate conditions. Clinical testing of genetically altered streptococcus mutans may start within the year. Research on vaccines against caries has been ongoing for several decades and continues to be active. Since dental caries is not a fatal disease, safety requirements make it difficult to justify clinical testing. No vaccine is on the horizon that may be put into practical use.

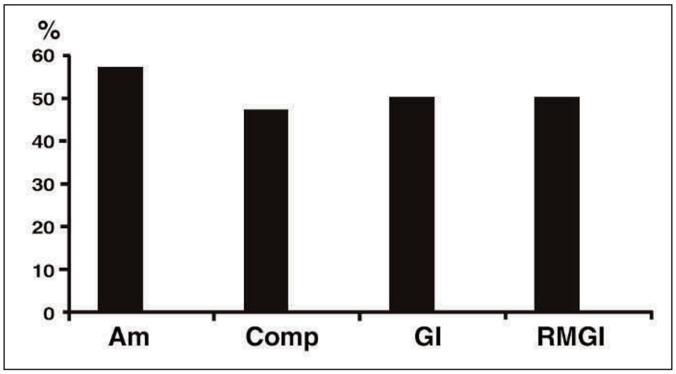

Figure 2. The percentage of the clinical diagnosis of secondary (recurrent) caries as the reason for replacement of amalgam (Am), composite (Comp), glass ionomer (Gi) and resin-modified glass ionomer (RMGi) restorations in general dental practice.

Secondary (recurrent) caries is the main reason for the replacement of all directly placed restorations in general dental practice (Figure 2). Given the diagnostic problems associated with this diagnosis and the short longevity of the restorations (3-15 years at replacement in general practice depending on the type of material and restoration), alternative techniques are being sought. For example, research in biometrics and tissue engineering based on the application of growth factors in a scaffold within the cavity of a tooth, is one approach that may lead to the development of tissue replacement therapies. Until such techniques have been developed, outcome research on repair and refurbishing of defective restorations must be considered. These techniques are likely to be cost-effective and will save tooth structure.

In the assessment of current dental education, there are many responsible partners in "dental education," including academia and its administration, licensing boards, reimbursement systems, organized dentistry, lay media and government. Neither faculty qualification requirements nor responsibilities for continuing education and updating of the faculty were touched upon. This updating could be achieved by international recognition of requirements for clinical faculty to do research. With reference to the Institute of Medicine Report on Dental Education (IOM Report), a strong call for simple studies was presented, that is, studies of immediate clinical relevance. Presently, there is a gap in research priorities. It is unlikely that many of the sophisticated, scientifically sound basic studies presently being supported will have any clinical application in the foreseeable future. Obviously, they must continue to generate new knowledge to improve dentistry in the future, but this effort should not leave today's everyday problems in dental practice by the wayside. Solving immediate problems in dental practice will improve contemporary care provided to the public at-large with the possibility of substantial revenue savings.

Dental care is widely available in industrialized countries, but on a world-wide basis, only a small proportion (about 25%) of the population can access regular dental treatment. This situation is a challenge to health care providers and the dental profession. It is also important to realize that underserved populations exist in industrialized countries, especially among rural families with low socioeconomic status. For these groups, preventive programs and alternative restorative techniques should be instituted.

Traditional specifications for dental materials are largely based on definition of physical and chemical requirements and rarely include specific clinical and biological requirements. In fact, most requirements are set after the materials have been in clin-

Metallic Restorative Materials and Historical Standards

ical use for sometime, that is, after they have stood "the test of time." This "cart before the horse" approach is also put into practice in the continuous process of revision of the specifications.

Most individuals accept the longevity of restorations as a good measure for the quality of restorations; however, restoration longevity studies in general dental practice are hampered by many problems, such as variation in diagnostic level, the practitioner's proficiency and lack of calibration of clinicians and factors like patient drop-out and oral hygiene variations. The "gold standard" for clinical testing is the "controlled clinical trial," but the results from such trials differ markedly from those obtained in general dental practice (Figure 3).

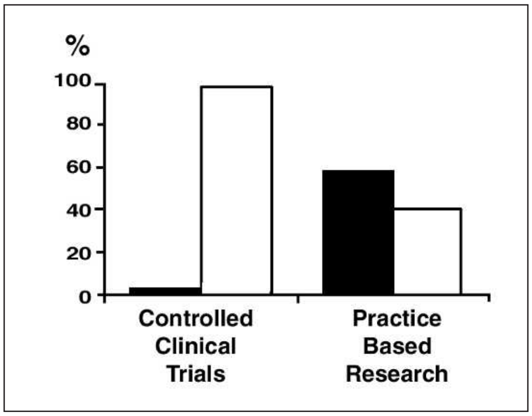

Figure 3. Typical percentages of secondary (recurrent) caries (black bars) and all other reasons pooled (open bars) as reasons for replacement of restorations in controlled clinical trials (left) and from practice based research (right).

Dental amalgam has certainly passed "the test of time." For more than 100 years amalgam, as the most common dental restorative material, has been repeatedly challenged on the basis of the toxicity of mercury, and more recently on its unsightly appearance. Improvements in the incidence of caries have also led to a need for materials with different properties. However, the cost-effectiveness of restorative amalgam therapy is a major reason for its continued use, but attention must be paid to mercury hygiene both with respect to the clinical team and the environment.

Cast and compacted gold restorations have been shown to have the greatest longevity of all restorations. Meticulous attention to detail in the placement of these restorations is important. They are initially expensive, but on a long-term basis, they are more cost-effective than the tooth-colored alternatives offered today.

Research into alternative non-mercury direct metallic restorative materials during the last 40 years has been focused on gallium alloys, and more recently on cold welding of intermetallic compounds. Commercially available gallium alloys have been introduced, but caution against their use has been issued for different reasons, including their biological properties and expansion of the materials leading to fracture of the restored teeth. The cold welded compounds have not yet been clinically tested and their future is uncertain, primarily because of their clinical technique and handling, but also because they, like amalgam and gallium alloys, are dark gray in color.

Conservative Dentistry Through Adhesion and Non-Metallic Materials

Development over the last 30 years of a great variety of resin-based, tooth-colored restorative materials both for direct and indirect use, together with cements and adhesives, has had a dramatic effect on dental practice. Detailed laboratory and clinical studies and clinical experiences with the use of these materials have demonstrated their efficacy and esthetic advantages. Unfortunately, the clinical acceptance of such materials has preceded controlled testing, especially in general practice. This has led to a flood of new and improved materials on the market. Results made available from clinical testing are, therefore, on "yesterday's materials." Improved materials are marketed based on laboratory data largely without correlation to the clinical problems associated with the materials. Minor attention has been paid to the longevity of the resultant restorations and the cost-effectiveness of the restorative techniques, both for the direct and especially the indirect alternatives. Over the last three decades, patients have paid for restorative care in the name of esthetics that has not been optimal. Research in this area still focuses on physical testing and chemical intricacies that may serve a marketing function, but only has minor clinical relevance.

The ionomer forms of materials received attention primarily because of: 1) their ability to chemically bond to the mineralized components of the tooth and 2) the release of fluoride from the materials. The development of ionomer materials has focused on both of these properties, but inherent clinical problems with the traditional acid-base reacted materials have led to so-called resin modified materials. Some materials, which are largely resin based, are now marketed but with the addition of fluoride compounds. This is quite amazing given that a "fluoride effect" from these materials has not been demonstrated in large scale clinical studies in general practice. In fact, with the widespread availability of fluorides, for example through toothpaste, it is unlikely that the fluoride released from restorative materials will have an additional beneficial effect except in selected patients. These materials have become the overall material of choice for most types of restorations in the primary dentition. However, the longevity of such restorations is currently of great concern pending a demonstration of their anti-cariogenic properties in general dental practice.

Future Materials and Biocompatibility

The clinical eminence of direct composite and ceramic systems was convincingly demonstrated at the final session of the Conference. Esthetically excellent restorations can be produced using existing materials. The main drawbacks of such materials are: 1) technique sensitivity and 2) cost in placement. These two factors are inherently connected because optimal clinical results are only obtained by meticulous attention to detail. As far as the composite and ceramic systems are concerned, the audience was left with the impression that ultimate esthetic results are possible. However, it must be realized that this type of dentistry is currently only available to discerning patients with sound financial resources. A major complicating factor in the practice of esthetic dentistry is the lack of training provided to dental students. Even Class II composite restorations have not been included in the clinical requirements of most dental schools worldwide up to the year 2000. Clinical teaching of ceramic techniques is virtually non-existent. Thus, the practice of these restorative techniques must be based on knowledge acquired through continuing dental education courses that traditionally do not include hands-on experience and by reviewing the literature in these areas. On these bases, clinicians are left with a "trial and error" approach towards developing skills in advanced esthetic restorative treatment.

Much research on esthetic restorative materials is ongoing, especially related to resin-based materials. Strong, suitable ceramic materials are available. The research in this area should focus on optimizing clinical techniques, including cementation (bonding) and reasons for failure in clinical practice.

The search for non-shrinking resin-based materials continues, but at this time it is largely limited to laboratory studies. If a breakthrough in this area is made, it will or should take several years of clinical testing before becoming available for clinical use. Today's composite materials are a result of continuous improvements over the last 20-30 years. Clinically, they provide more long lasting restorations than the early generations. It is hoped that the excellent laboratory research conducted will be supplemented by clinical and biological assessments. Any improvement in the physical properties of a material cannot be regarded as an improvement until it has been proved in clinical practice.

The biocompatibility of restorative materials has received additional attention as a result of the "amalgam issue." It is important to realize that many dental materials contain known allergens, some of which have been shown to result in allergic reactions in the sensitized individual. Sensitization may also occur from the use of dental materials. Members of the clinical team represent a risk group in this respect. A thorough knowledge of the potential problems and the use of non-touch techniques are essential for all materials used in dental practice. Patients experiencing toxic effects from dental materials is unlikely because the leachable components do not achieve toxic levels. However, the dental team, as the risk group for any toxic effects, must adhere to established guidelines for the use of the materials to prevent potential problems.

Concluding Remarks

The Charleston Conference on Carious Lesion and Management Alternatives clearly emphasized consideration for an initial non-restorative approach to carious management and treatment of dental caries as an infectious disease. The success of non-restorative, preventive methods based on active goal-driven monitoring of early lesions was convincingly demonstrated. It was recognized that this approach will change present day procedures and practices with a "drill and fill" attitude towards oral health care. Dental caries is a preventable disease, and the clinicians must act accordingly by providing the patients with the knowledge necessary to control the disease and its sequalae. This change in the practice of dentistry will take time and commitment. Appropriate remuneration systems must be established, along with the development of improved diagnostic methods.

The present day procedure-driven restorative approach to the treatment of caries focuses on the properties of the materials. However, it is important to recognize that restorations are only a treatment of the result of the disease—that is, the lesions of caries and not the disease itself. However, restorations, where indicated, are an integral part of any preventive program. Restorative materials research and development and associated biometics and tissue engineering techniques must continue. They must focus on technique insensitive approaches and clinical outcome measurements.

The Medical University of South Carolina and its College of Dental Medicine must be congratulated for their initiative to arrange the Conference and for providing excellent facilities for its implementation. This recognition is extended to Dr W Dan Sneed, who not only chaired the Conference planning, but also chaired the various sessions in an exemplary manner.

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OPERATIVE DENTISTRY

Supplement 6

Management Alternatives for the Carious Lesion

August 2001

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