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REVIEW ARTICLE

BIOCOMPATIBILITY: A REVIEW

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ABSTRACT

Introduction: Biocompatibility is fundamentally important to ensure the health of patients, dental staff members (including laboratory personnel) and practitioners themselves. Furthermore, the legal liability of dentists is often linked to biocompatibility issues. Practitioners should understand enough about biocompatibility testing methods to critically judge advertising claims and ask relevant questions of manufacturers.

Data: Articles from 1942-2014 were studied and relevant articles were included in this review.

Sources: The PubMed database search revealed that the reference list for biocompatibility of dental materials featured 1965 articles. A forward search was undertaken on selected articles, author names and contemporary dental material text.

Study selection: Only articles on biocompatibility of commonly used dental materials were included. Review articles on biocompatibility were included. Articles from 1942-2009 (Oct 2014) were considered.

Conclusions: Ultimately, each dentist must determine whether the benefits outweigh the risks for the patient under consideration. To avoid all risk is to deny the patient the tremendous benefits that materials have to offer.

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INTRODUCTION

Biocompatibility is fundamentally important to ensure the health of patients, dental staff members (including laboratory personnel) and practitioners themselves. Furthermore, the legal liability of dentists is often linked to biocompatibility issues. Practitioners should understand enough about biocompatibility testing methods to critically judge advertising claims and ask relevant questions of manufacturers.

Definition

Biocompatibility is "the ability of a material to elicit an appropriate biological response in a given application" (John, 2001; Williams, 1987).

History

Humans have attempted to improve life through the use of materials and devices of nonhuman origin as prosthetic devices and restorative materials in contact with tissues in the oral and maxillofacial environments (Kenneth, 2007). Some of the first publications to look at the evaluation of the tissue response to dental materials were those of Autian and his colleagues in the early 1970s, and an early review article was published in 1971 (Hauman 2003). Autian (1970) was the first to propose a structured approach as a concept consisting of three levels:

- Nonspecific toxicity (cell cultures or small laboratory animals);
- Specific toxicity (usage tests, e.g. in subhuman primates);
- Clinical testing in humans.

The following sequence was adopted by the ISO (1984) in Technical Report 7405:

- Initial tests (cytotoxicity, mutagenicity);
- Secondary tests (sensitization, implantation tests, mucosal irritation);
- Usage tests (Anusavice, 2004).

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Types of Biocompatibilty Tests

Testing for biocompatibility depends on the actual site of use and the duration of exposure (Craig, 1999).

Cytotoxicity measures:

- Cell number or growth,
- Integrity of cell membranes,
- Biosynthesis or enzyme activity or
- The genetic material of cell.

Current Biocompatility issues in Dentistry

Amalgam

The biocompatibility of amalgam, a product of the reaction of liquid mercury with silver and other metals, has been the subject of controversy for many years. There has been a concern that the mercury used in the reaction may leach out of the restoration as a result of unreacted material, dissolution in saliva, or corrosion reactions. It is known that mercury exists inorganically as the metal or in one of two charge states and in an organic form (methyl mercury). When present as methyl mercury, it is known to be highly toxic. Methyl mercury has been responsible for toxic reactions in the hat industry, in environmental disasters, and through consumption of seafood. Mercury in vapour form is easily taken up by the body. Studies reviewed by the US Public Health Service and the Food and Drug Administration suggest that based on available evidence, there is no proof of any mercury toxicity from dental amalgam to the patient, other than in cases of allergy. The authors in a review published in Europe concluded, ‘‘According to the conclusions of independent evaluations from different state health agencies, the release of mercury from dental amalgam does not present any non-acceptable risk to the general population’’ (Kenneth, 2007).

Amalgam restorations, in general, have been considered to be either inert or only mildly irritating to the pulp or body tissues in dogs, rats, and humans (Manley, 1942; Shroff, 1946 and Weider, 1956). Any pulpal response to amalgam seems to be related mainly to the physical insertion of the amalgam, that is, the pressure of condensation (Stanley, 1991), and is usually of short duration. Skogedal and Mjor (Skogedal, 1979) indicate that alloys containing the highest percentages of copper cause slightly more pulpal responses after 1 to 2 months in monkeys than conventional amalgam.

Polymeric materials and composites

In recent years the use of resin-based restorative materials has increased in dentistry because of better aesthetics, improved adhesion to enamel and dentine, and worries about adverse effects of mercury from amalgam. It has been shown that components of dental composite resins can be released from the materials (Michelsen *et al*., 2003; Ferracane *et al*., 1990; Spahl *et al*., 1998; Geurtsen, 1998; Moharamzadeh *et al*., 2007; Lee *et al*., 1998 and Arenholt-Bindslev *et al*., 1999). Unpolymerized monomers can be leached into saliva (Michelsen *et al*., 2008; Baker *et al*., 1988 and Hensten-Pettersen *et al*., 1998) and cause adverse reactions (Scott *et al*., 2004). These materials consist of monomers, fillers, initiators, accelerators and additives that are combined through some type of a curing reaction. If the proportions of the different components are not correct or if the curing reactions are not carried to completion, some or all of the components may be available to become dissolved in saliva, pass through tubules into the pulp chamber, or otherwise be released. Some monomer also may be released before curing occurs or during curing. Initiators and accelerators, depending on the type of curing reaction, may cause polymerization to occur or be accelerated without actually becoming a part of the polymer chain, which leads to the possibility that they may be free to diffuse out of the material and come into contact with tissues[3].

The primary risk of these materials- allergy (exposure to unpolymerized materials)–Type IV hypersensitivity reaction. Bis-GMA composites: Xenoestrogen: however studies have shown them to be 1000 fold less potent as estrogens than the native estrogen hormone. Although the estrogenicity of BPA has been confirmed, there is no evidence of dental composites having estrogenic effects in vivo or in vitro (Anusavice, 2004). In 1999 the national survey of adverse reactions to dental materials in the UK was established in Sheffield (Costa *et al*., 1999). In the adverse reaction reporting project (ARRP), green reporting forms were distributed to dental surgeries and laboratories in the UK. From 1999 to 2002, ARRP received 1,075 reports of suspected adverse reaction seen or experienced by dental staff and patients. The results of this study showed that, contact with acrylic resin was the main cause of hand dermatitis in dental technicians, and more than 12% of adverse reactions in patients were associated with resin-based dental materials. It has been shown that dentine bonding agents have toxic effects on immortalized odontoblast-like cells (Costa *et al*., 1999). Schmalz *et al*. using a three-dimensional culture of bovine pulp derived cells in a dentine barrier test, assessed the cytotoxicity of low-pH dentine bonding agents (All-Bond 2, Prime and Bond, Syntac Single, Syntac Classic, and Prompt L-pop) and demonstrated that these materials do not show toxic reaction in this dentine barrier test (Schmalz *et al*., 2002 and Keyvan Moharamzadeh, 2009). Therefore they concluded that pulp damage caused by the tested materials is unlikely if a dentine layer protects the pulp.

Metallic Materials

When metals and alloys are used in dentistry, there is the opportunity for adverse reactions caused by the release of metal ions or other products of the interaction between the physiologic environment and the metals. Except for certain noble metals, pure metals and alloys used in dentistry derive biocompatibility from the formation of a protective layer on the surface called a passive film, which is an oxide of one or more of the components of the alloy. These films are products of an oxidative (corrosive) reaction that reduces the corrosion rate by several orders of magnitude and essentially prevents further corrosion once the passive layer is formed. Contact between two different metals in the mouth or changes in the temperature or pH in the mouth can cause breakdown in protection and can, in the case of dissimilar metals, lead to galvanic corrosion. Even when the passive film is intact, the corrosion rate is not zero - just very small. Metal ions are being released at slow rates, but the body can have adverse reactions to those ions.

There may be local toxic responses, systemic changes in metabolic processes, or an allergic response to certain metal ions. Although uncommon, the metal most frequently responsible for an allergic response is nickel (Elgart, 1971 and Tomell, 1962), which is present in most stainless steels, most cobalt/chromium alloys (Hilderbrand, 1973), nickel-titanium alloys, and nickel-chromium alloys. If an adverse allergic response occurs, little can be done other than to exchange the metal component for one that does not contain nickel (Kenneth , 2007; Anusavice, 2004; Andreas Schedle, 2007 and Hauman, 2003). Another way that an adverse response can occur is if corrosion produces particles of corrosive product, which can induce the same type of tissue response that may result from the formation of wear particles.

Glass Ionomer cement

Smith and Ruse (Smith and Ruse, 1986) attempted to identify the mechanisms of potential sensitivity related to glass ionomer use. They measured the pH of cements following mixing and concluded that the initially low pH may produce chemically irritating conditions for the dental pulp. The actual pH depends importantly on manipulation procedures, such as the mixing ratio of components (Mount, 1986). Woolford (Woolford, 1986) also observed that the pH of glass ionomer cements remained very low during the first hour after setting, noting differences between varieties of commercial products. In screening and usage tests – pulp reaction to GIC: mild. Weak nature of polyacrylic acid, unable to diffuse through dentin because of its high molecular weight. As with other materials, hydraulic pressure and etching during placement of the restoration may cause irritation of the pulp.

Calcium hydroxide

Calcium hydroxide has been mainly used in pulp capping, pulpotomy, root amputation, apexificaiton and apexogenesis. The cement is alkaline in nature. The high pH is due to presence of free hydroxyl ions in the set cement. The high alkalinity and its consequent antibacterial effect helps in the formation of reparative dentin (Craig, 1999).

Latex

1991: FDA estimated 6-7% of surgical personnel allergic to latex. Hypersensitivity to latex-containing gloves (dermatitis-anaphylaxis). Ammonia added to the sap hydrolyzes and degrades sap proteins to produce allergens.

Ceramic materials

The tissue response to ceramic materials used in surgery falls into two basic categories:

(1) Porcelains and other hard ceramics used in crowns, inlays and onlays and
(2) Ceramics that are intended to react with surrounding tissues.

It is also important to note that the passive films that form on metals to protect them from corrosion are ceramic in nature and are the actual interface being presented to tissue on metals. In cell culture experiments, some ceramics were found to cause little suppression of mitochondria activity, some were found to be initially toxic, but that toxicity declined after an artificial aging process, one was extremely cytotoxic and became toxic again after repolishing, and one did not regain its toxicity with repolishing. The conclusion was that the aging process was removing cytotoxic chemicals from the ceramics but that the leaching was only from the surface in some cases while being from the bulk of the material in others. In reviewing reports of biocompatibility testing, it is important to review the condition of the materials being tested. In the referenced study, the ceramics that were not cytotoxic (feldspathic veneer porcelains) were fired before testing, but the other three materials tested were processed by pressing into molds according to manufacturer's instructions but had not been subjected to the final sintering treatment. It is possible that the sintering process would have bound up the toxic species into the bulk and prevented a tissue response.

The other class of tissue responses to ceramics concerns ceramics that are intended to interact with the surrounding tissues. In general, these materials do not have the necessary mechanical properties for use in crowns and other restorations but undergo at least a small amount of dissolution at the surface and are composed of compounds that contain calcium and phosphorus, two of the elements that comprise the mineral content of bone. Bioglass and calcium phosphate ceramics, such as hydroxyapatite and tricalcium phosphate, interact with surrounding bone to form a bond between the material and the tissue that can be stronger than either the bone or the material itself. In a process called osteointegration, the materials become integrated into the bone as it repairs itself and may reside permanently within the healed bone, although some are dissolved or resorbed and replaced by new bone. These materials are intentionally reactive with bone but are recognized and incorporated as if they were bone (Kenneth, 2007 and Messer, 2003). The relative incidence of biological side effects of dental ceramics compared with other restorative materials is considered to be low. In general, conventional dental ceramics are considered to be the most inert of all materials used for dental restorations. Ceramic restorative materials are not known to cause biological reactions, except for wear on the opposing dentition and/or restorations. No long-term data on the biocompatibility of these restorations are available (Roulett, 1990).

Conclusion

Biocompatibility is relevant to all dentists as we rely heavily on materials that remain in intimate contact with living tissues for long periods. Decisions about the biologic safety of materials are as much philosophical as scientific. Because no material can be proven 100% safe, the decision to use a material in the mouth must balance the potential risks and benefits.

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