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The Safety and Biocompatibility of Direct Aesthetic Restorative Materials

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Abstract

Restorative dental materials are among the most important medical devices in terms of the numbers of patients who benefit and the technical sophistication of the products. Many though contain toxic or noxious substances, including potentially sensitising resin monomers, photoinitiators, acidic polymers, and glass or ceramic filler particles. Despite this, dental materials are among the safest medical devices in use today, with very few reports of adverse reactions or injuries among both patients or the dental team. This paper considers the potential for adverse reaction to dental materials, current evidence for harm, and finally examines the reasons why in real world clinical use the likelihood of an adverse event is extremely low. Medical devices regulations, responsible manufacture, and clinical vigilance all appear to play important roles in ensuring that dental materials do not cause present a risk to patients. While this excellent in-practice safety record is welcome, there is now increasing interest in the “macro” scale biocompatibility of dental materials and their packaging in the environment, subjects that have been relatively neglected until recently. It was concluded that this should be a priority for future research and development, and support is needed from governments alongside manufacturing industry and the profession.

Introduction

Dental materials are arguably the most important synthetic biomaterials in clinical use today. Aesthetic direct restoratives are the most commonly employed medical devices for human tissue repair, where they effectively replace the functions of enamel and dentine to protect the pulp (alleviating pain) and restoring key functions related to eating, communication, and aesthetics. Dental materials therefore play a key role in healthcare, and make a major contribution to human quality of life. There use has increased over time, even gradually replacing dental amalgam in posterior dentition as they are both more aesthetic and – with continued improvements in design – are capable of providing a durable and long-lasting restoration. One further driver of the ongoing move away from dental amalgam are concerns around the use of mercury in a healthcare product, especially with respect to the potential for harm to the environment. These and wider concerns led to the Minamata Convention that is intended to ultimately eliminate mercury from all products, preventing the anthropogenic release of this toxic metal

Direct aesthetic restorative materials

The main types of direct aesthetic restorative are composite resins, glass polyalkenoate cements (better known as glass ionomer cements or GICs), and the so-called hybrids including polyacid modified composites and resin-modified GICs. The basic chemistry of these materials has not changed substantially since their respective inventions, although incremental improvements in formulation and associated technologies (e.g. bonding systems, light curing units, etc.) have resulted in improved clinical outcomes and sometimes greater complexity for modern systems. In brief, composite resin restoratives are composed of methacrylate monomers, glass and/or ceramic fillers, photoinitiators, and pigments.[1] GICs also contain a glass (albeit a basic fluoraluminosilicate with a larger particle size), an acidic polymer, tartaric acid, pigments, and water.[2] "Hybrids" represent an attempt to combine the chemistry and advantageous properties of these two classes of material in a single restorative. Resin-modified GICs contain all of the components of a GIC plus a water miscible monomer hydroxyethyl methacrylate (HEMA) and proprietary photoinitiators (and in some cases, additional complex chemicals to promote a "dark cure" following placement of the materials, where polymerisation does not then rely on solely photoinitiation).[3] Finally, polyacid modified composites (sometimes termed "compomers") are formulated as composite resins, but include ionomer glass fillers and unusual resin monomers that have carboxylic acid groups.[4]

The setting chemistry of these materials has been described extensively in the published literature and dental text books,[5] but what is particularly interesting in the context of safety and biocompatibility are the specific components including complex proprietary chemicals (where a wide range are in use today, including different glass and ceramic fillers, modified monomers, and photoinitiators). Moreover, detailed information on components may not be readily available for reasons of commercial sensitivity, and manufacturers are continuously seeking to innovate to produce clinical benefits that provide an advantage in the marketplace. These innovations are frequently underpinned by new intellectual property that may include development of modified or new substances. The range of chemicals that are present in high performance dental materials is therefore substantial and likely to increase, although there are also barriers to innovation such as the costs of research, and initiatives such as REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals, European regulations that entered into force on 1 June 2007) and now - after Brexit - UK REACH.

Risks and hazards

Many of the individual components of dental materials, including direct aesthetic restoratives, have the potential to harm not only patients but also the clinical team, and indeed people throughout the manufacturing and supply chain. Historically, public concern was heightened by both anecdotal stories of harm from dental materials, and unusual case reports where a dental material was suspected. For example, numerous reports have established that dental amalgam is safe when used correctly, but mercury spillages have resulted in illness and even deaths in practice.[6] Case studies describing potential adverse reactions to dental composites are uncommon, but some have been published. [7] Adverse reactions to GICs have not been published for dental materials, but serious events have been reported for these materials when used as bone cements. [8-10] Moreover, there are case reports for resin modified GICs, [11] reinforcing the concept that more complex dental materials might present a greater risk to human health. Examples of adverse reaction to dental materials are provided in Table 1, reinforcing the message that restorative dental materials have the potential to cause harm.

Case reports and adverse events from non-dental clinical settings suggest that these potential hazards may be translated into real harm, but they do not provide insight into the numbers of cases, the specific causes, or the actual numbers of incidents. Because of this – and also because of increased public concern around dental amalgam - a number of countries

including the UK invested in research to investigate the real risks of adverse reactions to dental materials. The most well-known of these initiatives were based in Umea (Sweden), Bergen (Norway), and Sheffield (UK), who have all published extensively on adverse reaction events. Condensing the findings thus far, adverse reactions to dental materials are exceedingly rare, and where they occur they are generally not severe or life threatening. Indeed in dentistry the more common adverse events were not to dental materials but to other materials such as gloves,[12] and the dental team were at far higher risk than patients (where the likelihood of even a suspected reaction was less than one in one hundred thousand).[13] Likewise in Sweden adverse reactions were very rare, and less than 6% of these unusual events were considered to be possibly linked to resin-based dental materials.[14] It is also noteworthy that restorative dental materials present the greatest risks before setting e.g. during placement, and elution of components from set or polymerised materials is minimal (so the risks are greatly reduced). There are of course related hazards not covered here, including injuries from instruments or eye damage from visible light curing units, emphasising very much that safety in a dental setting relies on the competence and vigilance of the team.

Why are restorative dental materials safe?

Despite the presence of hazardous materials in their formulation, direct aesthetic restorative materials are among the safest medical devices in clinical use today. In some ways this is a paradox, especially given their extensive use and composition, but Figure 1 illustrates the three major factors that should be considered that contribute most to this outstanding safety track record.

(Insert Figure)

Figure 1. It is the combination of a responsible, innovative manufacturing sector with a robust regulatory environment and a well-trained vigilant dental team that minimises the risks associated with the clinical use of restorative dental materials.

Industrial innovation. In their efforts to develop improved materials, the dental sector has significantly expanded the range of substances used in the manufacture of dental materials. They have in parallel though also greatly improved packaging and instructions for correct use

(so that for example the dental team is less likely to come into contact with sensitising resins). Moreover, the quality systems required for the manufacture of dental materials (as part of medical devices regulatory environment – see below) are rightly onerous, and include aspects of traceability from raw material through to final product (and increasingly end use).

The regulatory environment. The global regulatory environment has evolved over the past three decades, and today most countries have legal controls in place that cover the design, manufacture and sale of medical devices including dental materials. Many nations follow a model established by the US Food & Drug Administration (FDA), although the European Economic Area (EAA) has similarly well-developed regulations. Following departure from the European Union, the UK is developing its own framework. This is not expected to represent a major departure from established approaches, although there may be some confusion in Northern Ireland where it seems likely that both EU and UK regulations will operate. Medical device regulations are generally risk-based, require a design specification and detailed records, and frequently necessitate the application of a range of safety and usage tests prior to a new product being placed on the market. Where the dental team or public suspect an adverse reaction may have occurred, they are recommended to report this to the UK Medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card system (https://yellowcard.mhra.gov.uk/). Such post market surveillance contributes much to wider confidence in the safety of modern dental materials.

Clinical skills, professionalism and vigilance. Perhaps most importantly, the dentist, hygienist, therapist and/or nurse are all well-placed to observe an unexpected or adverse reaction to a dental material. Dental professionals are expected to follow manufacturer's instructions, use materials for the correct indication, and keep detailed records. The high degree of professionalism is a key factor underpinning the safe use of restorative materials.

To summarise, direct aesthetic restorative materials undoubtedly have the potential to cause harm, but through the combination of critical factors summarised in Figure 1 the real risk to patient health is negligible. That established, there is though now greatly increased interest in wider risks to human health based on the impact of dental materials on the environment. While the volume of materials used in a single dental procedure is tiny, hundreds of thousands of restorations are placed daily throughout the world, and additional waste is generated via partially used capsules or storing beyond the use by date. These emerging environmental concerns represent a shift of emphasis from patient safety and what might be

termed “micro” biocompatibility to “macro” biocompatibility, recognising that all human activities have an impact and healthcare must be as sustainable as any other sector. While further research is needed, the solution here is likely to mirror the patient safety challenge, where a combination of government regulations and responsible industrial behaviour will be coupled to high standards and vigilance in the hospital, practice and community settings.

Conclusions. Direct restorative dental materials are essentially safe for patients and the dental team when used correctly, although a low risk of adverse reaction remains, primarily to unpolymerised resin components that come into contact with human tissues. The excellent safety record is a result of the combined effects of a carefully written risk-based regulations, a responsible industry, and a high degree of professionalism on the part of the dentist and wider team. The emerging challenges are though now increasingly environmental - a form of macro-biocompatibility with life on earth - but lessons can be learned from our successes to date i.e. the combination of a sound regulatory environment coupled to a responsible industry – not just in manufacturing but also in packaging and distribution – with a professional healthcare community has the potential to deliver a circular economy where potentially hazardous substances are contained and ultimately recovered and recycled. Ultimately though, the most sustainable oral healthcare is based on a combination of prevention and high quality clinical intervention when necessary, where modern restorative dental materials make a significant contribution to human wellbeing.

Ethics declaration
The authors do not declare any conflict of interest.

Author contributions
All authors contributed equally to the manuscript, with PVH writing the first draft and all authors participating in the editing process and approving the final version.

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Dental material	Comments	Reference
Resin-modified glass ionomer cement	Dentist reported contact dermatitis following direct contact with the liquid from an RM-GIC, where HEMA was suspected but not confirmed.	11
Components of composite resins and bonding systems.	Review of patch sensitivity to detect allergic reactions to acrylic monomers in dental personnel. 8 dentists and 12 dental nurses were allergic to HEMA, and one dentist was allergic to 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy) phenyl]propane (bis-GMA).	15
Adhesive resin system	A patient experienced an adverse reaction following cementation of a zirconia bridge. Patch test results showed a positive allergic reaction to tooth primer light-cured adhesive resin.	16
Bonding agent	Three dental students in the USA each self-reported a rash after restoring a tooth with a composite and bonding system. Evaluation including assessment of glove permeability concluded that HEMA in the bonding agent was the most likely cause.	17
Composite resin restorative material	Female patient in India returned to a clinic with burning sensation and swelling on lips, two days after placement of a composite restoration. Patch testing suggested sensitivity to bis-GMA.	18

Table 1. Examples of published reports of adverse reaction to restorative dental materials or their components.

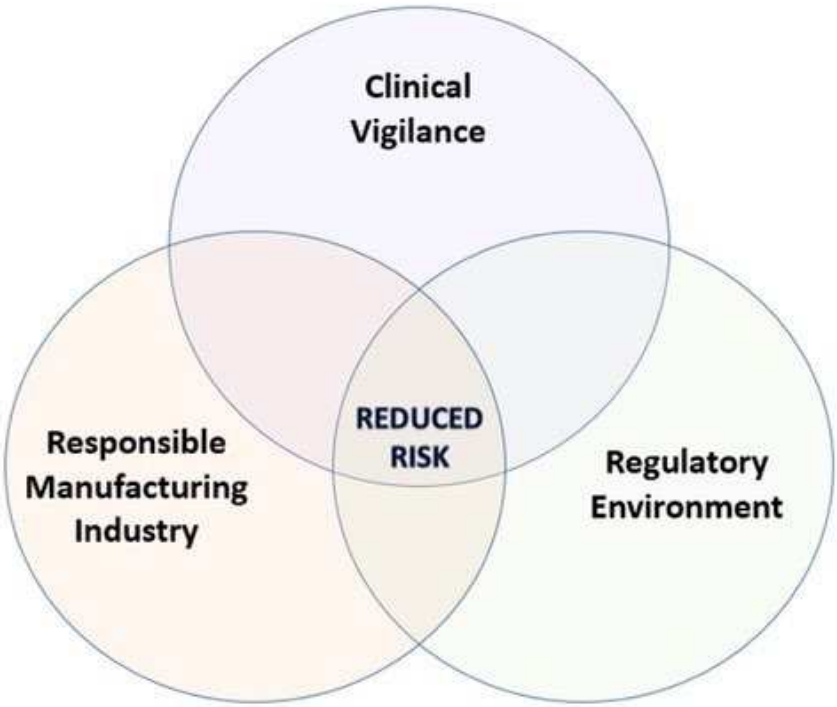

Figure 1. Reduced risk. The combination of a responsible, innovative manufacturing sector with a robust regulatory environment and a well-trained vigilant dental team minimises the risks associated with the clinical use of restorative dental materials