In dentistry, different types of materials are used to restore the decayed or to replace the missing teeth. These materials come into direct contact to the hard and soft tissue of oral cavity including dentin, periodontium, oral mucosa and body fluids. Though all these materials with long history of usage are tested for their biocompatibility in the oral cavity. Any adverse reactions due to the leaching of components from these dental materials into the oral environment is a clinical concern. The materials ranging from temporary to permanent or polymers to metals have different applications in dentistry. Besides their important role in restoring, healing or improving the function of oral tissues, the materials may show side effects which may lead to severe lesions or more serious illness. This review provides a comprehensive overview of side effects and toxicity by various materials in Dentistry. The side effects of the materials are discussed here based on clinical and cellular views.

Introduction:
Ideally the accepted fact is that a biocompatible biomaterial is a substance that does not elicit any adverse effects when it is implanted into the body because it is inert. Preferably, a dental material used in the oral cavity should not interact negatively with oral or dental tissue, it should be harmless to the pulp and the soft tissues. The material should contain no toxic diffusible substance that can be absorbed into the circulatory system to cause a systemic toxic response, should be free of potentially sensitizing agents that could lead to an allergic response and should have no carcinogenic potential. But a single material may not be biologically acceptable in all applications.

Over the time, the material may show many physical and mechanical changes including leaching out ingredient from restoration, long-term degradation, mechanical strength problems, and failure for secondary caries prevention. Mainly when the oral release of compounds from materials occurs with adverse reactions may lead to contact allergies in allergically vulnerable patients. The literature has documented many studies on the potential allergies from materials including mercury from silver amalgam filling, heavy metals in removable a partial denture, impression materials and irrigation materials used in endodontics. Despite being exposed to potential allergens and toxic substances, the oral mucosa seldom shows inflammatory and allergic reactions. In addition, wounds and lesions heal faster in the oral cavity compared to skin. This is proved to be due to diminished inflammatory response in the oral mucosa. It is therefore strong reasons to believe that the immune system of the oral cavity helps to diminish the degree of reactions to materials, to dental materials are unwanted reactions, either subjective or objective. An adverse reaction can be of allergic, toxic or psychological origin. An unwanted biological reaction can further be local (e.g. contact dermatitis) or general (systemic, for example a hormone-effect).

Contact dermatitis
Contact dermatitis on a cellular level can be divided in mostly two categories: Allergic or toxic (irritative). Allergic Contact Dermatitis is of allergic type IV origin while an irritative contact dermatitis is a non-immunological reaction with direct cell damage followed by an inflammatory reaction. Allergic contact dermatitis in dental personnel is predominantly confined to hand dermatitis (Figure 1), while patients with ACD to dental materials tend to experience stomatitis or cheilitis (type IV allergy) or contact urticaria with or without dissemination (Figure 2). Contact dermatitis is manifested by an itching or burning sensation at the site of contact, followed by erythema and then the appearance of vesicles. Once the vesicles ruptures, the erosion becomes more extensive may be followed by secondary infection. The oral manifestations, known as contact stomatitis or stomatitis venenata includes an edematous mucosa accompanied by a severe burning sensation.

Clinically it can be impossible to distinguish the different types of reactions without a deeper anamnesis or allergy test. The situation could arise when there is direct contact between body surface with allergen like Monomers of bonding agents, Acrylic component of dental cements, Nickel from orthodontic wires, Resin monomers, Latex gloves and Amalgam etc.

Genotoxicity
Genotoxicity is the ability of a material to break down or mutate DNA. Genotoxicity may have triggered by certain types of radiations used in diagnosis and also certain chemical compounds used in Dentistry. A genotoxic material is considered carcinogen because of its abilities to change DNA expression.

Amalgam tattoo:
The most common pigmentation found in the oral mucosa is the amalgam tattoo. The lesions are macular bluish grey or even black that usually seen in the buccal mucosa, gingivae, or palate near the amalgam restoration (figure 3). Such lesions are the consequence of an iatrogenic accident where the bur loaded with small amalgam particles accumulated during the removal of amalgam, accidentally turns into the adjacent mucosa and introduces the metal spots.

Beside this, there are several side effects of amalgam fillings attributed to Mercury as its main ingredient. Mercury poisoning also known as hydargyria or mercurialism, is a disease caused by exposure to mercury or its compounds with resulting side effects include damage to the brain, kidney, and lungs and several diseases, including acrodynia (pink disease), Hunter-Russell syndrome, Minamata disease etc.
Contact stomatitis: Contact allergy results from a delayed hypersensitivity reaction that occurs when antigens of low molecular weight penetrate the skin or mucosa of susceptible individuals. These antigens combine with epidermal-derived proteins to form hapten that bind to Langerhan’s cells migrates to the regional lymph nodes and present the antigen to T lymphocytes, which become sensitized and undergo clonal expansion. After re-exposure to the antigen, sensitized individual develops an inflammatory reaction confined to the site of contact. Since the reaction resulting from contact allergy appears as nonspecific inflammation, contact dermatitis is unknown, but it is believed to be significantly less common than contact dermatitis for the following reasons:

Saliva quickly dilutes potential antigens and physically washes them away and digests them before they can penetrate the oral mucosa. Since the oral mucosa is more vascular than the skin, potential antigens that do penetrate the mucosa are rapidly removed before an allergic reaction can be established. The oral mucosa has less keratin than the skin, decreasing the possibility that haptens will be formed. Contact stomatitis may result from contact with dental materials, oral hygiene products, or foods. Common causes of contact oral reactions are cinnamon or peppermint which are frequently used oral hygiene products, or foods. Common causes of contact oral reactions are cinnamon or peppermint which are frequently used.

Dental materials and related Toxicity:
Dental materials have been classified in many ways depending upon the usage (Table 1). Dental materials are divided upon the time of their application as provisional and permanent materials. The temporary or provisional materials are applied for a short period of time usually to heal a tissue or improve its function. Although the materials have often temporary effects, the effects may recur every time which they are applied. The permanent materials are often used to replace a tissue or recover its function and should keep the function. The materials used in dentistry may classified as following:

<table>
<thead>
<tr>
<th>PERMANENT MATERIALS</th>
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<tr>
<td>Restorative materials: Amalgam, composites, inlay cements</td>
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<tr>
<td>Reconstructive materials: Denture Base, Implants</td>
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<tr>
<td>Appliances: Denture with metal base, Metal and Metal Ceramic Crowns, Removable Partial Dentures</td>
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<table>
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<tr>
<th>PROVISIONAL MATERIALS</th>
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<td>Therapeutic materials: Mills, Mouth washes, Toothpaste, Dental Gels, Food Additives, Dentifrices</td>
</tr>
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<td>Devices: Brackets, Orthodontic Plaque, Wires, Space maintainers</td>
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<td>Impressions Materials, Gloves</td>
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Table 1: Classification of Dental Materials Causing Toxicity

Amalgam and mercury toxicity: Amalgam filling or silver filling are considered be the oldest and most commonly used type of restoration for restoring a decayed tooth. Amalgam consists of 50% mercury along with a combination of silver, tin, and copper. Studies have found that the amount of mercury vapor from amalgam varies from 1-3 ug/day (micrograms/day), at the low estimation, up to 27 ug/day. Mercury is a powerful neurotoxin and, at certain levels, can cause neurological issues, autoimmune disease, chronic illnesses and mental disorders. The burning question is whether an unknown quantity of mercury vapor in our silver fillings at a constant exposure poses a significant health risk.

Composite Materials: It has been reported that resin composite materials could trigger the development of lichenoid reactions in the oral mucosa. It may be related to formaldehyde formed in resin composite restorations. Formaldehyde causes more than one third allergic reactions caused by dental materials. Whether dental resin composites have improved their physico-chemical properties, the concern for its intrinsic toxicity remains high. Some components of restorative composite resins are released in the oral environment initially during polymerization reaction and later due to degradation of the material. During exposure to oral environment, biodegradation of resin composite materials can also be induced by fatigue, washing effect of saliva, thermal changes and microbial interactions.

Resin Cements: Even though dental resin composites have improved their physico-chemical properties, the concern for its intrinsic toxicity remains high. Some components of restorative composite resins are released in the oral environment initially during polymerization reaction and later due to degradation of the material. During exposure to oral environment, biodegradation of resin composite materials can also be induced by fatigue, washing effect of saliva, thermal changes and microbial interactions.

Denture base Resins: Denture base resins are extensively used in dentistry that can be classified as chemical, heat, light, and microwave polymerization materials depending upon the factor which starts the polymerization reaction. Their applications include use during denture base construction, relining existing dentures, temporary crowns and for fabrication of orthodontic removable appliances. Constant contact of saliva with the material cause’s expansion of the openings present between the polymer chains causing the unreacted monomer to diffuse out. Thus, the substances which are leached out from the denture bases into the saliva are transferred to the oral structures causing adverse allergic reactions.

Recurrent aphthous stomatitis (RAS): RAS is a disorder characterized by recurring ulcers confined to the oral mucosa in patients with no other signs of disease. The current concept is that RAS is a clinical syndrome with several possible causes. The major factors identified include heredity, hematologic deficiencies, and immunologic abnormalities. A detergent present in toothpaste, sodium lauryl sulfate, was suspected as an etiologic factor in RAS development.
with burning sensation include the palate, tongue, oral mucosa, and the oropharynx.\textsuperscript{[32]}

**Dental Impalnts:** Acute and chronic toxic effects of heavy metals including Titanium, Vanadium or metal implants can be cytotoxic for macrophages and fibroblasts that can be bound by iron proteins (ferritin and transferrin), which affects its distribution and accumulation in the body can incite local and systemic reactions; can inhibit cellular proliferation and can lead to kidney lesions.\textsuperscript{[39]}

**Impression Materials:** Polyether impression material has been known to cause allergic problems in the past, but since its composition has changed the problem has been eliminated. The material should be mixed thoroughly and contact of the aromatic sulfuric ester catalyst paste with the skin or mucosa should be avoided, because it may elicit adverse tissue reactions.\textsuperscript{[39]}

**Rubber Latex:** It is well known, that many health care workers who routinely wear gloves suffer from contact, or irritant, dermatitis. In contact dermatitis there may be a latent period following first contact with the allergen. Reaction may be immediate, or may take hours to develop and, if severe, may last up to 10 days.\textsuperscript{[31]}

**Eugenol-containing Materials:** Eugenol is a derivative of clove oil. It is used in dentistry in combination with zinc oxide inside the tooth as a dressing, in toothache drops and an impression material. Eugenol is highly soluble and is continuously released from zinc oxide-eugenol, which can lead to saturation of the oral environment with eugenol in a concentration sufficient to cause cytotoxicity. Therefore, eugenol periodontal packs, which used to be applied to open mucosal wounds, are no longer popular. The inflammatory response caused in mucosal tissue by eugenol should not, however, be confused with hypersensitivity reaction.\textsuperscript{[32]}

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**Local Anaesthetics**

The ester group of local anaesthetics (e.g., benzocaine, tetracaine, procaine) was previously in widespread use by dentists and their sensitizing potential is well known. In 1983, it was reported that tetracaine was the most frequent contact allergen for dentists. The newer amide local anaesthetics (lignocaine, mepivacaine, prilocaine, bupivacaine) currently used by dentists are less likely to cause allergy, both type IV and, arguably, type 1. A retrospective review of occupational hazards in dentistry demonstrated the virtual disappearance of reactions to local anaesthetics during the late 1980.\textsuperscript{[34]}

**Conclusion:** A single material may not be biologically acceptable in all Dental applications. The side effects may include a small lesion in oral cavity to a life-threatening situation ranging far from the application place of the materials or near. Dental materials may be categorized in provisional or permanent materials with their related side effects depending upon the quality and quantity of ingredients.

**REFERENCES**


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