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BIOCOMPATIBILITY OF DENTAL MATERIALS - AN UPDATE

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ABSTRACT

Biocompatibility is formally defined as the ability of a material to elicit an appropriate biological response in a given application in the body. Dentistry shares concerns with biocompatibility with the other fields of medicine. Dental materials have various means of being tested and evaluated. This review article briefly discusses the biocompatibility of dental materials particularly their correlation, testing methods to check their biocompatibility.

KEYWORDS: Biocompatibility, Dental materials toxicity, Inflammation, Allergy.

I. INTRODUCTION

Biocompatibility is defined as the ability of a material to elicit an appropriate biological response in a given application in a body.[1] In correlation with dentistry it refers to the study of interaction of various dental materials with the human tissues. Placement of a material in the body creates an interface that must exhibit both biological and structural stability during the lifetime of the implanted material or device. Materials used in dentistry more commonly come in direct contact with the oral tissues such as the teeth, oral mucosa, pulp and the periapical tissues.

II. Why are biocompatibility tests important?

- Safety of the patient and the practitioner
- Regulatory Compliance Issue
- Legal liability.

2.1 Safety of the patient and the practitioner: The primary purpose of biocompatibility tests is to protect the patient and the professional since no dental biomaterial is absolutely free from the potential risk of adverse reactions. An adverse reaction could be in the form of an allergic reaction, chemical burn, pulpal damage, pulp irritation or a thermal injury. The patient could have local and systemic effects depending on the contact with the material. The practitioner on the other hand may be chronically exposed .For example., the usage of dental amalgam causing the release of mercury vapours from amalgam during placement and removal is substantially higher .Also the use of latex and resin based materials can elicit a response not only to the practitioner but also to the dental technician.

2.2 Regulatory Compliance Issue: Regarding issues concerned with the use of mercury regulators have considered monitoring and restricting its usage.

2.3 Legal liability: Since dental materials can affect the well being of patients and dental auxiliaries, a knowledge of legal risk issues is mandatory.

III. History

A wide variety of relatively inert materials have been used to replace missing teeth and oral tissues .Bone, seashells, animal teeth have been used to replace missing teeth. **G.V.Black** in 1900 did the first controlled experiments on dental amalgam which is the earliest known testing on dental materials.

IV. How biocompatibility tests are carried out?

Autian in 1970 proposed a structured approach as a concept consisting of three levels[4] 1.Nonspecific toxicity (cell cultures or small laboratory animals) 2.Specific toxicity (usage tests, eg.in sub human primates) 3.Clinical testing in humans.

The current ISO technical report 7405 is based on the sequence suggested by Langeland in 1984 as follows

1. Initial test (cytotoxicity, mutagenicity);
2. Secondary tests (sensitization, implantation tests, Mucosal irritation).
3. Usage tests.

The initial tests Phase I and II are of short duration, simple and cost effective[3] .After completing initial testing, the material then progresses through testing hierarchy which is a series of tests ranging from simple in vitro test to more complicated which is briefly explained as follows.

4.1 In vitro tests

The candidate material is placed in direct contact or indirect contact with some biological system outside of an organism .Direct contact exposes a material directly to a biological environment whereas indirect contact involves a barrier such as agar, membrane filter or dentin .In vitro tests can be done in test tubes, cell culture dishes or other containers. Biological system may consist of mammalian cells, cellular organelles tissue, bacteria or certain enzymes.

1. ***Cytotoxicity tests-*** Membrane permeability tests.
2. ***Tests for cell function/cell metabolism-*** MTT, NBT, XTT, Almar blue tests.
3. ***Tests that use barriers(indirect tests)-***Agar diffusion tests, Millipore filler tests.
4. ***Mutagenesis tests*** -Ames tests and Styles' tests.

4.2 In vivo tests/Animal tests: Tests animals include-baboons, cats, dogs, ferrets, guinea, pigs, mice, monkeys etc. The tests that are categorized under the in vivo tests and the animal tests are 1. Mucous membrane irritation tests 2. Skin sensitization tests 3. Implantation tests An advantage of animal testing is that it permits an intact biological system to respond to or interact with the candidate material.

4.3 Usage tests: Usage test is the gold standard method of testing. It can be performed on animals or humans. Usage tests are likely to be performed on large animals whose anatomy is more similar to humans .when used on humans the term used is clinical trial. Relevance of usage tests depends on the extent to which the tests stimulate the clinical use of the product.[2]

1. Inhalation test[5]
2. Implantation test
3. Maximization test
4. Buehler's test
5. Pulp-dentin test for restorative material
6. Pulp capping and pulpotomy material test
7. Mucosal damage and mucosal usage tests
8. Periapical tissue damage and endodontic usage tests
9. Gingival usage tests.

4.4 Allergy tests: The allergy tests are classified as

1. **Patch tests**-Delayed hypersensitivity tests
2. **Prick tests**-Immediate hypersensitivity tests
3. **Radioallergosorbent tests RAST**-Alternative to prick tests

V. Standards that regulate the measurement of biocompatibility

First biocompatibility standard test, Document 41 for recommended standard practices for biological evaluation of Dental materials approved in 1972.

5.1 ANSI/ADA Specification 41

The initial tests include in-vitro assays for cytotoxicity, red blood cell membrane lysis (hemolysis), mutagenesis and carcinogenesis at the cellular level and in vivo acute physiologic distress and death at the level of the organism. The materials that pass the initial tests are then subjected to one or more secondary tests in small animals (in vivo) for inflammatory or immunogenic potential (e.g Subcutaneous and bony implantation, Dermal irritation and hypersensitivity tests).Materials that pass the secondary tests which still hold potential are then subjected to one or more in vivo usage tests , which are first experimented in larger animals, often primates and finally in humans after the approval from the Food and Drug Administration.

In accordance with the ANSI/ADA specification No. 41, 1982 addendum, two assays for mutagenesis have been added the Styles' cell transformation test and the Ames test. The standard was most recently revised to conform to the ISO (International Organization for Standardization) standard below, and was then released as ANSI/ADA specification No. 41, the Recommended Standard Practices for Biological Evaluation of Dental Materials (2005).

5.2 ISO Standard 10993

ANSI and ISO developed ISO 10993.This was not restricted to dental materials alone. Revision of the dental components of this document resulted in ISO7045:2008 "Preclinical evaluation of biocompatibility of medical devices used in dentistry—Test Methods for dental materials." Most recently the available standard for biocompatibility testing of dental materials is the ISO standard. The standard divides into initial and supplementary tests.

VI. Reaction of the oral tissue to dental materials[2]

Table 6.1: Dental materials and their immediate reaction and late consequence.

S. No	Materials	Immediate reaction	Late consequence
1.	Dental amalgam	1. Contact dermatitis/sensitization to metal elements 2. Symptoms of acute mercury toxicity	1. Oral Lichen planus[11] 2. Thermal sensitivity 3. Adverse pulpal response 4. Symptom of chronic mercury toxicity.
2.	Resin based composites	1. Contact dermatitis/sensitization to methacrylates 2. Post operative sensitivity due to polymerisation and marginal gaps 3. Most frequent allergens – Methacrylate[7] (HEMA, EGDMA), MMA	1. Estrogenic effects of bisphenolA. 2. Cytotoxicity or systemic effects. 3. Systemic effects of other free monomers /leached substance 4. Allergic reaction to dental acrylic resulting in burning mouth syndrome, lichenoid reaction, perioral eczema, urticarial.[9]
3.	Cast alloy and condensed foil	Contact dermatitis/ sensitization to metals especially nickel, copper, beryllium.	1.Oral lesions of lichen planus in cases of copper alloy[10] 2.Thermal sensitivity of pulp 3.Systemic effects of leached ions.
4.	Ceramic	Sensitization to ceramic	Respiratory effects from silica dust due to excessive wear of antagonist tooth structure.
5.	Titanium	1. Sensitization to titanium. 2. Relatively non toxic, non injurious, not physically reactive.	De-keratinized hyperplastic reactions of the peri-implant tissues and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome[13,14]
6.	Base metal and noble metal alloys	1. Gingivitis and periodontitis 2.Allergy to base metal alloy[8]	1. Nickel,[12] chromium, beryllium, copper increased cancer risk. 2. Beryllium has an increase risk of lung cancer 3.Beryllium and gallium salts show genotoxic effects

VII. Complication from use of a non-biocompatible material.

The four major complications one can come across can be

7.1 Toxicity

Toxicity describes the ability to damage a biological system by chemical means .Adverse effects evoked by foreign substances such as restorative materials and auxiliary dental products. Paracelus the father of Toxicology stated that "All substances are poisons; there is none that is not a poison". It's the dosage that differentiates a poison from a remedy. Toxicity can be categorised as immunotoxicity, local and systemic toxicity.

1. Immunotoxicity of a material describes adverse effects on the structure and function of the immune system leading to impaired host defence and tissue damage.
2. Local toxicity affects the adjacent tissues as the toxins are released into the adjoining oral mucosa ,gingiva ,the pulp and the periodontal tissue
3. Systemic toxicity involves the absorption, inhalation or ingestion of the toxin. Depending on the duration of symptoms present they could be acute, subacute and chronic toxicity.

7.2 Inflammation

Inflammation results from trauma toxicity or allergy.Histologically speaking, the inflammatory response is characterized by edema of tissues .there is an infiltration of neutrophils initially followed by the presence of monocytes and lymphocytes.

7.3 Allergic reactions

Abnormal antigen-antibody reaction can give rise to an allergic reaction .allergic reactions by dental materials can occur intraorally as well as extraorally.

7.4 Other reactions

***1. Genotoxicity*:** Ability of a substance to cause alterations in the DNA gnome.

2. *Mutagenecity:* Ability of a substance to pass genetic damage to the next generation. Beryllium, Copper, Nickel, resin based materials are known mutagens. Mutagenecity doesn't have same consequences as carcinogenicity. Mutagenecity can be repaired others could be irrelevant or insignificant. No dental material has ever been shown to be mutagenic.

3. *Carcinogenecity*: the ability to induce tumours. No dental material has ever been shown to be carcinogenic.

4. *Teratogenecity*: Causing malformation during embryonic development.

VIII. CONCLUSION

Clinicians should not simply accept statements such as "The material has been subjected to biocompatibility tests and no adverse effects were observed". Manufactures may be reluctant to divulge

biocompatibility information .In some cases MSDS sheet may be acquired. The practitioner should inform the patient of benefit and risks of the proposed treatment and of any alternative treatments. Patient should also give their consent if restorative treatment is needed to restore occlusion and function, risks can be accepted .informed consents must still be signed before the start of treatment.

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