TITLE OF THE CHAPTER:

BIOCOMPATABILITY BLUES IN RESTORATIVE DENTISTRY

AUTHORS:

1. Priyanka Sarangi
   Assistant Professor,
   Department of Conservative Dentistry and Endodontics,
   SCB Dental College and Hospital, Cuttack, Odisha

2. Subiksha K,
   Post graduate,
   Department of Conservative Dentistry and Endodontics,
   SCB Dental College and Hospital, Cuttack, Odisha

3. Dr.Ayushi Bajoria,
   Senior resident,
   Department of Conservative Dentistry and Endodontics,
   SCB Dental College and hospital, Cuttack, Odisha

4. Dr.Sukanta Kumar Satapathy,
   Associate Professor,
   Fakir Mohan Medical college, Balasore, Odisha.

INTRODUCTION:

In the process of manufacturing of any biomaterial, biocompatibility consideration is equally important to strength, aesthetics, and functional attributes of the material. Biocompatibility is an interdisciplinary field that incorporates information from a variety of disciplines, including material science, biochemistry, bioengineering, molecular biology, tissue engineering, and others. By definition, "Biocompatibility is the ability of a material to elicit an appropriate biological response in a given application in the body". When a substance is implanted in the body, an interface is formed that must be able to retain both biological and structural stability for the course of the implanted device's existence in the body. This stability is a high requirement because the interface is dynamic with constant interactions which may cause the body to alter the material or the material to cause changes in the body. Discussing about the interactions caused by the interface, in oral cavity four different types of interactions are possible, namely, between the material and oral cavity, with the dental pulp through the dentinal tubules, with the periodontium and between the material and the periapical bone. Concerns about biocompatibility of materials are shared by other medical specialties including dentistry. This chapter briefs about the basic concepts of biocompatibility and it's relevance to dentistry along with the tests used for evaluating biocompatibility of the materials, comparison among them with their advantages and disadvantages. The last part of the chapter is dedicated to discussing the biocompatibility of the various materials used in dentistry.

Factors affecting biocompatibility of a material are mentioned as follows:

1. The chemical nature of its components
2. The physical nature of the components
3. The types and locations of patient tissues that will be exposed to the device
4. The duration of the exposure
5. The surface characteristics of the material
6. The amount and nature of substances released from the material

EFFECTS IN THE BODY:

- ✓ **Side effects** of a biomaterial are defined as those effects that, besides the intended main function, are also characteristic for this biomaterial but are not wanted. Adverse effect is a word used synonymously.

- ✓ **Toxicity** of a material describes the ability to damage a biological system by chemical means. In higher organisms (animals, human beings), local toxicity – that is, adverse reactions emerging at the application site – is differentiated from systemic toxicity, in which adverse reaction appear in an area distant from the application site. In dentistry, local reactions primarily occur in the pulp, the periapical periodontium, and the gingiva/ oral mucosa.

- ✓ **Immunotoxicity** of a material describes adverse effects on the structure and function of the immune system, for instance on relevant cells such as monocytes. These effects

impair the host defense (e.g., against infection) or may cause tissue damage, such as by chronic inflammation.

Health effects can be subdivided into the following:

• Systemic toxicity

• Local reactions

• Allergic reactions

• Other reactions

SYSTEMIC TOXICITY:

Any biomaterial that is placed adjacent to a natural tissue in the body can induce biological effects. These effects are controlled by the substances that are released from the material and the biological responses to those substances. In case of systemic toxicity, the application site may be in a different location from the effect. Their routes of entry into the body include the following sources: (1) ingestion and absorption (2) inhalation of vapor (3) leakage through the tooth apex and (4) absorption through the oral mucosa. The final systemic reaction is influenced by four important factors: (1) concentration of the substance; (2) time of exposure; (3) excretion rate of the substance; and (4) organ of importance or site at which exposure occurred. However, reviews of the scientific literature conclusively demonstrate that a link between exposure to dental materials and persistent systemic health issues has rarely been established.

LOCAL REACTIONS:

In dentistry, it's common to witness local reactions, and their diagnosis is very significant for appropriate treatment measures. Local effects might occur in the pulp tissue, in the periodontium, at the root apex, or in nearby oral tissues such as the buccal mucosa or tongue. Also, the periodontal ligament is a crucial tissue since it is adjacent to the pocket or attachment area, which is frequently a site for the accumulation of biofilms and ions, atoms, or molecules of substances released from the cervical region of dental restorations that can extend into this area. The reaction maybe an inflammation or necrosis. Further, the release of pro-inflammatory mediators may occur if cell metabolism is affected. These local effects are a function of the ability of substances to be distributed to these sites, their concentrations, and exposure times, which may range from seconds to years.

ALLERGY:

An allergic reaction to a substance can be triggered if the organism was previously sensitized to this compound. Four different types of allergic reactions are differentiated. Type I, II, and III are antibody mediated (IgE,IgG), whereas type IV is related to cells. Type I (immediate reaction) and type IV (delayed reaction) are most commonly seen in dental materials. Some materials, such as latex, can cause allergy directly by activating antibodies to the material. These are classified as Type I, II, or III reactions. Dental materials may cause localized intraoral allergic reactions or more distant extraoral reactions, such as those produced due to contact

with nickel. Also, if a patient develops sensitivities to chemicals that are chemically related, a cross-sensitivity is indicated. A dentist should be aware of such conditions before opting the dental material. For example, Palladium and nickel are both members of the same periodic table main group. Patients with nickel allergies are frequently also allergic to palladium.

OTHER REACTIONS:

These include teratogenic, mutagenic, and carcinogenic consequences. The DNA in the human genome can be altered by substances released from materials (genotoxicity). Numerous methods exist in cells to reverse genotoxic damage. Alternately, planned cell death (apoptosis) can prevent the transmission of certain abnormalities to a cell's subsequent generation. However, this consequence is known as mutagenicity if these genetic damages are passed on to the following generation. For compounds that directly attack DNA, mutagenicity can be used as a potential predictor of carcinogenic potential. The aforementioned health risks associated with this group are typically more theoretical in respect to dental materials because, as of yet, no such clinically documented damages have been associated with the use of dental materials.

MEASUREMENT OF BIOCOMPATIBILITY:

The main goal of biocompatibility tests is to protect the clinical staff and lab technicians who will be handling the materials as well as the dental patients who will be treated with them. Testing for biocompatibility is related to risk assessment because no dental biomaterial is completely devoid of the possibility of adverse reactions. A material's biocompatibility cannot be determined by a single test but rather by a combination of different evaluation methods. Different types of tests are mentioned in the fig. 1. The initial tests (phases I and II) are quick, easy, and reasonably priced. The material only progresses from simpler in vitro tests to the more complicated in vivo tests after completing the initial test. Animals or humans can be used in usage tests (clinical trials). In that they provide the final determination of whether a material is biocompatible or not, these usage tests are gold standard tests. One has to remember that assessing biocompatibility of materials using invitro assays and extrapolating the same in-vivo, anticipating the same results in oral tissues still remains debatable.

1. **INVITRO TESTS:**

   These tests are done outside the body. Placement of a material or a component of a material in contact with a cell, enzyme, or some other isolated biological system. The contact can be either direct, when the material contacts the cell system without barriers, or indirect, when there is a barrier of some sort between the material and the cell system. Direct tests can be further subdivided into those in which the material is physically present with the cells and those in which some extract from the material contacts the cell system.

Invitro measures-

- ✓ cytotoxicity or cell growth
- ✓ some metabolic or other cell function
- ✓ effect on the genetic material in a cell (mutagenesis assays

- **ADVANTAGES:** relatively quick, generally cost less than animal or usage tests, can be standardized, are well suited to large-scale screening, and can be tightly controlled to address specific scientific questions.
- **DISADVANTAGES:** As already mentioned questionable relevance to the final in vivo use of the material.

CYTOTOXICITY TESTS: The term "cytotoxicity" is used to determine biocompatibility, The potential impact a substance may have on cell survival is a clear indicator of biocompatibility. The term **'cytotoxicity'** is used to describe the cascade of molecular events that interfere with macromolecular synthesis, causing crystal clear cellular, functional and structural damage. It assesses cell death caused by a material by measuring cell number or growth before and after exposure to that material.

a) **MEMBRANE PERMEABILITY:** Membrane permeability tests are used to measure cytotoxicity by the ease with which a dye can pass through a cell membrane, because membrane permeability is equivalent to or very nearly equivalent to cell death.

b) **CELL METABOLISM/ CELL FUNCTION:** Some in vitro tests for biocompatibility use the biosynthetic or enzymatic activity of cells to assess cytotoxic response. A commonly used enzymatic test for cytotoxicity is the MTT (MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] test, as well as the NBT (nitroblue tetrazolium), XTT [2,3-Bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide salt], and WST (a water-soluble tetrazolium), all being colorimetric assays based on different tetrazolium salts.

c) **INDIRECT TESTS:** Because direct contact often does not exist between cells and materials during in vivo use, several in vitro barrier tests have been developed to mimic in vivo conditions. These tests include an agar overlay method, which uses agar to form a barrier between the cells and the material, and the Millipore filter assay, in which a monolayer of cells is grown on a filter that is turned over so that test materials are placed on the filter and leachable diffusion products are allowed to interact with the cells.

d) **MUTAGENESIS ASSAY:** It assess the effect of a biomaterial on a cell's genetic material. The Ames test is the most widely used short term mutagenesis test and the only short-term one that is considered thoroughly validated. A second test for mutagenesis is the Styles' cell transformation test. This test on mammalian cells offers an alternative to bacterial tests (Ames test), which may not be relevant to mammalian systems.

2. **ANIMAL TESTS:**

Animal tests for biocompatibility, usually involving mammals such as mice, rats, hamsters, or guinea pigs. Different from usage tests such that the material is not placed in the animal with regard to its final use.

- **ADVANTAGES:** The biological responses in animal tests are more comprehensive and may be more relevant than in vitro tests
- **DISADVANTAGES:** Difficult to interpret and control, are expensive, time consuming, and often involve significant ethical concerns.

a) **MUCOUS MEMBRANE IRRITATION TEST:** determines whether a material causes inflammation to mucous membranes or abraded skin.
b) **SKIN SENSITISATION TEST:** materials are injected intradermally to test for development of skin hypersensitivity reactions, followed by secondary treatment with adhesive patches containing the test substance.
c) **IMPLANTATION TESTS:** evaluate materials that will contact subcutaneous tissue or bone.

According to OECD Guideline, the following two guinea pig testing techniques are suggested - maximization test and Buehler test.

a) **MAXIMIZATION TEST:** In order to perform the maximization test, Freud's Complete Adjuvans (FCA) and the substance under investigation are first intradermally injected into the test subject. The same chemical is applied topically for two days at the same location seven days later. Its goal is to enhance the immunological impact of FCA and thereby increase the test's sensitivity. After this induction period of fourteen days, an additional portion of the skin is treated with the test chemical and appropriate response is evaluated.

b) **BUEHLER TEST:** The procedure is same as that of the maximization except the application of FCA. It is considered safer test to maximization test.

c) Other tests like the mouse local lymph node assay (LLNA) and mouse ear swelling test (MEST) are becoming increasingly significant.

3. **USAGE TESTS:**

Animals or human study subjects may be used in usage tests. They differ from other animal experiments in that the substance must be exposed to conditions corresponding to its intended clinical application. Usage testing typically involve larger animals, such as dogs, mini-swine, or monkeys, whose oral environments are similar to those of humans. The usage test is referred

to as a clinical trial if it involves using humans. The primary targets of usage testing in dentistry are gingival or mucosal tissues, periodontium, and dental pulp.

ADVANTAGE: Relevance - these tests are the gold standard, in that they give the ultimate answer to whether or not a material will be biocompatible and clinically useful.

DISADVANTAGES: Extremely expensive, over extended periods of time, raise numerous ethical and frequently legal issues, are incredibly challenging to correctly manage, and could potentially damage test subjects.

a) **DENTAL PULP IRRITATION TESTS:**
In healthy, intact teeth with class 5 cavity preparations, materials to be evaluated on the dental pulp are inserted. After the study is complete, the teeth are extracted out and sectioned for microscopic analysis. Tissue necrosis and inflammatory reactions are then graded based on their intensity.

b) **MUCOSAL AND GINGIVAL TESTS:**
Placing the materials in cavity preparations with subgingival extensions allows for the assessment of the tissue response to materials that come into direct contact with the mucosa and gingiva. According to the quantity of mononuclear inflammatory cells, the material's impact on gingival tissues is detected, and reactions are classified as mild, moderate, or severe. This type of study is challenging because gingival tissue frequently has some level of preexisting inflammation brought on by the presence of bacterial plaque, the roughness of the restorative material's surface, open or overhanging borders, and the over- or under-contouring of the restoration.

STANDARDS REGULATING BIOCOMPATIBILITY:

The American Dental Association (ADA) made its initial attempts to create standards for dental materials in 1926.

Unfortunately, the technological advancement of dental materials has evolved more compared to the biological compatibility recommendations and conditions of materials .

This is due to the following factors:

(1) rapid advancements in cellular and molecular biology

(2) a wide range of tests available to evaluate the biocompatibility of materials

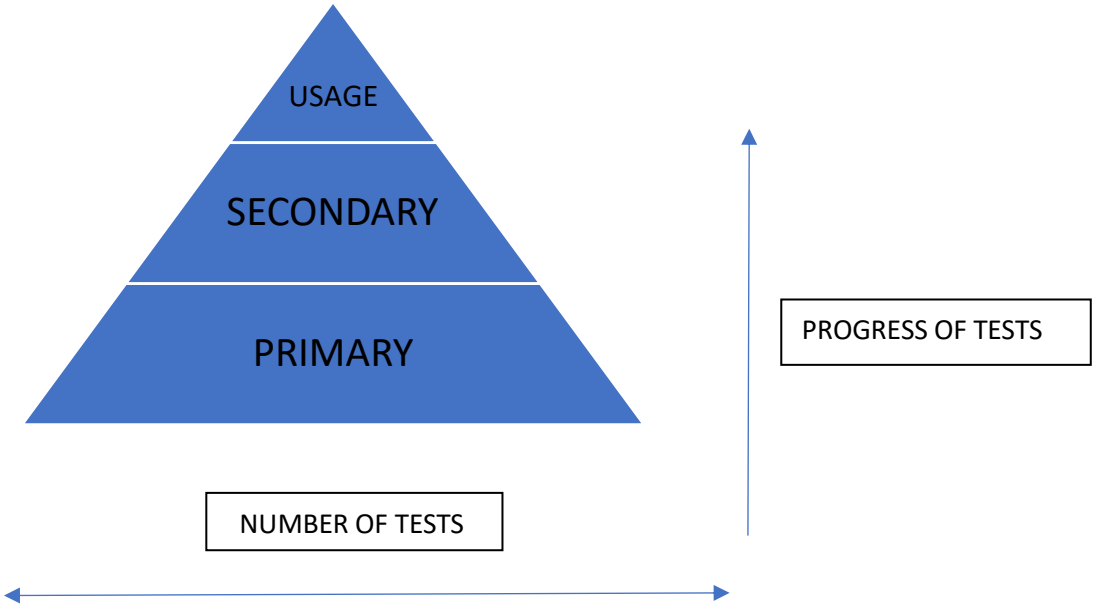
(3) a lack of standardization of these tests.

The research conducted by Dixon and Rickert in 1933, in which the toxicity of the majority of dental materials then in use was studied by implanting the materials into pockets in subdermal tissue, was one of the earliest attempts to provide a universal test for all materials. Gold, amalgam, guttapercha, silicates, and copper amalgam were sterilized and inserted into uniformly sized compartments inside skeletal muscle tissue in small, standard-sized pieces. After six months, biopsy specimens were examined under a microscope. Other preliminary

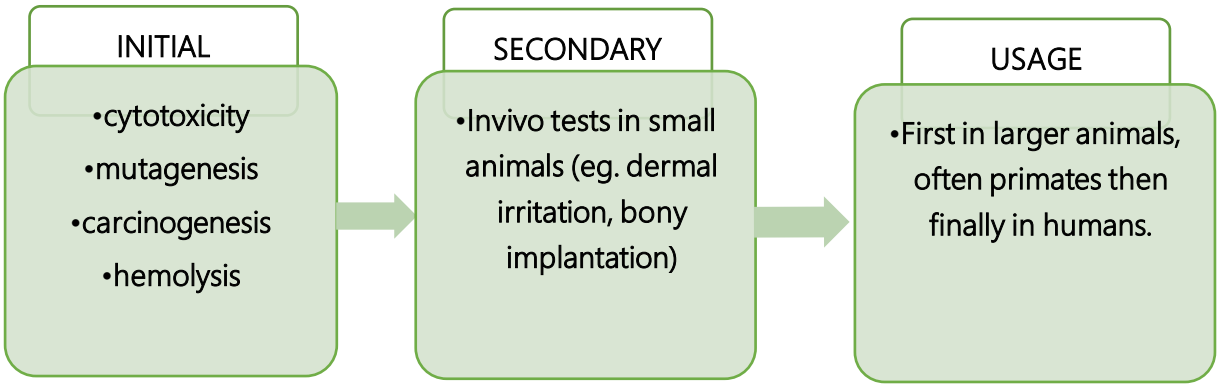
attempts to standardize methods were made on connective tissue by Mitchell (1959) and on tooth pulp by Massler (1958).

Specification No. 41 for Recommended Standard Practices for Biological Evaluation of Dental Materials was approved in 1972 by the ADA Council on Dental Materials, Instruments, and Equipment (now the Council on Scientific Affairs). This document advocated the use of **sequential testing of materials and standardized testing** procedures in order to reduce the variety of materials that would require clinical testing. This document was modified in 2005 to its current version after an addendum was added in 1982.

ANSI/ADA Specification 41



Three categories of tests are described in the 2005 ANSI/ADA (American National Standards Institute/American Dental Association) specification: **initial, secondary, and usage tests.**



ISO 10993

In the 1980s, international efforts were initiated by several organizations to develop international standards for biomedical materials and devices. Several multinational working groups, including scientists from ANSI and the ISO, were formed to develop standard ISO 10993, published in 1992. Revision of the dental components of this document resulted in ISO 7405:2008 "Preclinical evaluation of biocompatibility of medical devices used in dentistry—Test methods for dental materials." This is the most recent ISO standard available for biocompatibility testing of dental materials.

BIOCOMPATIBILITY OF RESTORATIVE DENTAL MATERIALS:

I.RESTORATIVE MATERIALS:

a) **AMALGAM:**

Amalgam fillings, which are commonly referred to as silver filling, are one of the first materials used for restoring teeth. Since many years, there has been debate concerning the biocompatibility of amalgam, which is a byproduct of the interaction between liquid mercury and silver and other metals. It is well known that mercury can be found in an inorganic form (methyl mercury), as a metal, or in one of two charge states. It is well known that methyl mercury is extremely hazardous when present. Methyl mercury (free mercury) has caused hazardous effects like contact dermatitis in the hat business, in environmental catastrophes, and when seafood is consumed. The body is capable of absorbing mercury vapor easily. Inhaled mercury vapor can cause damage to the brain, kidneys, and other major organs. After being inhaled into the lungs, it is transported through the blood to the brain. If eaten, the metallic form of mercury present in an

amalgam reaction is difficult for the digestive system to absorb. Due to the chemical reaction that unites it with the other metals in the amalgam to create an alloy, it is entirely combined with them.

Tests on cell cultures have shown that the free Hg in amalgams is harmful.

Amalgams are toxic to cells in culture when copper (Cu) is added, but when set for 24 hours, so-called low-Cu amalgams (i.e., 2-5% Cu), do not even inhibit cell growth. Low-Cu amalgams are well tolerated according to implant studies, whereas so-called high-Cu amalgams (i.e., 20–40% Cu) induce severe reactions when in direct contact with tissue.

CAVITY TYPE	RESPONSE FOR AMALGAM
Shallow, deep lined cavities	Minimal response, no irreversible damage
Deep unlined cavities (>0.5-1mm remaining dentin thickness)	Pain

Hg from amalgams in humans and dogs does not get to the pulp, according to research. According to the conceptual terms, Hg does not dissolve but rather seeps back into the amalgams and continues to react with the alloy cores that had not yet been reacted to it. An "amalgam tattoo"—a benign discoloration of the mucosa caused by embedded amalgam particles. Any pulpal reaction to amalgams appears to be primarily linked to the physical insertion of the amalgams, specifically the pressure of condensation and tends to be of very short duration. Some people are still concerned about the presence of amalgam fillings and even want them to be removed. But removing the filling for no other dental-related reason could be more detrimental than helpful. This is due to the fact that drilling existing fillings would result in the production of more mercury vapor and the unnecessary inhalation of increased mercury vapor by the patient. There is no proof of any mercury poisoning from dental amalgam to the patient based on available evidence, according to studies examined by the US Public Health Service and the Food and Drug Administration, with the exception of cases of allergy. Although amalgam appears to be safe for use in the mouth, dental practitioners who are exposed to it on a regular basis may have concerns. A recent study showed that those who handle amalgam while working in a dental setting have higher amounts of mercury in their blood. Implementing adequate regulatory safety precautions, such as donning protective masks and gloves, could help prevent increasing mercury levels in dentists' blood. It can be concluded that amalgam remains a viable option for restorations since it seems to be a biocompatible material that does not cause harm to the human body. The increased exposure to electromagnetic fields brought on by everyday objects like Wi-Fi routers, computers, mobile devices, and MRIs also raises a fresh question about the safety of amalgam fillings. Further future research is required on this aspect for continued usage of amalgams.

b) GLASS IONOMER CEMENTS:

Wilson and Kent were first to introduce glass ionomer cements, which have been utilized in dentistry since 1969. Glass ionomer has been used as a cement (luting agent), liner, base, and restorative material. A freshly prepared ionomer is slightly cytotoxic, but this effect lessens with time, according to screening studies. In vitro cytotoxicity is caused by the fluoride release

from these compounds. Glass ionomer materials' overall pulpal biocompatibility has been linked to the high molecular-sized polyacrylic acid's inability to diffuse into dentine. Histological investigations reveal that any inflammatory infiltration from an ionomer is low or absent after 4 weeks, and usage tests suggest that the pulp reactions to these cements are often mild. Following the insertion of glass ionomers into cervical cavities, pulpal hyperalgesia has been reported for brief intervals (days). The enhanced dentin permeability following acid etching is most likely the cause of this phenomenon. In any case, it has been demonstrated that glass ionomer, used as a direct pulp capping agent, is not well tolerated when applied directly to living pulp tissue.

c) ZINC OXIDE EUGENOL:

Upon direct contact, eugenol (4-allyl-2-methoxyphenol, C10H12O2) emitted from Zn oxide (ZnO) eugenol cements (ZOE) fixes cells, inhibits cell respiration, and decreases nerve transmission, according to investigations conducted in vivo and in vitro. Eugenol has dose-dependent effects, and eugenol is significantly diluted by diffusion through dentin. The ability to seal and the antibacterial effect seem to speed up pulpal healing but eugenol is an irritant when it comes into contact with connective tissues.

d) ZINC PHOSPHATE CEMENT:

According to in vitro screening experiments, Zn phosphate Zn3(PO4)2, cement causes strong to moderate cytotoxic effects that weaken over time due to Zn ion leaching and a low pH, preserving the pulp. Zn3(PO4)2 cements were injected into rat dental pulp during implantation studies, and the resulting focal necrosis validated the cement's cytotoxic effects on pulp tissue. Deep-cavity preparations have demonstrated moderate to severe localized pulpal damage within 3 days of usage tests, which is likely due to the initial low pH (i.e. pH 4.2 in 3 min). After 48 hours, the pH of the set cement, however, approaches neutrality. Under Zn3(PO4)2 cement in deep cavities, it is advised to apply a protective layer of a dentine-bonding agent, ZOE, cavity varnish, or Ca(OH)2.

e) ZINC POLYCARBOXYLATE CEMENTS:

In short-term tissue culture assays, the release of Zn and fluoride ions into the cell culture media as well as a lower pH have all been associated with the cytotoxicity of freshly-set and fully-set cements. Additionally, tissue culture assays suggest that polyacrylic acid doses greater than 1% are cytotoxic. However, testing on bone implants and subcutaneous tissue conducted over a year did not reveal these cements' long-term cytotoxicity. As a result, additional mechanisms, like buffering and protein binding of these chemicals, may eventually neutralize these effects in vivo. These cements have low reparative dentine generation, hence they are only advised for use in the floor of cavity preparations with intact dentine.

f) LINERS:

Cavity liners made of Ca(OH)2 are available in variety of forms, including modified versions that contain ZnO, titanium dioxide (TiO2), and certain resins, as well as saline suspensions with a high alkaline pH (>12). Ca(OH)2 in suspension has a high pH, which causes severe cytotoxicity in screening assays. When pulp tissue is exposed to these extremely alkaline aqueous pulp-capping compounds, the immediate reaction is necrosis to a depth of 1 mm. Any hemorrhagic exudates of the superficial pulp are also helped to coagulate by the alkaline pH. Neutrophils invade the subnecrotic region shortly after necrosis develops. Only a minor inflammatory reaction is left after 5-8 weeks. The necrotic zone experiences dystrophic calcification within weeks to months, which then appears to be a stimulant for dentine bridge development. A number of in vivo investigations using various resin-modified glass ionomer cements as liners had no pulp damage reported as well. Due to their antibacterial properties, thermal isolation, and biocompatibility with the pulp tissue, hard-setting cements such Ca(OH)2 have been used as bases or liners.

g) BLEACHING AGENTS:

These products are frequently found in the form of a gel that can be administered to the teeth by a dentist or a patient at home. The peroxide in these products is either hydrogen peroxide or carbamide. Depending on the material's formulation, the agents may remain from a few minutes to many hours in contact with the teeth. Peroxides can quickly (within minutes) and in high enough quantities to be cytotoxic cross the dentin, according to in vitro research. The amount of peroxide in the bleaching chemical has a big impact on how hazardous it is to cells. Even more research has revealed that peroxides can quickly penetrate healthy enamel to get to the pulp in a matter of minutes. Bleaching has been shown to have harmful pulpal effects in in vivo investigations, and the majority of research concur that there is cause for concern over the prolonged use of these treatments on teeth. Although the exact cause of these reactions is unknown, using these medications frequently results in tooth sensitivity, according to clinical research. If the agent is not used properly, bleaching agents will also chemically burn the gingiva.

h) ETCHANTS:

The mineral acid H3PO4 (PHOSPHORIC ACID) is moderately potent yet highly corrosive, and if it were to come in contact with the gingiva or the lip, it might cause severe burns of the soft tissues. As a result, etchants that spill onto tissues from the teeth should be thoroughly washed off with water.

Hydrofluoric acid, on the other hand, is toxic and has a potent corrosive impact on living tissues, hence it should only be used extra orally.

i) BONDING AGENTS:

Several bonding substances have been created and are used in dentin while restoring a tooth. The biocompatibility of these bonding systems has been the subject of numerous research. If

evaluated in vitro alone, several of these chemicals are harmful to cells. To decrease cytotoxicity, the manufacturer recommends applying to dentin and rinsing with water in between applications of additional reagents. The components of the bonding agents, however, may permeate the dentin up to 0.5 mm, according to longer-term in vitro investigations, and significantly restrict cellular metabolism for up to 4 weeks after application. In tissue culture, the hydrophilic resin hydroxyethyl methacrylate (HEMA), which is present in a number of bonding systems, is at least 100 times less cytotoxic than Bis-GMA. However, studies employing long-term in vitro systems have demonstrated that when exposure times are raised to 4 to 6 weeks, detrimental effects of resins occur at considerably lower doses (by a factor of 100 or more). The presence of a dentin barrier considerably lessens the cytotoxic effects of many resin components. The dentine surface that is left after being cut, such as during a cavity preparation, is covered by a 1-2 lm layer of organic and inorganic debris known as the "smear layer".The smear layer not only covers the dentine's surface but is also deposited inside the tubules to create dentinal plugs that, when viewed under an electron microscope, seem impenetrable. This debris considerably decreases the flow of tubular fluid. For restorative materials to adhere and be biocompatible, the presence of this smear layer is crucial. There is however some proof that HEMA is harmful in vivo if the dentin in the cavity preparation's floor is thin (0.1 mm). But still, but HEMA has been shown to stimulate the expression of growth factors in mouse odontoblast-like cells. Most commonly used resins in bonding agents, including Bis-GMA, triethylene glycol dimethacrylate, urethane dimethacrylate (UDMA), and others, have been shown to be in vitro cytotoxic in other investigations. HEMA and other resins included in dentin bonding agents could collaborate synergistically to have cytotoxic effects in vitro.

j) RESIN BASED MATERIALS:

Resin-based composites (RBC) have been employed as cements and restorative materials for tooth restorations. They are known as resin composite materials because they combine organic and inorganic components. These materials consist of monomers, fillers, initiators, accelerators, and additives that are combined through some type of a curing reaction.

These fillings could include substances like Bisphenol A (BPA) that become toxic when released as monomers. Several monomers that make up RBC are synthesized using BPA, including BPA-glycidyl methacrylate (BisGMA). BPA residues are frequently present during the process of creating RBC material. BPA is in the class of xenoestrogens. Xenoestrogens are chemicals that are known to be endocrine disrupters, and they inhibit normal hormone function. One test commonly used to assess xenoestrogenic activity is the E-screen assay. This in vitro test relies on the growth response of breast cancer cells, which are sensitive to potential estrogenic compounds.

The mean degree of conversion (DC) for each of the composites was between 60 and 70%. Depending on the type of composite, the total monomer release varied significantly. The composite that resembled paste had the least amount of monomer elution. This can be attributed to the fact that it initially contains less resin. It is also applied in layers, allowing for better healing. Lower DC and more monomer release were obtained with four mm bulk placement. Evidently, complete polymerization of the material is less successful when curing through a

thicker layer of composite material. As a result, greater amounts of toxic monomers are released.

It's interesting to note that dental professionals are more likely to experience asthma attacks and other respiratory problems, while a specific explanation is unknown. This observed phenomenon might be caused by composite dust particles that were released into the atmosphere. It is necessary to take further steps to limit the inhalation of composite dust. To lessen the exposure to harmful composite dust, perhaps improved safety masks should be used.

Freshly set chemically cured and light-cured resins frequently produce mild cytotoxic responses in vitro after 24 to 72 hours of exposure in cultured cells. Evidence suggests that light-cured resins are less cytotoxic than chemically cured systems, however the effectiveness of this impact depends greatly on the type of resin system and the light's curing efficiency. The pulpal inflammatory response to chemically and light-activated resin composites was low to moderate after 3 days when they were placed in cavities with approximately 0.5 mm of remaining dentin. The response of the pulp to resin composite materials is negligible in the presence of a protective liner or a bonding agent. Although the long-term consequences of placing resins directly on pulpal tissue are unknown.

The allergic reactions associated with resin-based materials, such as resin composites, affect patients, as well as the dental personnel working with such materials. About this in- vivo effects of released composite components on soft tissues, very little is known. Although there haven't been many clinical investigations, there is some evidence that methacrylate-based composite components may significantly increase the likelihood of hypersensitivity. On the other hand, allergic reactions to acrylic resins have been linked to contact dermatitis, thus there is a risk.

k) CERAMICS:

Other than wear on the opposing teeth and/or restorations, indirect ceramic restorative materials, sometimes known as dental porcelains, are said to have no biological effects. Dental ceramics are thought to have a relatively low relative incidence of biological side effects when compared to other restorative materials. However, according to Roulet et al., ceramics have no long-term consequences.

Zirconia (also known as zirconium dioxide, ZrO_2) is an incredibly dense, inert, and hard material that is also quite biocompatible. ZrO_2 is currently employed for a variety of applications, including as root canal posts to strengthen non-vital teeth.

II.ENDODONTIC MATERIALS:

a) SODIUM HYPOCHLORITE:

The most commonly used irrigation fluid for root canal preparation is sodium hypochlorite (NaClO) because of it's pulpal dissolution and strongest antimicrobial property. At high concentrations, NaClO is extremely toxic and tends to irritate tissues when it comes into contact with them. According to reports, 0.025% NaClO is the safest concentration to employ since it has bactericidal actions without tissue-toxic effects. A concentration as low as 1:1000 in saline can completely hemolyse red blood cells in vitro. Because a pH level close to neutral has the best antibacterial effect with the least amount of tissue irritant effect, it may be reasonable to use 0.5–1% of NaClO in endodontic irrigation. The majority of problems associated with the use of NaClO seem to be caused by its unintentional injection beyond the root apex, which may result in strong tissue reactions characterized by pain, edema, and bleeding. It has been observed that NaClO might cause hypersensitivity reactions, paraesthesia, and secondary infections in some cases.

b) EDTA

The chemo mechanical enlargement of root canals is enhanced, the smear layer is removed, and the dentinal walls are cleaned and disinfected using EDTA frequently in endodontic therapy. When EDTA leaks into the periapical tissues during root canal preparation, this may decrease macrophage activity and change how the periapical lesions respond to inflammation.

c) CALCIUM HYDROXIDE MEDICAMENT:

In vivo studies have shown that Ca(OH)2 intracanal dressings effectively removes the majority of bacteria from infected root canals 7 days, 4 weeks, and 3 months afterwards. Ca(OH)2 intruded to the periapical area seems to be well tolerated and is thereafter reabsorbed.

d) GUTTA PERCHA:

80% of gutta-percha is made up of ZnO, which is what gives gutta-percha its radiopaque quality (60–70%). The added complication of heat generation during obturation, which could be harmful to periodontal tissues, is imposed by warm gutta-percha procedures. It has been claimed that some commercially available gutta-percha points are highly cytotoxic due to the substances added to the base material, particularly Zn, as this might leak into the surrounding soft tissues, which is regarded as a critical level at which irreversible damage to the periodontal tissues can occur. Because no impact has been noted on the incidence of chromosomal abnormalities in in vitro tests, pure gutta-percha can be regarded as completely biocompatible.

e) CHLORHEXIDINE:

Human keratinocytes and fibroblasts were used in the wet disc assay to investigate the cytotoxicity of the antiseptic CHX and other antimicrobial compounds as well as their microbic impact.The CHX that was tested was consistently effective against six strains of frequent microorganisms found in burns, however it was unsuitable for clinical usage due to its significant cytotoxicity. Therapeutic mouth rinses used to treat gingivitis contain CHX digluconate as one of the active components.

f) MINERAL TRIOXIDE AGGREGATE:

Mineral trioxide aggregate (MTA) has been a popular a root-end-filling material over the past decade. In one study, Portland cement was discovered to contain the same chemical elements as Mineral Trioxide Aggregate (MTA), which suggests that Portland cement has the potential to be used as a less expensive root-end-filling material in dental practice. Additionally, it has been demonstrated that Portland cement has the same biocompatibility as MTA.

g) CHITOSAN:

A macromolecule called chitosan is generated when D-glucosamine, which comes from the deacetylation of chitin found in the shells of marine crustaceans, particularly crabs and prawns, is repeated. It is a fiber that is indigestible and chemically comparable to cellulose. Chitosan is a natural polysaccharide that is non-toxic, biocompatible, and biodegradable and has been shown to have antibacterial properties .

OTHER MATERIALS:

LATEX ALLERGY:

Natural rubber latex is a substance that can be found in a variety of dental supplies, including gloves, rubber dams, and toys that kids utilize during dental procedures including pacifiers, nursing bottles, and balloons. Patients with latex hypersensitivity can be categorized as type IV or type I, and dermatitis, swelling, redness, and irritation have been described after contact with latex.

CONCLUSION:

The manufacturer is in charge of guaranteeing the safety of its products when used in accordance with instructions, but the healthcare professionals should validate that all necessary testing has been carried out. Dentists should be aware that no material is completely free of potential adverse effects. It should be clear that dental professionals cannot select restorative materials for their patients by just using a guidebook method. Instead, they must ensure that any possible risks are reduced by using their best clinical judgment, which is supported by scientific data, their own dental experience, and, when appropriate, statements from patients, their doctors, and prior dentists. The patient should be told of the advantages and disadvantages of the suggested treatment as well as any potential alternatives after the practitioner has made a treatment decision. The patient must thereafter give consent for the suggested treatment in order for medical and legal requirements to be addressed.

REFERENCES:

1. Chiayi Shen, H. Ralph Rawls, Joséphine F. Esquivel-Upshaw, Eugene W. Skinner, Ralph W. Phillips, Kenneth J. Anusavice, Phillips' science of dental materials, English, 2022, 13th edition, Elsevier, St. Louis, Missouri.

2. Ronald Sakaguchi, Jack Ferracane and John Powers, Craig's Restorative Dental Materials,2019, 14th edition, Elsevier.

3. Gottfried Schmalz Dorthe Arenholt-Bindslev, Biocompatibility of Dental Material, 2009 Springer-Verlag Berlin Heidelberg.

4. Murray PE, García-Godoy C, García-Godoy F. How is the biocompatibilty of dental biomaterials evaluated?. Med Oral Patol Oral Cir Bucal 2007;12:E258-66

5. Mallineni SK, Nuvvula S, Matinlinna JP, Yiu CK, King NM. Biocompatibility of various dental materials in contemporary dentistry: a narrative insight. J Investig Clin Dent. 2013 Feb;4(1):9-19.

6. Noble, A. (2020). The Biocompatibility of Various Dental Materials. The Science Journal of the Lander College of Arts and Sciences, 13(2), 13-20.

7. St John KR. Biocompatibility of dental materials. Dent Clin North Am. 2007 Jul;51(3):747-60.

8. Shahi,Shahriar;Özcan,Mutlu;MalekiDizaj,Solmaz;Sharifi,Simin;Al-HajHusain,Nadin;Eftekhari,Aziz;Ahmadian,Elham(2019).Areviewonpotentialtoxicity of dental material and screening their biocompatibility.Toxicologymechanismsandmethods,29(5):368-377

9. Dr. Dakshita Joy Sinha, Dr. Ashish Amit Sinha, Dr. Agrima Vasudeva Review", International Journal of Current Research, , 7, (6), 17379-17382