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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – I - BIOMATERIALS AND ARTIFICIAL ORGANS– SBMA7001

I. INTRODUCTION

Biomaterials is defined as the synthetic material that is used to replace or restore function to a body tissue and is continuously or intermittently in contact with body fluids.

Characteristics of Biomaterials

i) Biocompatable
ii) Nontoxic
iii) Noncarcinogen
iv) Good physical mechanical properties

Modulus: Elastic modulus = stress / strain, young's modulus – when force is applied, the object is deformed.

v) Low cost
vi) It must be readily available
vii) Moulded into different shape
viii) Resistant to degradation
ix) Acceptable strength
x) Resistant to wear

Application of Biomaterials

1. Orthopedic – prosthetics used to replace joint affected by arthritis. Eg. Fixation devices.
2. Cardiovascular application – artificial heart valve, stunt, etc.
3. Ophthalmology – intraocular lens and contact lens
4. Dental braces, filling, dental cap.
5. Wound healing – sutures and graft.
6. Drug delivery system – controlled and targeted delivery of drugs (doctor delivers drug to patient in remote areas).

History of Biomaterials

- Earliest operation were performed by surgeons for restoration of missing parts.
- Susbruta in 600 B.C. he repaired injured nose with a patch of living flesh taken off from the region of the cheek.
- Sicilian Laymen in 1430, nose construction was done by using skin flap taken from arms.
- In 19th Century, modern implant development was seen by repairing long bone and joints.
- In 1893 – 1912 plate using steel was designed for fracture.
- In 1930 use of polymers was designed.
- In 1950, heart valve implantation was possible only after the development of open heart surgery.
- In 1944 dialysis of human beings was discovered.

Classification of biomaterials

Biomaterials have been classified into 4 different types.

i) Metals
ii) Polymers
iii) Ceramics
iv) Composites – stainless

Metals.

- Widely used for load bearing implants
- Wire, screw, plates, artificial joint for hip, knee, shoulder etc.
- Metal used as stainless steel, titanium and its alloy and cobalt based alloy.

Polymers

- Polymers resembles soft tissues and their application range from facial prosthesis to tracheal tubes, bladder, lens, tendons, etc.
- It can be used as sutures, catheters.

Ceramics

- Ceramics have been widely used in restorative materials in dentistry. The includes materials for crown (baby), cement, dentures (adult).

Composites

- The most successful composite are used in the field of dentistry as restorative material or dental cement.
- Carbon – carbon and carbon – reinforce polymer composites are used for bone repair and joint replacement because of the low elasticity modulus level.

Impact of biomaterials

- In the early days, relatively few engineering materials such as stainless steel, chromium, etc. were used to make artificial hearts with simple design.
- Today field of biomaterials has evoked more than 50 different materials in various types of complex prosthetic devices.
- The development of biomaterials used in medical devices as occur in response to growing number of patient afflicted in traumatic and non traumatic conditions.

Examples

- Arthritis – leading to joint disorder which needs correction.
- Total knee and hip replacement are achieved by using implants that are composites of metal polymer and ceramics
- Implants which are regularly used in ophthalmology includes lens implants, corneal transplant and protective corneal shields.
- Facial implants – purely cosmetic surgery
- Oral implants is of two types: i) artificial teeth or dentures, ii) implants is totally implanted in oral cavity.
- Vascular graft are made of synthetic polymer which are routinely used to replace aorta.
- Cancer a large number of implants are used for reconstructive surgery of the breast.

Strength of the (biological tissue) biomaterials

- Strength of the biological tissue can be determined by static and compression tension, torsional and b ending, dynamic impact load (or) fatigue oscillative.

Interfacial phenomenon

- There are 4 types of biomaterials in term of interfacial response of tissue.
- Type 1 – hearty inert, smooth surfaces
- Type 2 – nearly porous surfaces inert
- Type 3 – controller reactive surfaces
- Type 4 – Reasonable

Type 1: These materials achieve suitable combination of physical properties with a minimal of physical properties with a minimal toxic response in the host. The physical response of the implant always produce some response in the adjacent tissue which yield thin fibrous capsules (0.1 – 10 μm(surrounding the implant. In these cases, the lack of adherence of the capsule to implant results in motion of the tissue implant interface and under stress are flow and its responsible for the lifetime limitations of many devices.

Type 2 & 3: Improving interfacial stability, when the rate of surface reaction are correctly controlled where repairing tissues are incorporated structurally within the reactive layers on the implant surface, rendering stability to the implant.

Type 4: Biomaterial designed to the ultimately replaced by regenerating tissue, eliminating the original interface altogether and there is no discernible difference between implant site and host tissue after resorption is complete.

Metal and alloys for orthopedics implants

i) Stainless steel (SS)

- The first stainless steel used for implant material was 18 – 8 (type 302) which is stronger than vanadium steel and more resistant to corrosion.
- Vanadium steel is no longer in use in plants since it is corrosion resistant.
- Later 18 – 8s MO (molybdenum) SS was introduced which contains MO to improve the corrosion resistant in salt water.
- This alloy is known as type 316 SS. In 1950 the carbon content of 316 SS was reduced from 0.08 wt% - 0.03 wt%.
- This is better for corrosion resistance in chloride solution. This alloy is known as 316L.
- Chromium is the major component of corrosion resistant SS. The minimum effective conc. of Cr is 11 wt%
- Cr and its alloy gives an excellent corrosion resistant. The SS especially type 316 and 316LL are most widely used for implants. This group of SS is non-magnetic and possess better corrosion resistance than any other.
- American society for testing a material recommends type 316 L rather than 316 for implant fabrication.

Properties of SS

- A wide variety of properties can be obtained depending on the heat treatment – to get soft materials.
- Cold working of implant is done to get greater strength and hardness.
- The designer must be careful when selecting materials even the type 316L stainless steel may corrode inside the body due to high stress and oxygen depletion.
- So it can be used as a temporary devices such as facture plates, screws and hip nails.

Manufacture of implant

SS cannot be cold work with intermediate heat treatment

↓

Heat treatment should not induce Cr carbide which may cause corrosion

↓

It can be overcome by controlling the uniformity of heating

↓

Another undesirable effect of heat treatment is the formation of surface oxide scales

↓

↓

Which can be removed either chemically by acids

After scales are removed

↓

Surface components is polished to a mirror or map finished

↓

Surface is then cleaned degreased with nitric acid

↓

Component is washed and cleaned again before packaging and sterilizing

Biomedical application

- Orthopedic implants
- Major uses includes fracture, fixation and joint replacement
- It is used in hip joint, ankle joint, knee joint, intramedullary pins bone plates and screws.
- Cobalt based alloys
- These materials are usually referred to as Co-Cr alloys
- There are basically 2 types
- (a) Co Cr Mo alloys which is usually a cast product (b) Co Cr Ni Mo alloy which is usually wrought by hot togging
- The castable Co Cr Mo has been widely used in dentistry and recently in making artificial joints
- The wrought or forged alloy – Co Ni Cr Mo alloy is used for making the stems of prosthesis for heavily loaded joints such as knee and hip
- Types of cobalt based alloy
- ASTM listed 4 types of cobased alloy that are applicable for surgical implant application.

i) Co Cr Me alloy (F76)
ii) Wrought Co Cr W Ni alloy (F90)
iii) Wrought Co Ni Cr Mo alloy (F562)
iv) Wrought Co Ni Cr Mo W Fe alloy

(F563) are widely used alloy at present

Properties of cobalt based alloys

The two basic elements of a cobalt based alloy form a solid solution upto 65% wt cobalt (Co) and the remainder is Cr.

- The molybdenum is added to produce fine grains which results in higher strength after casting or forging.
- Wrought cobalt based alloys is the Co ni Cr Mo alloys which has high degree of corrosion resistance to sea water.
- Cold forging can increase the strength of the alloy
- Hot forging can be used to fabricate and implant with an alloy (hip joint stem)

- Cast and wrought alloys have excellent corrosion resistance.

Manufacture of co based alloys.

- Cobased alloy can be used in one of three forms

i) Cast
ii) Wrought
iii) Forging

Casting

- The orthopedic implant of Co – Cr alloy are made by casting process
- Wax model of the implant is made
- Ceramic shell is built around the wax model
- Ceramic shell is pot fired to obtain the required mold strength
- Match metal alloy is then cold into the shell after cooling the shell is removed to obtain metal implant.

Wrought

- It possess a uniform structure with fine grains
- Wrought Co Cr Mo alloy can be further strengthened by cold wrought

Forged alloy

- Forged alloy is produced by hot forging process
- Forging of Co – Cr – Mo requires sophisticated and complicated tooling press
- These factors make it more expensive to fabricate a device from Co Cr Mo forging then from casting
- Disadvantage of casting produce large grains and metallurgically, imperfection when compared to wrought alloy and forged alloy.

Application

- Porous coated Co Cr implants have been extensively used for bone in growth application
- Sintered beads, plasma flame sprayed metal powders are used as coating on Co Cr orthopedic implants.
- Ti and Ti based alloys Its low density and good mechanochemical properties are salient features of implant applications.
- It is relatively high cost and reactive in nature.
- Pure Ti is a very useful material have produced better results.
- The most important one Ti alloy is Ti (6% Al, 4% is widely used to manufacture implants.

- The main alloying elements of the alloy are Al (5.5 – 6.4 wt%) and Va (3.5 – 4.5 wt%)
- Mostly recently this alloy has been used for the production of hip prosthesis, fracture equipment and has largely replaced pure metal in many applications.

Structural properties of Ti and Ti alloys

- Ti is a two allotrophic materials that exists as a hexagonal crystal structure (□-Ti), temperature is 882.5°C.
- Centre cubical structure above that temperature (□-Ti)
- Al tends to stabilize the □-phase, that is increase the transformation from □ to □
- Vanadium in a titanium – aluminium alloy tends to form □, □ two phase system at room temperature.
- Ti-Al 4V is generally used in one of three conditions.
  i) Wrought
  ii) Forged
  iii) Cast
- Wrought alloy is available is standard shape and size and it is annealed at 700°C at using furnace cooled to 600°C and air cooled to room temperature.
- Forged alloy – the typical hot forging temperature is between 900 to 980°C. Hot forging produces a fine grained □-structure with the dispersion of □-phase.
- Cast alloy metallurgically stable homogeneous structure casting or annealing at approximately 840°C.
- Ti is very reactive material and its surface can be modified by
  i) Oxide layer may be enhanced by suitable oxidizing treatment such as anodizing
  i) Surface can be hardened by the diffusion of interstitial atoms into surface layers.
  ii) Flame spraying of metals on the surface.
  iv) Metals can be electroplated on the surface.

Manufacture of implants

- Ti is very reactive at high temperature and burns readily in the presence of oxygen.
- It requires inert atmosphere for high temperature processing are processed by vacuum melting
- Oxidises diffuses rapidly in Ti and embedded in metals
- So hot forging should be operated at 925°C followed by electrochemical machining to obtain a metal implant.

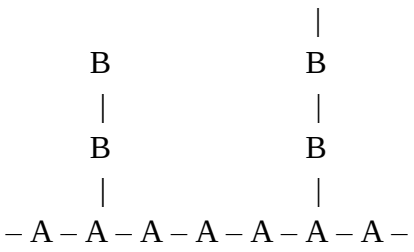
POLYMERS IN BIOMEDICAL USE

Polymers: Polymers are large molecules built by repetition of small simple chemical unit (monomers)

Polymers are of various types.

i) Linear
ii) Branch
iii) Cross-linked

- Homopolymer is the simplest and made up of identical units linearly
- Oligo polymer
- It has less than 10 monomer units eg. Oligostyrene, copolymers made up of two monomer units by polymers. Eg: methylvinyl ether copolymer.
- Types of copolymer chain
- Random : –A – A – B – A – B – A – A – A – B –
- Alternate: – A – B – A – B – A – B –
- Block: – A – A – A – B – B – B – A – A – A –
- Graft:



Classification of polymers

Natural and synthetic

- It occurs naturally in the nature eg. Cotton, silk, protein, wool and rubber
- Synthetic: it is from low molecular weight compound eg: polyethylene, PVC and nylon

Inorganic and organic

- The main side chain is made up of carbon atom eg: H, N, 0 is attached to main chain

Inorganic

- It main chain is made up of atom other than carbon eg: glass, silicon, rubber

Thermoplastic	**Thermosetting**
Heat is applied It becomes soft then its reshaped	Heat is applied It is infusible and insoluble mass

Eg: PE, PVC Eg: Epoxy resins

Plastics, Elastomers, fibres and liquid resins.

Classification of ultimate forom

Plastics: It shaped to hard and tough particles eg: PVC and PMMA

Elastomers

- It is vulcanized into rubbery product with strength and elongation. Eg: Silicon rubber and natural rubber.

Fibres

- Long filament with length 100 times the diameter. Eg. Nylon.

Liquid resins

- It is used as adhesive and ceiling agent. Eg. Epoxy adhesive.

Synthesis of polymerisation

- Takes place by two mechanism: i) addition polymerization, ii) condensation polymerization.
- Addition polymerization: Rearrangement of bond, Double or triple bond breakage. It requires 3 steps: i) initiation, ii) elongation, iii) termination.
- Condensation polymerization: elimination of small molecules or atoms (H_2O).
- Polymers in biomedical use: it is widely used in surgery, dentistry, ophthalmology, orthopedic, pharmacy, etc.
- Polyethylene: Simplest hydrocarbon polymer. $-(CH_2 - CH_2 -)_n$
- Preparation: Reacting ethylene gas at high pressure (100 – 300 MPa) at 180 – 250^oC in presence of O_2 (0.1%) or peroxide catalyst.
- Grade: LDPE – 6000 – 40,000 – branched polymer high density
  HDPE > 40,000 – 2 Million – Linear polymer
  UHMWPE > 5 million – ultra high molecular weight ethylene

Specific properties

Low cost

i) Easy processability
ii) Excellent chemical resistance
iii) Toughness and flexibility
iv) Excellent electrical insulation

Properties of different grade of PE

v) LDPE

- High to ear strength
- Low density
- Extreme flexibility
- Chemical and moisture resistant

vi) HDPE

- High density
- Stiffness
- Low gas permeability
- High tensile strength
- Chemical resistance

Applications

- LDPE : It is used widely in sheet and film
- HDPE: It is widely used in container, drum and gas tank
- KHMWPE: It is widely used in orthopedic implant, total knee and hip joint replacement.
- Fabrication of acetabular up in artificial joints.

Polypropylene (PP)

$$-\left(CH_2 - \underset{\displaystyle CH_3}{\underset{|}{CH}}\right)-_n$$

- It has 2 conformations
- Isotactic – methyl group on one side
- Syndiotactic –methyl group on alternate side
- Molecular weight : 5 □ 10^5
- Lightest polymer

Properties

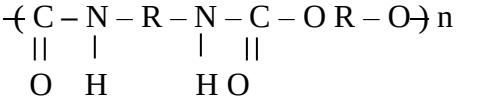
□ High stiffness and hardness

- High tensile strength
- High strength to weight ratio
- Meltingpoint is 100^{o}C. It can be sterilized.

- Insoluble at room temperature
- Good mechanical and dielectrical property
- When heated at above melting point, it is dissolved, chlorinated to aromatic hydrocarbons.

Applications

- It is used as a sutures, i.e. monofilament of PP for prolene



- Common urethane linkage (– O – CO – NH)
- Presence of additional O_2 atom gives flexibility

Properties

- It is not resistant to abrasions
- High resistance to breaking
- High modulus of elasticity
- Resistant to fatigue
- Good bio and blood compatibility

Applications

- Segmented PV used in extruded blood tubings.
- Crosslinked PU – long term surgical implants
- PU copolymers – used to fabricate heart arrest device and aortic patch grafts
- Polyether PV – commonly used for heart surgery. It has good mechanical property and hydrolytic stability.
- Polymethyl methacrylate (PMMA)
- It is prepared by radical polymerization of acetone (acrylic acid derivative)
- It is cast molded (or) machined
- It is referred as plexi glass (or) organic glass
- Available as 2 components
- Powder – small PMMA spheres / beads
- Liquid – having monomers
- It is mixed in ratio 2:1 and donga made which cures in ten minutes.
- It is used in dental fillings.

Properties

- Very brittle, excellent light transparency
- High refractive index (1.4 g)

- Excellent chemical resistivity
- Highly biocompatible
- Good strength and life period
- Soluble in ketone, chlorinated hydrocarbon
- Amorphous in nature.

Application

- Used in contact lens preparation
- Implantable ocular lens.
- Bone cement for joint fixation
- Dentures
- Maxillofacial prosthesis
- In orthopedic surgery, it is used in hip replacement.
- Polytetrafluoroethylene (PTFE)
- Teflons
- It is similar to PE but replaced by fluorine
- Molecular weight 610 □ 10^6
- It has unique stability – extreme inertness, strength of covalent bonds

Properties

- Good chemical and thermal stability
- High crystalline melting point (> 250^{o}C)
- High thermal stability
- Extremely resistant to chemical attack
- High dielectric strength
- Unique non adhesion and anti frictional property
- High density (2.15 – 2.2 g/cm^3
- Low tensile strength
- Low modulus of elasticity
- Low surface tension.

Applications

- Tissue tolerance of PTFE graft is good healing and rapid.
- Used in cardiovascular circulation
- Sutures used for fixation of heart valve prosthesis
- Tabe fine application it is used as graft
- Sheets and films used for in bypass surgery reconstruction madillofacial area
- PTFE shunt is used to carry CSF from brain to venous system for the treatment of hydrocephalus
- Polyhydroxyethylmethacrylate (PHEMA) (hydron)
- Rigid acrylic polymerization dry and in water becomes a gel

- Depending on fabrication, (3 – 90%) can be made of water.
- Easily machined while drying
- It is used in preparation of contact lens

Polyvinyl alcohol (PVA)

- Tensile strength
- Wear resistance
- Semipermeability

Application

- It is used for preparation of synthetic cartilage reconstructive joint surgery.
- It holds synorial fluids in joint.

Disadvantage

- It cannot be steam sterilized

Hydrogels: eg: P-HEMA and PVA after uses of hydrogel

- The first hydrogel polymer developed is the polyhydroethyl methacrylate (PHEMA) or poly HEMA which can absorb water more than 30% of its weight.
- This property makes it useful for soft lens application.
- Hydrogels are made by polymerization of certain hydrophilic monomers with small amount of cross linking agents such as ethylene glycol dimethacrylate (EDGA).
- The hydrogel can change its structure according to pH, salt concentration and temperature.
- They are basically cross linked polymer with hydrophic group. They also contain carboxylic acid group.
- A common polymer used to make hydrogel is sodium polyacrylate
- The polymer usually exist in the shape of randomly coiled molecules in the absence of Na^+ if the salt is removed, the changes on the oxide ions along the polymer chain repel each other and the chain tend to uncoil.
- In this state, the hydrogel can absorb over 500 times its own weight of pure water.
- This ability of hydrogel to absorb much water is useful for making soft contact lenses, baby napkins, wound dressing and drug delivery system.
- When salt is added to the hydrogel the chain starts to change their shape and water is lost from the gel.
- Na^+ now take up the place of water and hydrogel gets coiled again.

Use of hydrogel ini wound dressing.

- A wound dressing is put over a cut to keep the skin healed.
- The hydrogel is applied as a thin layer which is moist and smoothening.
- It stops the wound drying out and protect it from infection.
- The hydrogel can control bleeding and does not stick to the surface so it can be removed easily without damaging the stain.

Silicon rubber

- Silicon natural and synthetic rubber have been used for fabrication of implant.
- Rubber (or) elastomer are defined as a material that at room temperature can be stretched repeatedly to at twice its original length and upon release of the stress returns immediately with force to its approximate original length.
- This phenomenon helps in the cross linkage between the chain that holds the chain together.
- The amount of cross linking for natural rubber controls the flexibility of the rubber, the addition of 2 – 3% of sulfur results in flexible rubber
- While addition of 30% of sulfur makes it a hard rubber.
- Rubber contain antioxidants to protect them against decomposition by oxidation, hence improving aging properties.
- Fillers such as carbon black or silver powder are also used to improve the physical properties.
- Silicon rubber is one of the few polymers developed for medical se.
- The repeating unit is dimethyl siloxane which is polymerized by condensation polymerisation to give (PDNS) polydimethyl siloxane.
- Low molecular weight polymers having low viscosity.
- It can be cross linked to make high molecular weight rubber like material.
- Medical grade silicon rubbers contain Stannous octate as a catalyst and can be mixed with base polymer at a time of implant fabrication.
- There are three grades of si8licone rubber : i) Hard, ii) Medium, iii) Soft

Properties of silicon rubber

- They are chemically resistant
- They are stable over a wide range of temperature
- They are easily sterilized and biocompatible
- They are durable: good electrical insulation, possess thermal and oxidative stability at high temperature, flexibility and elasticity at low temperature.

Advantages

- Due to flexibility, silicone implants can be compressed through a small incision.
- Since the body cannot bond with silicon or grow into it, it builds a scar tissue wound it.
- And silicone implants can be removed easily.

Disadvantage

- Silicone has a sticky surface structure, hence there will be more contamination.
- It may contain toxic materials.

Applications

- It is used in cardiovascular appliances because of blood compatibility.

- They are mostly used as breast implant it can be replaced in disease or destroyed finger joints.
- It can be used for maxillofacial surgery

Biodegradable polymer (BDP)

- Biodegradable of synthetic polymer is developed only in recent years and primarily response in growing problem of waste disposal of plastics.
- All biopolymer undergoes enzymatic degradation.
- Factors affecting rate of degradation.
- Polymer site (molecular weight presence of functional group in or on main chain
- Physical or morphological state: crystalline, amorphous
- Environmental condition: ph – temperature – salt concentration.

Major applications

- Adhesives, temporary scaffolding, temporary barrier, drug delivery matrix.

Temporary scaffold: Eg. Absorbable sutures

- Surgery causes temporary weaknesses and needs artificial support
- Sutures hold tissues together until collagen synthesis takes place
- 70-80% of collagen synthesis occurs at first third week and 20 – 30% of collagen synthesis occurs in 3 – 5 months.

Temporary barrier

- It is important in the field of tendon, spinal coral and open heart surgery.
- After surgery, surgical adhesions caused by blood clotting and fibrosis between sliding surface of tendons and between cardiac and pericardiac stack which causes pain.
- So this biodegradable polymer act as a temporary barrier to prevent adhesion and they degrade gradually.
- Drug delivery matrix: Drug Delivery Biodegradable (DDB) matrix is used to deliver the drug and degrades at a predictable rate by drug diffusion mechanism from the matrix where the drug is incorporated.

Design

- Solubilisation, ionization followed by solubilisation, enzymatic hydrolysis, simple hydrolysis

BDP in Biomedical use or in medicine

PVA

- It is used in creams and cosmetics as a water soluble thickening agent.
- Used as an artificial tears in dry eyes.
- In contact lens, it acts as a wetting system.

- Copolymer of methyl vinyl ether and maleic anhydride
- It is used as a coating agent on the surface of drug to prevent damage of drug in stomach by acetic environment.
- Co-polymer of PE Oxide : It act as a temporary mechanical support to tissue.
- Degradation by simple hydrolysis within 2 – 12 weeks.
- It is made as film or fiber and used as a BDP.
- Copolymer of L-latic, Dlatic and glycolic: It should bear load during bone fracture heating.
- Copolymer polyglycolic acid / polylactic acid
- It act as suture material and it is
- Under the name DEXON VICRYL
- It is used to deliver the drug at a predicable absorption rate
- It is also used as a drug delivery matrix
- Polydioxanone: under the name PDS.
- Monofilament structure and act as a suture
- Advantage it has less affinity, for the attachment of bacteria.
- Polyglyconate: copolymer of trimethylene carbonate and polyglycols acid.
- Under the name MAXON
- Less inflammation and scar tissue formation.

Microorganism in polymerizing implant.

Microorganism posses variable capacities to adhere to the polymer surface.

- Staphpylococci is predominant organism followed by Pseudomonas, Klebsiella, Serratia (curd contaminant red colour pigment) followed b y Candida.

Polymeric sterilization

- Most polymeric implant materials cannot be treated by steam or dry heat.
- As their thermosensitive, in such situation treatment by gamma radiation or chemical agent employed
- □-radiation with dose of 2.5 M radiation has been found to be suitable to sterilize PE tetraphthalate (PET)

Built materials for biomedical application

- This process results in destruction of all form of microorganism (bacteria and spores)
- The only disadvantage of this irradiation of polymer, it can alter the chemical nature of polymer
- Ethylene oxide is a gas mostly used for the sterilization of medico surgical materials.
- Advantage is it is very efficient, rapid and large spectrum action.
- Formaldehyde is utilized as aerosol or in gaseous state in operation theatre.
- Gluteraldehyde has been employed in concentration of above 2 – 2.5% for the decontamination of medico surgical materials at room temperature.
- Gluteraldehyde should be removed as much as possible by rinsing with water.

Deterioration of polymers

Biodeterioration of polymers involves primarily enzyme-catalyzed chemical reactions which can occur due to endoenzymes and exoenzymes The former results in random chain cleavage with a substantial decrease in molecular weight where as the later in which the immediate effect on molecular weight of the residual polymer will be much less results in removal of only terminal units, which are generally either monomers, dimers or trimers. Deterioration of polymeric materials is caused by adhering microorganisms that colonize their surfaces, forming biofilm. The formation of a biofilm is a prerequisite for substantial corrosion and deterioration of these materials to take place. Polymeric materials have gained a wide influence due to their excellent mechanical and thermal properties and high stability. They are very unique in chemical composition, physical forms, mechanical properties and applications. Because of this structural versatility, polymeric materials are widely used in aerospace applications, aviation and space industries as paints, adhesives, sealants, plastics, composites, rubbers, lubricants, fuels, matrix materials for fiber reinforced polymeric composites etc. Polymeric materials are potential source of carbon and energy for heterotrophic microorganisms including bacteria and fungi in several ways. The actions of microorganisms on polymers are influenced by two different processes:

1. Direct action: The deterioration of plastics which serve as a nutritive substance for the growth of the microorganisms
2. Indirect action: The influence of metabolic products of the microorganisms, e.g., discoloration or further deterioration.

Biodegradation of a polymeric material is chemical degradation brought by the action of naturally occurring microorganisms such as bacteria and fungi via enzymatic action into metabolic products of microorganisms (e.g., H_2O, CO_2, CH_4, biomass etc.). In contrast to the biodegradation of polymers, where a near complete conversion of the material components takes place only a change in the polymer structure or the plastic composition is observed in many cases in polymer biodeterioration or biocorrosion. The biological environment includes the biological agents such as bacteria, fungi and their enzymes responsible for the deterioration of polymeric substances. They consume a substance as a food source so that its original form disappears.

Composites

- Composite materials are a combination of more materials having different set of properties from their consequent material thus the combination of two or more discrete type of materials results superior properties not exhibited by the individual materials their significant properties are: high strength, heat resistance, stiffness and stability.

Classification of composite material

- It is classified into two types.
- Natural composites
- Artificial composites

Natural composites eg: Wood, bone, bamboo, concrete tc.

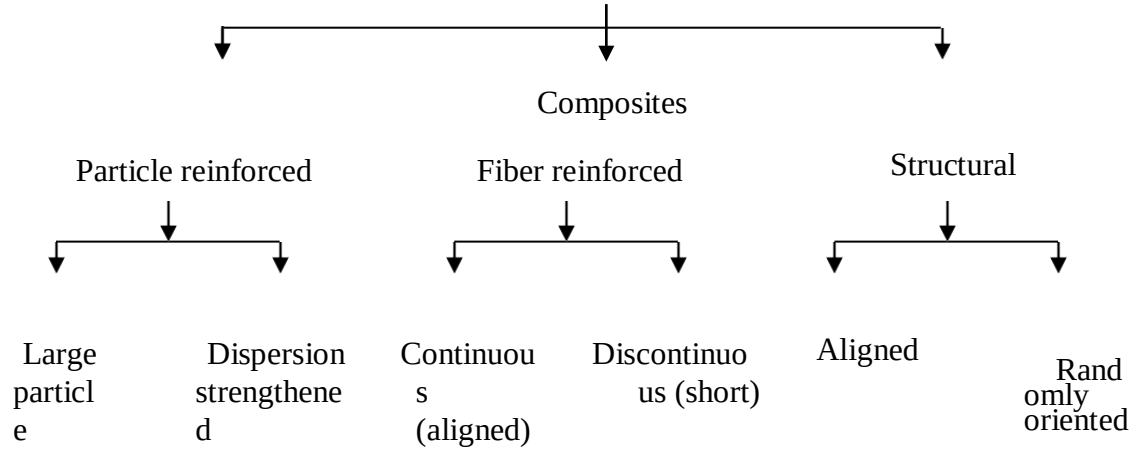
- Wood consist of organic material (lignin and cellulose fiber) in its structure which

provides the required strength for various application.

- In bone the fibrous protein called collagen is apetite which produces the required strength.
- Artificial composite: Reinforced carbon (RCC) in this steel rods are embedded in the concrete mix and produces the required strength.
- The concrete mix is added with steel rods results in RCC structure which leads to take heavy load, which cannot be carried out by concrete alone.
- Glass Reinforced Plastic (GRP) which has combined properties of glass, glass fibers and plastic.

Structure of composite material

- Matrix and reinforced material
- This matrix is base material which is surrounded by other material known as reinforced material
- The base material can be continuous while the reinforcement is more essential, it may be by means of chemical reaction.
- Mechanical stability between the matrix and reinforcement, physical bonding between matrix and reinforcement through Vanderwall's force.
- Particle reinforced: Large particle composites: Constituents are metal, polymer and ceramics. Eg. i) Concrete in which cement is a matrix while sand and gravel act as a particular to form the composites, Cermets which are made up of ceramics and metal matrix Ceramic like carbides are enhanced on metal like Cobol, Ni, Fe, form metal matrix.
- Application: the addition of hard carbide result in high strength high tensile modulus.
- Dispersion strengthened: They are produced to improve the mechanical strength.



- The uniform dispersion of fine particle of hard and inert material are used. Eg. Strength of nickel alloy can be enhanced by adding fine dispersed particle 30% volume of thoria nickel (TD).

Fiber reinforced composites:

- Continuous and aligned fiber component
- The fiber is aligned parallel in single direction
- The longitudinal aligned fibers are brittle in nature
- They show uniaxial stress strain relationship with more efficiency
- They are anisotropic in nature (different properties in different direction)
- Two important parameters should be considered: i) specific strength = tensile strength / specific gravity, ii) specific modulus : modulus elasticity / specific gravity.
- Discontinuous and alignment fiber composites.
- The fiber reinforced are not continuous that is aligned partially in the longitudinal direction.
- More demand due to increased moduli of elasticity (90%) and tensile strength (50%)
- The discontinuous reinforcement material are known as filter.
- There are in different shape like microsphere, platelets, viscous etc.
- Discontinuous and randomly oriented fiber composite: The fiber are short and discontinuous this type leads to increase in modulus only, in some portion of the volume, fraction of the fiber.

  Preparation of composite material

Fiber reinforced material

↓

Pre peg (bulk of material in cold condition) method

↓

Mostly used for silica and oxide of composite material

↓

Fiber is feeded to up drum

↓

Slurry contains matrix powder

↓

Fiber reaches the slurry

↓

Matrix fiber coated on the fiber

↓

Pre peg is obtained

↓

Dried and cut

↓

Arranged in form of stack

↓

Binder is removed at high temperature using furnace 1800^{o}C

↓

Stacks are removed

↓

Hot pressed

↓

Reinforced composite material are obtained

Applications of composite

- Dental filling composites: silver amalgam and gold are commonly used for posterior and anterior teeth.
- Acrylic resin and silicate cement are used in the anterior teeth but they have less life and clinical failure
- Dental composite resin – widely used for posterior and anterior teeth.
- Porous implant: It allows tissue in growth.
- Porous implant has permanent anchorage.
- Porous implant composites are of two types: a)Porous filled with tissue, b) implant filled with tissue.
- It is widely used on bone compatible implant.
- Pore size of the implant is of biological important larger than 150 µm has good tissue in growth and permanent anchorage.
- Pore size less than 75 µm does not posses tissue in growth.
- Porous coating: It is widely used to anchor artificial root canal treatment of dental implant.

- Fibrous and particulate composite in orthopedic implant.
- Inclusions are added to increase stiffness, strength, fatigue and other properties.
- Carbon fiber incorporated into High Density Polyethylene (HDPE) in total knee replacement.
- Fiber are added to provide near resistance
- Fibers are also incorporated into PMMA bone cement which improves the mechanical property.
- Metal wires are used as macroscopic fiber to reinforce PMMA cement in spinal cord stabilization surgery.
- Inclusions of bone particles in PMMA cement improves stiffness and fatigue life.

BIOCERAMICS

- Refractory, polycrystalline compound, inorganic in nature
- Oldest synthetic material
- It can be single crystals (sapphire) polycrystalline (alumina HAP), glass ceramics (bioglass).

Physical Properties

- Generally hard
- High melting point
- Low conductivity for electricity and heat
- Low tensile strength
- Difficult to shear

Classification: based on chemical reactivity

- Bioinert – alumina, zirconia, titania, carbon,
- Bioactive – ceravital and bioactive glasses, HAP
- Resorbable ceramics – TCP and HAP
- Nonresorbable ceramics: Alumina and carbon

Bioinert ceramics

- Alumina: Chemically inactive
- Available in □-alumina
- For implant use, 99.5% pure almina +0.1% SiO_2 and alkali (Na_2O)
- Natural alumina : Sapphire (or) ruby

Properties

- High corrosion and wear resistanace
- High rigidity and hardness
- Good biocompatibility
- Reasonable strength (depends on grain size and porosity)

- Mechanical properties depend on its grain size.

Application

- Orthopedic application hip and knee prosthesis
- Reconstructive maxillofacial surgery
- Dental implants – teeth roots (porous)

Important pre requisites of alumina

- Surface finish
- Small grain size
- Biomechanically correct design
- Exact implantation techniques
- Good manufacturing technology

Zirconia yttria stabilished zirconia

- Properties : Structure changes with temperature, at room temperature, monoclinic structure, 1000 – 1100^{o}C, 2000^{o}C: cubic
- High bending strength and fracture toughness.

Application

- Orthopedic prosthesis
- HAP coated zirconia used in dental implants have a longer life.
- Shoulder prosthesis

Carbon

- Iinert bioceramic material has unique properties.
- Possess two bonds
- Covalent bonding: between hexagonal layers, high strength
- Vanderwaal's bond: between parallel layers, less stiffness and strength.
- Between parallel layers
- Less stiffness and strength.

Properties.

- Good biocompatibility
- High strength and modulus

Types

- Low temperature isotropic carbon (LTI)
- Good bonding strength
- Good thrombo resistance

- Frictional properties and high elastic strain.
- Vitreous carbon
- Glass blocking appearance
- Small size
- Good resistance, strength, less than LTI
- Ultra LTI – (ULTI)
- Used as coating in implants
- High biocompatibility

Application

- Isotropic pyrolitic carbon – vascular implants
- Carbon coatings – heart valves, blood vessel grafts, percutaneous devices.
- VLTI – Valve coating (carbon absorb protein easily)
- LTI – restorative dentistry
- Surface reactive ceramics: gives controlled surface reactivity based on chemical bond
- Glass ceramics – bioglass – applied as coating for stainless steel, Co – Cr alloys – high mechanical stability biocompatibility
- Excellent mechanical and thermal properties
- Vary only in composition.

Surface reactivity composition

- Inclusion of 5 – 15% of B_2O_3 more reactive
- Drawback : Brittle, not used in joint implants.
- **Application**: Fillers for bone cement, dental composites and coatings.
- **Bioglass**: SiO_2 CaO Na_2O P_2O_5
- **Ceranital**: SiO_2 $CaONa_2OP_2O_5$ $MgOK_2O(Al_2O_3TiO_3Ta_2O_6)$
- **Layer formation**: Calcium phosphate $\longrightarrow$ SiO_2

Properties

- Good tensile strength
- Good resistance to scratching, abrasions

Hydroxyapatite (HAP)

- $Ca_{10}(PO_4)$ $(OH)_2$
- Hexagonal structure
- Ratio of Ca/P – 1.66
- Synthesis – $Ca(OH)_2$ + H_3PO_4 – in aqueous solution: 105ºC – powdered and sieved.
- Chemically equivalent to bone mineral – forms strong biological bond.
- Stimulates osteo induction – osteogensis
- Osteo integration – interface between implant and must happen else implane bone rejected.

- Biological performance based on osteointegration with an increased load bearing capacity.

Thermal behavior of MAP

- Increase in temperature – structure is modified
- Shows presence of : i) lattice water, ii) absorbed water
- HAP subjected to ~ 1200^{o}C – water is driven out – produces partially hydrated HaP
- Above 900^{o}C – weight loss
- 1050^{o}C HAP decomposes
- $Ca_{10}(PO_4)_6(OH)_2 \longrightarrow 2$ $Ca_3(PO_4)_2 + CaP_2O_9 + H_2O > 1350^{o}C$
- $(Ca_3PO_4)_2$ $Ca_3(PO_4)_2 \longrightarrow$ irreversible reaction.
- Ceramic degrade in the order : Tricalcium phosphate (TCP) > TCP > HAP

Application

- Used as fillers to replace amputated bone or as coating to promote bone ingrowth.
- HAP is widely and used as bone implants
- Experiment done with dog's tibia and femur
- There is direct chemical attachment to bone and there is no degradation.
- Used as synthetic roots and healing place without complications.
- No rejection is seen
- Used in biological chromatography as support material for protein purification.
- HAP column used in HPLC
- It is used as sealing agent
- Used as coating materials on metals

Properties

- Lacks toxicity
- It possess direct contact with bones
- Stimulates bone growth

Disadvantages

- It is brittle in nature and it posses or mechanical properties

QUESTION BANK:

PART-A

1. Define Biomaterials.
2. List the characteristics of biomaterials.

3. State some examples of biomaterials.
4. Using an example explain elastic behaviour of materials.
5. Analyze different ways of wound healing techniques.
6. Develop the methods used to categorize biomaterial surfaces.
7. Sketch the structure of Ti and Ti based alloys.
8. Categorise bioactive ceramics.
9. Design the synthesis procedure of nano alumina.
10. Estimate the drawback of Glass-ceramics based biomaterials

PART-B

1. Describe the properties, merits and demerits of ceramics.
2. Interpret the characteristic features of metals and itsapplications as implants.
3. Examine the use of ceramics in medical applications withexamples.
4. Develop an application for ceramics in medical field andexplain its characteristics.
5. Tabulate how polymers is used as biomaterials.
6. Compare and contrast the types of synthetic polymers.
7. Classify the polymeric biomaterials and analyze its characteristics, merits and demerits.

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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – II - BIOMATERIALS AND ARTIFICIAL ORGANS– SBMA7001

II. TISSUE RESPONSE TO IMPLANTS

TISSUE GRAFT

Grafting refers to a surgical procedure to move tissue from one site to another on the body, or from another person, without bringing its own blood supply with it. Instead, a new blood supply grows in after it is placed. A similar technique where tissue is transferred with the blood supply intact is called a flap. In some instances a graft can be an artificially manufactured device. Examples of this are a tube to carry blood flow across a defect or from an artery to a vein for use in hemodialysis.

Classification

Autografts and isografts are usually not considered as foreign and, therefore, do not elicit rejection. Allografts and xenografts are recognized as foreign by the recipient and are rejected.[1]

- Autograft: graft taken from one part of the body of an individual and transplanted onto another site in the same individual, e.g., skin graft.
- Isograft: graft taken from one individual and placed on another individual of the same genetic constitution, e.g., grafts between identical twins.
- Allograft: graft taken from one individual placed on genetically non-identical member of the same species, e.g., the majority of grafts are allografts.
- Xenograft: graft taken from one individual placed on an individual belonging to another species, e.g., animal to man.

A tissue graft is a medical procedure in which tissue from a donor is used to replace missing or damaged tissue on a patient. Numerous type of human tissue can be used including veins, skin, tendons, bone, and ocular materials. One of the most common types of tissue graft is a skin graft for a burn victim, but other patients can benefit from tissue donation as well. Because the surgery which accompanies this type of graft is often invasive, the patient will have to take antibiotics and observe special precautions until the surgical site heals.

In an autograft, donor tissue is taken directly from the patient. Autografts are frequently carried out with skin, which can be removed from the thigh and used elsewhere on the body. This type of tissue graft tends to absorb more quickly into the body, although the patient will have to take care of two recovery sites, the grafted site and the donor site, until he or she heals. In an

emergency situation, an autograft is often the graft of choice, if it is possible, because the tissue does not have to be processed for safety.

An allograft is a tissue graft using materials donated from someone else. In most cases, this uses materials recovered from a deceased person. Typically, the deceased has indicated a desire to donate organs or tissues, and his or her family consent to the procedure. The cadaver is treated exactly like a regular patient in surgery, to ensure the utmost respect and to create a sterile environment. Tissues are harvested from the cadaver and processed in clean laboratories before being placed in storage.

When cadaver tissues are processed, they are tested for potential pathogens and cleaned. Technicians carefully label the tissue parts and place them into sterile bags which are then sealed. Stored under subzero temperatures, tissue products can keep for quite a long time.

When a patient requires a tissue graft, it is either because of an emergency like a severed tendon or serious burn, or due to a degenerative condition. The doctor may discuss several options with the patient, and if the decision to graft is taken, the patient is prepared for surgery. Typically, the patient needs to take prophylactic antibiotics to ensure that infection does not set in at the graft site. The patient is given an anesthetic or put under general anesthesia, depending on the procedure, and the tissue graft is performed. Afterwards, it is of the utmost importance that the patient continue taking antibiotics and keep the graft site clean.

Types of grafting

The term grafting is most commonly applied to skin grafting, however many tissues can be grafted: skin, bone, nerves, tendons, neurons, blood vessels, fat, and cornea are tissues commonly grafted today.

Specific types include:

- Skin grafting is often used to treat skin loss due to a wound, burn, infection, or surgery. In the case of damaged skin, it is removed, and new skin is grafted in its place. Skin grafting can reduce the course of treatment and hospitalization needed, and can also improve function and appearance. There are two types of skin grafts:

1. Split-thickness skin grafts [epidermis + part of the dermis]
2. Full-thickness skin grafts [epidermis + entire thickness of the dermis]

- Bone grafting is used in dental implants, as well as other instances. The bone may be autologous, typically harvested from the iliac crest of the pelvis, or banked bone.
- Vascular grafting is the use of transplanted or prosthetic blood vessels in surgical procedures.
- Ligament repair, as with anterior cruciate ligament reconstruction or ulnar collateral ligament reconstruction.

Reasons for failure

- Hematoma (a collection of blood) development when the graft is placed over an active bleed
- Infection
- Seroma (a collection of fluid) development
- Shear force disrupting growth of new blood supply
- Inappropriate bed for new blood supply to grow from, such as cartilage, tendons, or bone

Soft Tissue Grafting

Soft tissue grafting is often necessary to combat gum recession. Periodontal disease, trauma, aging, over brushing, and poor tooth positioning are the leading causes of gum recession which can lead to tooth-root exposure in severe cases.

When the roots of the teeth become exposed, eating hot and cold foods can be uncomfortable, decay is more prevalent and the aesthetic appearance of the smile is altered. The main goal of soft tissue grafting is to either cover the exposed root or to thicken the existing gum tissue in order to halt further tissue loss.

The three different types of common soft tissue grafts include:

- **Free gingival graft** – A strip of tissue is removed from the roof of the mouth and stitched to the grafting site in order to promote natural growth. This type of graft is most commonly used for thickening existing tissue.
- **Connective tissue graft** – For larger areas or root exposure, subepithelial tissue is needed to remedy the problem. This subepithelial connective tissue is removed from a small flap in the mouth and sutured to the grafting site. This is the most common treatment for root exposure.

- **Pedicle graft** – This type of graft involves the "sharing" of soft tissue between the affected site and adjacent gum. A flap of tissue is partially cut away and moved sideways to cover the root. The results of this type of graft are excellent because the tissue that is moved to the adjacent area includes blood vessels that are left in place.

Reasons for soft tissue grafting

Soft tissue grafting is an extremely versatile procedure that has many uses. Recent developments in dental technology have made soft tissue grafting more predictable and less intrusive. Here are some of the main benefits associated with soft tissue grafting treatment:

- **Increased comfort** – Root exposure can cause substantial pain and discomfort. Eating hot, cold or even warm foods can cause severe discomfort. Soft tissue grafts cover the exposed root, decreases sensitivity and restore good health to the gum area.
- **Improved aesthetics** – Gum recession due to periodontal disease can cause the smile to look "toothy" or the teeth to appear uneven in size. Soft tissue grafting can be used as a cosmetic procedure to re-augment the gums, and make the smile appear more symmetrical.
- **Improved gum health** – Periodontal disease is a progressive condition that can destroy soft tissue very rapidly. When used in combination with deep cleaning procedures, soft tissue grafting can halt tissue and bone loss, and protect exposed roots from further complications.

Indications

Soft tissue implants are used for the following purposes:

- To reconstruct surgically or traumatically created tissue voids
- To restore bulk to aging tissues in order to correct soft tissue folds or rhytides
- To augment tissue for cosmetic enhancement
- They should be sterilizable.
- They should be low cost.

Other important factors are feasibility of mass production, aesthetic quality, etc.,

In soft tissue implants as in other applications that involve engineering, the performance of an implanted device depends on both the materials used and the design of the device or implant. The initial selection of material should be based on sound materials engineering practice. The final judgment on the suitability of the material depends on observation of the *in vivo* clinical performance of the implant. Such observations may require many years. This requirement of *in vivo* observation represents one of the major problems in the selection of appropriate materials for use in the human body. Another problem is that the performance of an implant may also depend on the design rather than the materials *per se.*

The success of soft tissue implants has primarily been due to the development of synthetic polymers. This is mainly because the polymers can be tailor-made to match the properties of soft tissues. In addition, polymers can be made into various physical forms, such as liquid for filling spaces, fibers for suture materials, films for catheter balloons, knitted fabrics for blood vessel prostheses, and solid forms for cosmetic and weight-bearing applications.

It should be recognized that different applications require different materials with specific properties. The following are minimal requirements for all soft tissue implant materials:

1. They should achieve a reasonably close approximation of physical properties, especially flexibility and texture.
2. They should not deteriorate or change properties after implantation with time.
3. They should not cause adverse tissue reaction.
4. They should be noncarcinogenic, nontoxic, nonallergenic, and nonimmunogenic.

SOFT TISSUE REPLACEMENT:

SUTURES, SURGICAL TAPES, AND ADHESIVES

The most common soft tissue implants are sutures. In recent years, surgical tapes and tissue adhesives have been added to the surgeon's. Although their use in actual surgery is limited to some surgical procedures, they are indispensible

SUTURES

There are two types of sutures, classified as to their long-term physical in nit o integrity: absorbable and non absorbable. They may also be distinguished by their raw material source: natural sutures (cai2ui, silt, and ostton) and synthetic sutures Inylon, polyethylene, polypropylene, stainless steel, and tan-talu m). Sutures may also be classified according to their physical form: monofilament and multifilament

The absorbable suture, catgut, is msde of collagen derived from sheep intutinal «ubmucnsa. It is usually treated with a ehromie salt to increase its strength and is cross-linked to retard resorption. Such treatment extends ihe life of caigut suture from 3-7 days up to 20-40 dayx. Table 11-1 gives initial strength data for caigut sutures according to their sizes. The calput sutures are preserved

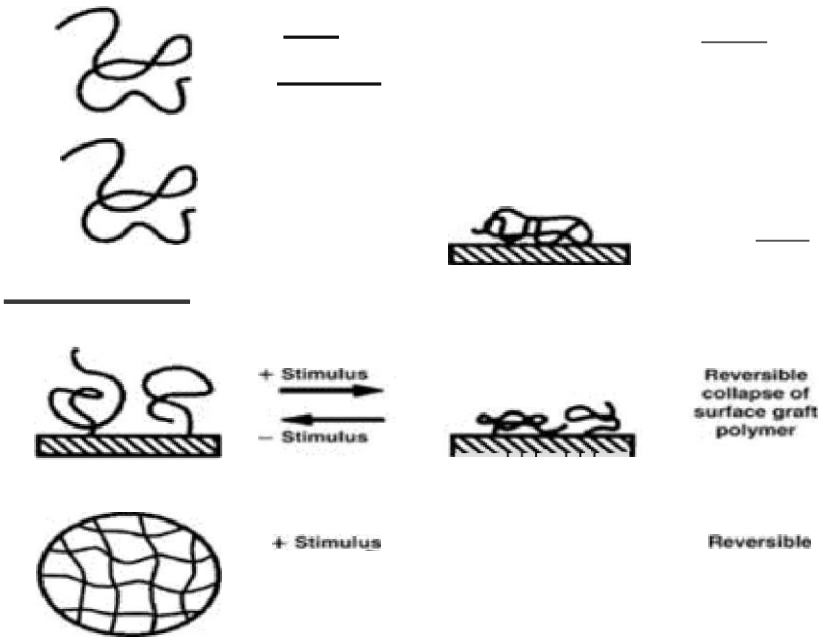


Fig:1 SUTURES

– Stimulus

The most common implants are the futures. In recenl years surgical tapes and tlssue adhesives have added io the surgeon's armamentarium- Although their use in actual surgery is limited for some surgical proce- dures, tt ey are indispensable,

The types of sutures are classified by their physical integrity, i.e.. absorbable and nonabsorbable. The may be distinguished according to their source Df raw materials, i.e., natural sutures (catgut, silk, and cot- ton) and synthetic sutures (nylon, potyeih y gene, polypropylene, and stain- less steel), Sutures may also be classified by their physical forms, i.e., monofilament and multifilament.

An absorbable suture, cat8ui, is made of collagen and derived from sheep intestinal submucosa. It is usually treated with a chromic salt to increase its strength and retard resorption by cross-linking, Such treat- ment extends the life of a catgut suiute from L7 days up to 2M0 days. Table 9-1 gives some of the original strength of catgut sutures according to their sizes.

It is interesting to nole that the surgical knot decreases the suture strenslh of catgut by half, no matter what kind of knotting technique is used, because of stress concentration. It is suggested that the most effec- tive knotting is the square know with three ties to present loosening. Whether it is need loosely or tightly makes no measurable diPerence in the rate of wound healing, according to one study.

The catguts and other absorbable sutures (polygiycolic acid, PGA) invoke tissue reac(ions, although the effect diminishes as they are absorbed, This is true with other natural non-absorbable futures like silk and cotton, which showed higher reaction than such synthetic sutures as polyester, nylon, orpolyacrylonitrile.

If thesuture is contaminated even slightly, theincidence of infection increases many fold. The most significant factor of infection is the chemical structure; the geometric configuration seems to have no influence on infection. Polypropylene, nylon, and PGA sutures develop least infection compared to other suture materials, such as stainless steel, plain and catgut, and polyester sutures.

Surgical Tapes

Surgical tapes are supposed to offer a means of avoiding pressure necrosis, scar tissue formation, problems of stitch abscesses, and weakened tissues. The problems with surgical tapes are similar to those experienced with Band-Aids, i.e. , (1) misalignment of wound edges, (2) poor adhesion

Artificial Skin

Artificial skin is another example of pericutaneous implants and has similar problems. Most needed for this application is a material that adhere to a large (burned) skin surface and prevent the loss of fluid, electrolytes, and other biomolecules until the wound is healed, Although a permanent skin implant is needed, it is a long way from being developed because of the same reasons given for pericuineous devices proper, Autografting and homografting are the only methods presently available.

Several polymeric materials, including reconstituted collagen, have been tried. Among them are the copolymers of vinyl chloride and acetate and methyl-2-cyanoacrylate.

Maxillofacial Implant

There are two types of maxillofacial implant materials (often called prosthetics, which implies extracorpore&1 attachment): extraoral and intraoral. The latter is implanted and the former is not. Maxillofacial implant is defined as "the art and science of anatomic, functional or cosmetic reconstruction by means of artificial substitutes of those regions in the maxilla, mandible, and face that are missing or defective because of surgical intervention, trauma, etc.
Many polymeric materials are available for the extraoral implant, which requires that
1. color and texture should be matched with that of patients;
2. it should be mechanically and chemically stable, i.e,, it should not creep and change colors or irritate skin; and
3. it should be easily fabricated.
Polyvinyl chloride and acetate (5-20%) copolymers, polymethylmetacrylate, silicone, and polyurethane rubbersarecurrently used.

Maxillofacial implant types

Titanium implants comprising of bone plates, screws and dental implants have transformed the concept of management in maxillofacial trauma, correction of dentofacial deformities, reconstruction of jaws after ablative surgery and restoration of lost stomatognathic apparatus. Cranio-maxillary facial region is a complex structure having structural elements arranged in a series of columns, arches and buttresses with intervening thin bones providing lateral support to primary structural members. Bone plates and screws when engaged to secure thin plates of bone, fractured bony fragments and osteotomised segments, provide rigid fixations.

Moreover approximation, fixation and stabilisation of bony fragments in anatomic alignment promotes healing of bone by primary intention with direct in-growth of capillaries and osteogenic cells across the fragments and thereby restoring the lamellar bone. Although bone plates were introduced into Maxillofacial surgery by Christiansen (1945)and thereafter plates borrowed from orthopaedics were modified and employed to manage unstable fractures, but it was only after 1970s that with technological advances, principles of fixation and knowledge of biomechanics was incorporated in bone plates system. Initially bone plate implants were fabricated in stainless steel, then in vitallium. Currently the material of choice is Titanium. Titanium dental implants support dental prosthesis in fully or partially edentulous patients having compromised alveolar ridges where conventional methods will not deliver satisfactory results.

Implant materials
The basic requirements for successful outcome of material are that it should be biocompatible, corrosion resistant, must possess adequate mechanical property to withstand stress, produce least artifacts under imaging like CT Scan and MRI and interfere minimally in normal growth, remodelling and development of bone. The materials used for implants at present are metals, ceramics and polymers. Metallic components are exclusively used in bone plate, screws and dental implants because of their higher strength and contourability. Ceramics including calcium phosphate preparations, bioglass and alumina have excellent biocompatibility but they are brittle and cannot be contoured or adapted to anatomic site. Polymers like polylactic and polyglycolic acid implants which are bioresorbable cannot be used in stress areas as they do not have adequate strength and rigidity. Metallic components currently in use are stainless steel, chrome-cobalt alloy and titanium.

Stainless steel possesses good structural and mechanical characteristics but has compromised biological response. It is susceptible to corrosion, lacks homogenicity and exhibits porosity which provides undesirable stress concentration area. Vitallium has got better biocompatibility and resistance to corrosion vis-a-vis stainless steel but is too rigid and is difficult to adapt along anatomical geometry. The metal which fulfils the requirements of ideal material currently is Titanium.

Titanium

Titanium possesses all the requisite properties. Biocompatibility and resistance to corrosion is due to ability to form a stable dioxide layer of 2 to 20 nm thickness in milli seconds when exposed to air, water and electrolytes. This layer protects the metal from any chemical attack even in aggressive body fluids. Even if this layer is distorted by shear forces from relative movement, repassivation occurs in biological environment in presence of oxygen and electrolytes. The modulus of elasticity of titanium is 10 $(PSI\ x10^6)^2$ which is nearer to bone having the modulus of elasticity of 2.4 $(PSI \times 10^6)^2$. This allows distribution of shearing stress evenly at the implant bone surface. Titanium also osteointegrates with bone tissues and is a base metal for dental implants. Surgeon has successfully used indigenously developed Titanium bone plates and screws in maxillofacial surgery.

Bone plate and screws

The bone plate and screw implant for osteosynthesis are fabricated either in pure commercial titanium or from alloyed form. Titanium and its alloy provide mechanical properties specific for bone plates and screws. A plate is made with lower elasticity, better deformability and lower hardness, so that it can be adapted accurately to anatomic contours whereas screws are fabricated to have higher elasticity and tensile strength and low deformability.

Bone plate systems available in Maxillofacial surgery are compression and non compression mini plate type. Another type is a microplate system which is indicated for a nasoethemoidal, infraorbital and frontal sinus wall fractures.

Dental implants

Titanium is the base metal for dental implants. The ability of the metal to osteointegrate with the bone surface and getting anchored within bone tissue enables implant to withstand the masticatory load transmitted through prosthesis. Titanium possesses molecular binding sites that facilitate the absorption of proteoglycans in presence of dioxide layer formed on its surface which then serve as a substrate for biological and cellular adhesions. This leads to direct ingrowth of bone cells on the implant surface with no intervening connective tissue. The other factor influencing osteointegration is the minimal adsorption of platelets on the titanium surface, thus clot formation on the implant surface is hindered which is otherwise responsible for fibrous tissue formation. To achieve the higher success rate and bone anchorage, surface area of implant is increased by plasma spraying either with titanium particles or by hydroxyapatite (HA) coating. The HA becomes ionised and is converted into plasma stream that condenses in multiple layer on the metallic implant surface in the form of partially amorphous and partially crystalline ceramic coatings.

In plasma coated implants the particles of titanium in plasma state is sprayed over the smooth commercially pure titanium to prepare titanium plasma spray (TPS) implants. It not only increases the surface area by six times but also increases the bone strength of the surface coating by 33%. This results in more implant bone interface and good osseointegration.

HARD TISSUE REPLACEMENTS:

Types of Orthopedic fixation devices design

- The design principles, selection of materials and manufacturing criteria for orthopedic implants are safe for engineering products undergoing dynamic loading.
- Although it is tempting to duplicate the natural tissue with materials having same strength and shape. This has not been desirable since the natural tissues and organs have an advantage over the man made implants.
- That is their ability to adjust new set of circumstances by remodelling their micro and macrostructure.
- When we try to replace the joints or heal a fractured been it is logical that the bone repairs should be made that the tissues should follow.
- If the bone heals faster when a compressive force is exerted, then we should provide compressing through an appropriate implant design.
- Unfortunately, the effects of compressive or tensile forces on the repair of9 the bones are not fully understood.
- Historically speaking, until aseptic (sterile) surgical techniques was developed various metal devices such as cures, pins constructed of iron, gold silver, platinum etc were not successful largely because of infection after implantation.
- Most of the modern implant developments have been centered around repairing long bones and joints.
- Although the exact mechanism of bone fracture repair is not known at this time stability of the implant with respect to wound surface is clinically an important factor to be considered.
- Whether the fixation is accomplished by compressive or tensile force. The reduction should be anatomical and bone ends should be firmly fixed so that the healing process cannot be disturbed by unnecessary micro and macro environments.
- Surgical techniques usually involve the use of metallic fixation devices.

Wires: The type of wires used is called as Kirschner wires. The simplest but most versatile implants are the various metal wires called Kirschner wires the diameter is 2.38 mm

- **Pins**: The Steinmann pins which can be used to along with Kirschner wires to hold fragments of bones together. Wires are also used to reattach greater trochanter (femun and hip) hip joint replacements. The common problems are corrosion of metals may weaken the cures . The added necessity of twisting and knotting of wires attenuates the problems since strength can be reduced by 25%.
- Pins: Steinman pins is also versatile implant and often used for internal fixation in cases when it is difficult to use a plate or when adequate stability cannot be obtained.
- The tip of the pin is designed to penetrate the bone easily when the pin is screwed into the bone.
- 3 types of tip designs are trochanter, diamond and cone.

- The trochanter tip is a most efficient in cutting and often used for cortical bone insertion.
- The fracture bones can be held together by two or more pins inserted percutaneously away from the fracture site and the pins are fixed by a device such as Hoffmann external fixation.
- **Screws**: Screws are the most widely used devices for fixation of bone fragments to each other. There are basically two types of screws: i) self tapping, ii) non self tapping.
- As the name indicates the self tapping screw cuts it own threads as it is screwed.
- The non self tapping makes less favourable although the holding power (pull out strength) of the two types of screws is about the same.
- The variations of thread design do not influence holding power.
- The radial stress transfer between the screw thread and the bone is slightly less for V shape thread than buttress thread indicating the lather can hot a longitudinal load betters.
- Pull out strength / holding strength of the screws is an important factor in the solution of particular screw design.
- Larger screw has higher pull our strength.
- Corticol bone plates.
- They are different types of fracture plates since the forces generated by the muscles in the limbs are very large bending movements the plates must be strong.
- This is especially true for the femoral and tibial plates.
- Adequate fixation of the plate to the bone with the screws over tightening may result in necrotic bone as well as deformed screws which may fail due to corrosion process.
- A bone plate divides to compress the end of the fracture bone can be achieved by using self compression plate and screw system.
- Compression plate is more favourable sign of healing.
- Large amount of callous formation results in good healing.

- The amount of callous formed is proportional to the amount of motion between plates and bone.
- Rigid plate fixation the drawback is weakening of underlying bone such that refracture may occur followed by removal of plates.
- The stiff plate carry so much of load and reabsorbed by the body
- A considerable amount of care must be exercised when fixing callacinous bone since this kind of bone has lower density, lower stiffness.
- The fixation of the end of a long bone are fixed with a combination of screw, plates, balls, nails and nut.
- Spinal fixation devices.
- When the spinous element of the back bone are deformed in such a manner that the length of the element is longer than the length of posterior one.
- The resulting structure is bend back ward is called “Lordosis”.
- The opposite condition is called kyphosis.

- There are forward and backward curvature in normal spine.
- Spinal deformities internal and external fixations can be corrected.
- These are several designs which stability or strengthen the curvature.
- The main problem with these devices are fatigue failure and necrosis occurs due to concentrated
- As the spine is straightened it is hardened to the when fixation deice in distract the curved hooks.
- Since they liberate the spine become smaller.
- Thus multiple hooks are sometimes attached to overcome the problem.

Intramedullary devices.

- Intramedullary devices are used to fix the fracture of long bones.
- The devices inserted inside the medullary cavity.
- This type of implant should have spring could exert some elastic force inside the bone cavity to prevent rotation of the device and to fix the fracture firmly.
- Compared to plate fixation the intramedullary device is better positioned to resists bending since it is located in the centre of the bone.
- IMD destroys the intramedullary blood supply although it does nt disturb the persisteal blood supply.
- The advantage of IMD is that it does not require the opening of a large area to operate and the device can be nailed to a small insertion.
- The long bone blood supply comes from 3 sources, i) the nutrient, ii) metaphyseal arteries, iii) periosteal arteries.
- Fracture occurs the extra osseous circulation from the surrounding soft tissue becomes active and forms the fourth source of blood supply.
- Intra medullary devices usually plates for the fixation of femoral neck
- The femoral fracture fixation which usually made to compress the broken bones together by tightening to compress the broken bones together by tightening screw which also helps to stabilize the fracture.***BIOELECTRIC EFFECT***

Bioelectric Effect

According to experiments, bone is considered as piezo electric material similarly collagen and apatite are considered as semiconductor which produce a PN junction diode.

- Stress on bone induces a cement which influences the alignment of tropocollagen molecules.
- SGP is a non linear functions of bone structure stress generated potential and has been found to be proportional to the cross linking of collagen.
- Negative potential develops in areas of bone under compressive stress that stimulates bone deposition where as tensile stress gives positive SGP which stimulates bone reabsorption.

- During bone tissue injury, a bioelectric potential develops between injured site and isolated tissue.
- This potential can range from a few mvolt to 100 mvolt.
- Tissue in active growth and regeneration shows electrode negative potential
- The bioelectric potential induces an electric current that concentrates protein electrolytes and polarisable molecule at wound site.
- Damaged tissue tend to respond to pulse electromagnetic field which results in normal structure and recovers more rapidly.
- Electrostatic field is being applied in correction of osteoporosis and osteogenesis.

Bone healing

- Blood vessels break and leads to clotting and formation of callous.
- The pH of the fracture region drops about 7.4 to 5.4.
- This change of pH aids in decalcification reabsorption and remodeling of necrotic bone.

First 2 days – 1st week

- Fibroplast from peristoneum moves to fracture site
- Capillaries proliferate into wound region.
- Osteogenic cells migrate from peripheral region to the fractures site.

1st – 2nd week

- Mucopolysacchride level decreases while collagen production is significant.
- Collagen fibre bridges between the fractures gap and the pH becomes normal

2nd – 3rd week

- Collagen matrix replaces entire clot
- Chrondoblast seen between matrix and bone growth
- Calcium and phosphorous in take increases and results in bone mineral deposition.

3rd – 4th week Trabecular bone replaces chrondoblast

5th – 6th week

Remodelling of trabecular bne to compact bone.

Healing process occurs in two ways

Primary fracture healing

- Secondary fracture healing

- Resorption of fracture fragments
- New bone formation
- Remodelling
- Osteosynthesis
- Remodelling of osteons between 2 fracture ends.

JOINT REPLACEMENTS – UPPER AND LOWER EXTREMETIES TOTAL HIP

REPLACEMENT

Current hip prosthetic devi ces and techniques claims high success rate above 90% for last 10 years.

A hip replacement consists of a femoral component that is, a ball mounted on a shaft and an acetabular component having a socket into which ball is placed.

Co-Cr and Ti-Al-Va alloys are used by different manufacture for the femoral head and HDHMWPE (High density high molecular weight Polyethylene) is to cover the socket.

Several designs types with different strength are available.

Surgical Insertion procedure

i) Femoral head is diseased; the infected region is removed off.
ii) Medullary canal of femur is drilled to prepare stem of prosthesis.
iii) Cartilage of acetabulam is also reamed.
iv) PMMA bone cement is prepared and packed into medullary canal
v) Femoral strength is inserted.
vi) Alignment and articulation is verified

Materials used are

I) Metal – metal
II) Metal-HDHMWPE
III) Ceramic-HDHMWPE
IV) Ceramic-Ceramic

Solution - Bone cement act as a shock absorber (viscoelasticity) polymer and it even spreads load uniformly over large area

Disadvantages of bone cement

- Monomer vapors interfering with body functions alter the blood pressure rapidly.
- Polymerization caused temperature increases cell necrosis.
- Intramedullary cavity preparation results and blocks the bone sinusoid

- Difficulty in removal of implant
- Friction between ball and socket
- SS-PE and Co-Cr-PE reduces frictional movement
- Loosening of ace tabular and femoral components
- Improper surgical and cementing technique
- Blood clot during surgery
- Shrinkage of bone cement during polymerization

TOTAL KNEE REPLACEMENT

- Prosthesis consists of femoral, tibial, patellar components.
- It has some complicated geometry and movement
- Knee joints are two types – hinge and non-hinge
- Implantation can be done with or without cement

  Femoral component – Co-Cr alloy

  Tibial component – UHMWPE

  Patellar component- UHMWPE& Ti alloy
- Patella is vulnerable, small size and force is applied
- Selection of implants depends on the health of the knee, types of diseases, range of activities required
- Porous coated implant is used which allows tissue in growth giving interface of bone and implant
- It is used only for healthy knees as it requires tissue in growth
- Femoral components have fairly thin, rigid, shell with an attached fixation system to bone
- Shell should be stiff, high strength and low wear rate
- Tibial portion has broad plateau covering fibia
- Stiff metal tray supporting the polymer is used.

Disadvantages

- Loosening
- Infection
- Shrinking of tibial plateau

NORMAL WOUND HEALING PROCESS CELLULAR

IMMUNE RESPONSE

The body reaction to foreign material is to reject

them.

- The foreign material may be walled of if it cannot be removed from the body
- If the material is particular of fluid, then it is ingested by the giant cell macrophage and removed.
- A typical tissue response is appearance of polymorphonuclear leucocytes near the

implant followed by macrophages.

- If the implant is inert to the tissue, then the macrophages may not be present near the implant, only a thick collagenous layer encapsulates the implant.
- If the implant is chemically or physically irritating to the surrounding tissue then the inflammation occurs at the implant site.
- Porous implants are fixed by in growth of surrounding tissue.
- Some implants may cause necrosis of tissue by chemical, mechanical and thermal trauma.

Various mechanism involved in Tissue response to implants

- Inflammation (normal wound healing process)
- Cellular response to implants
- Systemic effect of implants
- Blood compatibility
- Carcinogenicity

Inflammation

Tissues are injured or destroyed.

↓

Adjacent cell repair them soon after injury

↓

Construction of capillary occurs

↓

Dilation of blood vessel occurs

↓

Followed by increased activity in the endothelial cells lining the capillaries

↓

Capillaries become covered by leucocytes, erythrocytes and platelets Leakage

↓

of fluid of plasma from capillary occurs

↓

Migrating leucocytes and dead tissue combined with leaked fluid form exudates Local

↓

lymphatics are also damaged

↓

Capillary damage will provide fibrinogen

↓

Elements of the blood which will quickly plug the damaged lymphatic Localising

↓

the inflammatory reaction.

Chronic inflammation occurs after 3 – 5 days, this is marked by the presence of multinucleated giant cell. The macrophages and phagocyte remove foreign materials, sometimes the mononuclear cell evolved into histocyte skin macromphage which regenerate collagen. This regenerated collagen is used to unit the wound or remove foreign materials by encapsulation.Cellular response to implants

- Systemic effect of implants
- The polymethylmethacrylate (PMMA) bone cement is applied in femoral shafts in douth state is known to lower the blood pressure.
- Biodegenerable implants such as adsorable sutures surgical adhesives and corrosion particles released by metallic implant reduces systemic immune response.
- Corrosion resistant metal alloys are not completely stable some ion concentration in the elements are released into t he body which interferes with the normal physiological activity.
- The divalent metal ions may also inhibit various immune enzyme activity.
- Polymeric materials which contains additives induces cellular and systemic reaction.

Blood compatibilit

- Blood coagulation is the most important factor for the blood compatibility
- The implant should not damage proteins, enzymes, RBC, WBC and platelets.
- If the blood is coagulated it is called as clot.
- Sometimes the clot formed inside blood vessel is referred to as thrombus or embolus depending whether the clot is fixed or floating

Blood vessel damage

↓

Exposure of collagen

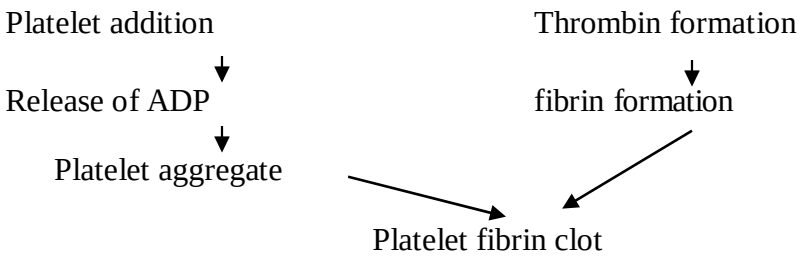
↓

Tissue damage

↓

Release of thromboplastin

↓



- The surface roughness is an important factor since roughness the surface, the more area is exposed to blood.
- Rough surface promotes faster blood coagulation than the highly polished surface of glass PMMA, polyethylene stainless steel.

Carcinogenicity

- A variety of chemical substance are known to induce the onset of cancerous disease in human beings are known as carcinogens. Eg: Sheets or film of many polymers produce cancer when implanted in animals especially rats.
- It was later found that the physical form of the implant was important and fibre and fabrics produce less tumour then sheets of same material
- But powder produce almost no tumours.

PART-A

1. Summarize the function of soft tissue augmentation.
2. What is blood compatibility? How it is affecting the bodyresponse to different materials?
3. State the applications of soft tissue augmentation
4. Show the difference between soft tissue and hard tissue.
5. Interpret the pros and cons of different types of suture materials.

PART-B

1. Interpret the pros and cons of different types of suture materials.
2. With the help of technological advancements, describe therecent advancement in the soft tissue repair technique.
3. How to choose a best biomaterial in application of skinreplacement and explain in detail.
4. Develop a dental implant system by stating the materials usedand it compatibility .
5. Describe about the hard tissue replacements.

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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – III - BIOMATERIALS AND ARTIFICIAL ORGANS– SBMA7001

III. CHARACTERIZATION OF OPTHALMIC AND DENTAL MATERIALS

CORROSION OF METALLIC IMPLANT

Metallic implant materials that are implanted in the human body should withstand aggressive environment with several ions present in the body fluid with pH 7 and temperature of 37°C. Hence the need for high corrosion resistance of these materials is high. To substantiate this titanium and titanium alloys exhibit elevated corrosion resistance in biological environment when compared with other conventional biomaterials like 316L grade stainless steel and cobalt-chromium alloys. The reason for this performance of titanium is the formation of thin adherent passivating oxide layer formed on the surface of Ti when exposed to body fluid environment. Ti implants undergo wear due to accelerated corrosion and result in the formation of Ti debris near the implant region, which in turn results in the blackening of the tissues, leading to catastrophic failure of the implant. several Mg alloys like Mg-Cd, Mg-Al, and Mg-Al-Mn were developed as an alternate for pure Mg for fracture fixation. The time taken for wound healing is approximately 12 weeks, however, all these alloys failed to survive this time period and underwent rapid corrosion. Electrochemical studies performed in simulated body fluid (SBF) on pure Mg are influenced mainly by pH of the solution, temperature in which the test is performed, and the presence of blood plasma and proteins, which mimics the real composition of the human body condition. Corrosion in the presence of serum solution leads to release of gas bubbles when Mg stents are employed. This leads to the blockage of blood vessel causing death. The presence of secondary phase and impurities in van lead to localized corrosion and pitting, which are the most predominant types of corrosion that occur in Mg and its alloys. In a primary study on 31 Mg alloys tested for corrosion almost 29 underwent rpitting and localized corrosion whereas only 2 samples underwent uniform corrosion.

To enhance the mechanical strength of Mg alloys intermetallics (secondary phases) are of high importance. Majority of the alloying elements and impurities are nobler compared to Mg, and hence, the intermetallic particles act as cathode and the Mg matrix will act as an anode and hence when exposed to biological environment the potential difference between them results in a galvanic coupling and rapidly increases the corrosion rate of Mg. It is important to note that temperature at which the corrosion testing is performed is a key to analyze the exact corrosion behavior of Mg and its alloys. The corrosion behavior of Mg alloys in minimum essential medium at 20°C and 37°C and found

that the samples tested at 37°C exhibited 100% higher corrosion. Hence, it becomes evident that the body temperature alters the electrochemical reactions and accelerates the process resulting in the variation of corrosion mechanism of these Mg alloys compared to that of room temperature. It becomes evident that corrosion tests carried out at room temperature underrate the corrosion behavior of Mg alloys.

CORROSION OF CONVENTIONAL ALLOYS

The commonly used surgical implants are usually made from one of the three types of materials: austenitic stainless steel, cobalt-chromium alloy, and titanium and its alloys and out of these, 316L austenitic stainless steel is the most commonly used implant material as it is cost effective.

- Austenitic Stainless Steels
- Cobalt-Based Alloys
- Titanium-Based Alloys
- Magnesium and its Alloys
- Cardiovascular Implants
- Corrosion of Dental Implants
- Corrosion of Orthopedic Implants

DENTAL MATERIALS AND ITS APPLICATIONS

- Dental materials are generally considered to compromise those materials which are employed in restoration dentistry.
- Dental materials include impression materials to copy the contour of the gum, restorative material to correct defect in natural material, appliances and dentures to replace or correct the deficiency of the grinding surface.
- Oral implants fall into 2 categories:
  - **i. Artificial teeth and**
  - **ii. Dental appliances those support and anchor artificial teeth**
    - These are specialized type of transcutaneous devices that must penetrate the oral cavity. The other type of implants are totally implanted. They include devices for repairing damaged or diseased mandibles; supports for rebuilding the alveolar rich and packing for stimulating the growth of bone to correct lesions associated with periodontal diseases.
    - There are 4 main group of materials used for dental applications which includesPolymers, Composites, Ceramics material and Metal alloys.

Anatomy

- All the teeth are made up of two portions:
  - i. Crown and
  - ii. Root
- The crown and root are demarcated by gingiva(gum).
- The root is placed in a socket called alveolus in maxillary and mandibular (lower) bone.
- The enamel (outermost layer of the teeth) is the hardest substance found in the body and consists of almost calcium apatite crystals.
- The periodontal is another mineralized tissue whose distribution of organic matrix mineral is similar to that of regular compact bone.
- The pulp cavity collagenous fiber running in all direction and aggregated into bundles.
- The ground substance, nerve cells, blood vessels are also contained in the pulp.
- The periodontal membrane anchors the root firmly into the alveolar bone and is mostly collagenous fiber and glycoproteins.

Materials used for Dental

i. Impression materials

- Impression materials are used to make a reproduction of gum surface as a mold or model based on which dentures and restoration materials are fabricated.
- They are used mostly for the preparation of cost of an artificial denture.
- The most commonly used impression materials are plaster of plastic ($CaSO_4$ - hemihydrate), dental stone ($CaSO_4$ - hemihydrate), elastic impression material which includes hydrocolloid and elastomeric materials.
- Reversible hydrocolloid - example: agar.

- Irreversible hydrocolloid – example: ground seaweed polymer.

ii. Bases, liners and varnishes for cavities
- There is a large diversity of organic and inorganic materials for the purposes.
- They can be used as barrier against other materials with aggressive pH for thermal and electrical insulation or to provide hardness and mechanical barrier.
- These materials include Zinc polycarboxylate, cement, ionomer glass cement and varnishes.

iii. Filling and restoration materials
- Dental amalgam has traditionally being employed for cavity filling but use of this material is controversial due to toxicity & environmental pollution by mercury.
- Amalgam is obtained by mixing silver, tin, copper alloy powder with liquid and mercury.
- The liquid is a paste that hardens as mercury dissolves on the surface of the alloy.
- Alternatively cavities are filled using PMMA resins.

iv. Materials for deep cavities
- Necrosis of the tissues at the pulp chamber and the root canal of the teeth occurs by deep cavities.
- The nature of materials employed is very important since they contact internal tissues at root apex.
- The materials include cement, polymers such as polyethylene, epoxy, silicon, polycarbonate which contribute to the hardness of final product and also seal the internal part of the canal.

v. Metals in dentistry
- Metals in dentistry are mainly used to construct crowns, orthodontic wires.
- The alloys used are gold alloy containing silver, copper, palladium, platinum and zinc.

vi. Oral Implants

vii. Dental Implants
- The endosstosis implant is inserted into the site of missing or extracted teeth to restore the original function.
- This implant is made up of stainless steel, Co-Cr alloy, Ti-Al-Va alloy and stainless steel.
- The surface of implant is coated with ceramic or polymers.

viii. Mandibular reconstruction
- Mandibular defects are more often due to some trauma or neoplasm.
- Urethane elastomer has been used as a substitute to medical devices for reconstruction of mandible at room temperature and no special equipment is required for surgery.

ix. Collagens in dentistry

- Collagen is widely used in prevention of oral bleeding, healing of mucosal lining

Use of collagen in dentistry

Collagen has wide applications in the dental field. For example, collagen plugs are used for control of bleeding, and resorbable forms of collagen are used to dress oral wounds, for closure of graft and extraction sites, and to promote healing.

Collagen is a highly versatile material that is extensively used in the medical, dental and pharmacological fields. Collagen is capable of being prepared into cross-linked compacted solids or into lattice-like gels. Use of collagen in the form of tendons as suture material goes back to millennia and can hold its ground with catgut, which is still representing a useful suture material in surgery. Resorbable forms of collagen have been used to dress oral wounds, for closure of graft and extraction sites and to promote healing. Collagen-based membranes have also been used in periodontal and implant therapy as barriers to prevent epithelial migration and allow cells with regenerative capacity to repopulate the defect area.

It has been reported that collagen has the following properties:

- It controls the evaporation of fluid, keeping the wound pliable and flexible.
- It promotes the development of granulation tissue,
- It diminishes pain and
- It provides mechanical protection against physical and bacterial insult.

Collagen powders exhibit excellent adhesion to the wound, hemostatic properties, tissue fluid binding and an adequate stimulation of cell reactivity. Collagen has the ability of enhancing wound healing following dental therapy by clot formation and stabilization, neovascularization and epithelial cell rejuvenation thus acting as a natural hemostatic agent. Collagen also serves as a biologic scaffold for ingrowths of endothelial cells and progenitor cells from the periodontal ligament.

For oral applications, homogenized reconstituted collagen mixed with cell culture media has been used for endodontic repair. Notably, collagen-based membranes have been widely used in periodontal and implant therapy as barriers that prevent the migration of epithelial cells and encourage wound repopulation by cells with regenerative potential. Type I collagen as a possible membrane barrier for use in guided tissue regeneration (GTR) procedures. Collagen is absorbable, does not require a second surgical procedure for removal and has some unique properties. Type I collagen has the capacity to support regeneration of periodontal tissues.

Collagen is used as a membrane due to the following reasons: It is the major extracellular macromolecule of the periodontal connective tissue and is physiologically metabolized by these tissues, it is chemotactic for fibroblasts, it has been reported to act as a barrier for migrating epithelial cells *in vitro* and it is a weak immunogen that has been used experimentally in animals and humans. The collagen membrane barrier may act to enhance and protect the initial clot formation onto the root surface by acting as a scaffold for cell adhesion and in growth. It may also attract fibroblasts to the area, which may aid in the formation of new attachment and regeneration during GTR procedures. A combination of dexamethasone and platelet derived growth factors (PDGF) in a collagen carrier matrix (CM) has been tested on local experimental periodontitis lesions in monkeys. It was observed that application of PDGF/dexamethasone/CM produced five-fold more new cementum and ligament and seven-fold more supracrestal bone than the control treatments that had a collagen carrier only.

OPHTHALMOLOGY

Introduction

Eye implants are used to restore functions of cornea, lens, vitreous humor, etc. to maintain

and improve the eye vision.

Various biomaterials used in ophthalmology are:

i. Viscoelastic solutions
ii. Intraocular lens
iii. Contact lenses
iv. Eye shields
v. Artificial tears
vi. Vitreous replacements
vii. Correction of corneal curvature (lasik laser surgery)
viii. Scleral buckling materials.

Contact lenses

It is used to correct ametropias (refractive index error).
It is used cosmetically to improve the appearance of damaged eye and enhance eye color.
In ocular surfaces, disorder such as:

- Chronic corneal ulcers
- Recurrent erosions
- Pain in bulbous keratopathy (corneal edema)
- Entropion
- Therapeutic – bandage lenses

Therapeutic contact lenses may be considered a bandage on the cornea and thus they have also been called Bandage lenses.
Lenses placed in direct contact with the cornea to correct vision.

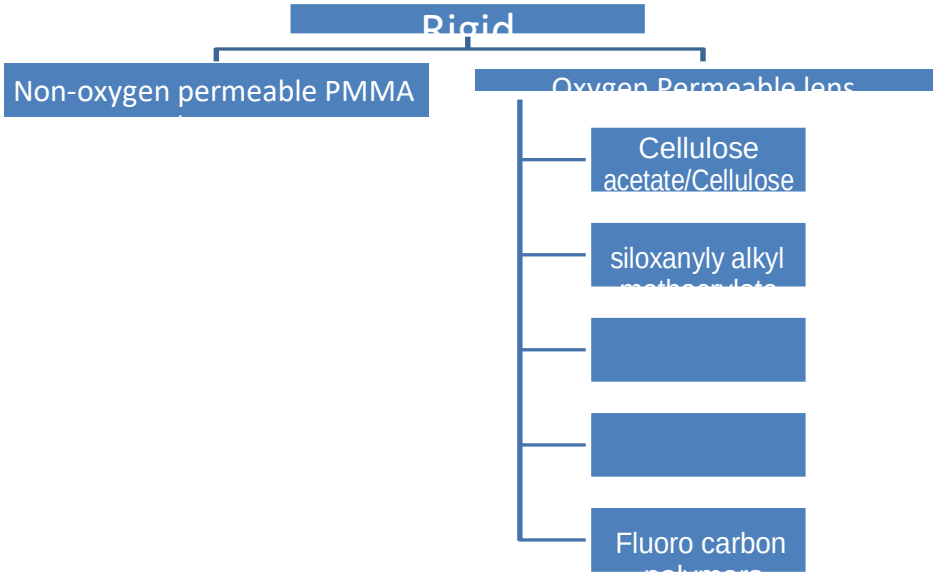
Desirable properties of contact lens

i. High oxygen permeability to minimize lens interference with corneal respiration.
ii. Good wettability by tears and resistance to deposition of protein, mucous, lipid, microorganisms and other foreign substances on the lens surface.

Materials used for contact lenses

i. Rigid
ii. Elastomer
iii. Hydrogel

Materials used for construction of contact lens



Contact lens must be thin with sufficient flexibility.

Elastomeric lens

i. Silicone rubber
   - Made of cross-linked poly-methyl-phenyl-vinyl silicones.
   - It has highest O_2 permeability of all contact lens materials.
   - Silicone rubber lenses-Good O_2 permeability (drawback is hydrophobic ocular intolerance).
   - It interacts with lipid components from tears and preservative solutions.

ii. Acrylic rubber
   - Made of cross-linked co-polymers of n-butyl acrylate with n-butyl methacrylate.

Hydrogel lenses (Also known as Soft contact lens)

i. Low water content
   - Made from cross linked 2-hydromethyl methacrylate polymer.
   - Contains methacrylic acid to inhibit growth of fungi, bacteria, protein & mucous layer.

- Determines the hydration and reactivity of lens to diverse contaminants.
- Another approach to increase oxygen permeability of polymeric material to increase the diffusion of O_2 by creating small channels in lens materials.

ii. Medium and High water content

- Consists of co-polymers of vinyl pyrrolidone with 2-hydroxyethyl methyl acrylate or methyl methacrylate

Eye Shields

These are used in the treatment of basement membrane associated diseases corneal abrasions, erosions, epithelial defect, cataract extraction penetrating kertoplastin and other diseases the cause eye inflammation.

Once applied to eye these shield absorb fluid from ocular surface and begins to dissolve.

The surface polymers in use are: Hydrogels, polyvinyl alcohol, silicone rubber and collagen.

Eye Shield – thin clear, pliable, collagen film (0.0127-0.77mm thick).

In a spherical shell shape with the diameter of 14.5mm and base curvature of 9mm are used as eye shield of relief of discomfort.

Eye shield is used to prolong the delivery of antibacterial, antifungal, antiviral and anti-inflammatory agents.

Artificial tears

Keratoconjunctivitis sicca is a dry eye syndrome characterized by either decreased tear formation.

Symptoms range from mild ocular discomfort to severe ocular pain.

Artificial tears are added as substitute. The commonly used are methyl cellulose, polyvinyl alcohol, hyaluronic acid, chondroitin sulphate.

Corrosion of metallic implant

Corrosion is one of the major process that affects the metal and alloy that are used as implants in the body.

Corrosion may be regarded as the unwanted reaction of the metallic component with the environment which it exists.

During this process, metal ions are lost from the metal surface to form either a solid corrosion product or one that is soluble in the environment.

Corrosion Reaction

Corrosion in the aqueous medium of the body fluid is an electrochemical process.

The electrochemical reactions that occur on the surface of the surgically implanted alloy are identical to those observed during exposure to sea water.

The metallic components of the alloy are oxidized to ionic form and the dissolved oxygen is reduced to hydroxyl ion.

The electrons that are released during oxidation are consumed in the reduced reaction.

Corrosion of stainless steel implant is mainly affected by pitting.

Pitting Corrosion

- It refers to the formation of small cavities or holes at the surface of material which is protected by the presence of an adherent tenacious and self-healing thin films.
- The formation of pit is attributed with the interaction of certain aggressive ions with the films at location where it is defective or weak in nature.
- The pit may be visible to naked eye in some cases but in general they are invisible and dangerous to the extent they can allow the formation of stress, corrosion, cracking or fatigue crack.
- The importance of pitting significantly depends on the nature of the surface layer or due to the film that has formed on the surface due to the interaction of material with the environment.
- Thus it state of passivity is forced on the material which safeguard the material from general corrosion slowing down the dissolution process at the surface.

Types of failure of orthopedic implantation material

- An orthopedic implant is considered to fail if it had to be prematurely removed from the body.
- Failures of implant are usually classified as: mechanical, electrochemical and biological.
- Mechanical failures include overload fracture, fatigue fracture and permanent deformation.
- Electrochemically failures are related to different forms of corrosion.
- Biological failures are due to infection, inflammation or adverse reaction by the host induced by the presence of implant.
- The remedies to overcome such failures are surface modification of the implant.

Corroboration of Failure Mechanism

- Unawareness of the patient on the load bearing capacity of an implant.
- Improper fitting of the implant by the surgeon.
- Biomechanical forces.
- Corrosion attacks due to hostile body environment.
- Fabrication problem.

Surface modification of orthopedic implants

- Corrosion is a major problem affecting the service life of orthopedic implant.
- There are number of ways to reduce corrosion.

i. Altering the environment.
ii. Addition of chemical inhibitors.
iii. Changing the electrolyte concentration.

- These techniques cannot be adapted for orthopedic implant since the body environment is fixed and cannot be altered without biological effect.
- The alternate way to reduce corrosion of orthopedic implant are:
  i. Material selection.
  ii. Surface modification by protective coating which improves corrosion resistance of the currently used implant material.
    - Materials should possess adequate mechanical strength to tolerate body movement and biocompatibility to overcome the adverse effect on the surrounding tissue.
    - The coating should not impair the properties of bulk material.
    - The deposition process must not change the size and shape of implant.
    - Surface treatment must be cost effective with reduced time consumption.
    - Stainless steel, Co-Cr alloy and Ti and its alloy possess the required mechanical strength and biocompatibility by coating the metal surfaces with ceramic powder HAP coating and plasma sprayed metal powder, etc. which are widely used in orthopedic applications.

Biocompatibility Testing (Biological Test)

- Theoretical part should be followed before developing a medical device.
- Biological test for three different groups:

i. Surface devices.
ii. External communicating devices.
iii. Internal devices.

Various Biological Test

i. Cytotoxicity

- Invitro interaction of material with simplest organisms like cell, the cytotoxicity test can be done. There are three ways to the extract of biomaterials:
  - Exposing the cells to the extract of biomaterials
  - Indirect contact via diffusion layer like agar.
  - Direct contact with surface.
- Direct contact:

Immersing biomaterial in an extractant (culture medium) Incubation

↓

at 37C for 24 hours.

↓

Extractant liquid filtered off

↓

Diluted

↓

Cells exposed to these dilutions for different periods of time.

- Cells are directly inoculated onto the material surface, the disadvantage is that it is difficult to obtain reproducible number of cells on test material as they are easily washed off when it is flooded with the medium.
- The suitable way is to inoculate small drop of extract and incubate such that cells adapt to the surface and then the well is filled and the cytotoxicity is observed.
- It is simple technique and less experience.

ii. Genotoxicity

- Mutagenic material increases the rate of mutation of either individual genes or chromosal mutation.
- Genotoxicity can be determined by both invivo and invitro condition.
- Invitro, the gene mutation can be done by AMES test.
- Invivo chromosal damage can be done by Micronucleus test.
- There are two types of mutagens: One type can damage DNA directly and the other damages DNA indirectly with intermediate conversion step.

- This genotoxicity test determines the mutagenic potential of extract material on a mammalian cell culture.

iii. Carcinogenicity testing

- Carcinogenicity potential is evaluated through implantation on rodents using non carcinogenic material polyethylene as control.
- It needs a extended time period 1 year to exhaustive.
- If the test is negative, it is not sure that they may not induce carcinogenic response once induced.
- Example: Breast Prosthesis.

iv. Reproductive toxicity/Reproducibility toxicity

- It is similar to carcinogenicity and mutagenicity test.
- This test is usually done to determine the toxic level of intra uterine devices, energy depositing devices and resorbable devices.
- The test is designed to determine the toxicity during reproductive cycle of the cell.
- New experiments have been done using transgenic animals whose DNA is replaced by human DNA.

v. Irritation and Sensitization

- To estimate the potential of irritation of the extract.
- The amount of leachable causes allergic reactions.
- Allergic to nickel containing metal alloys in contact with skin, in women wearing non-noble jewels.
- Patch test is done to determine the host is susceptible to allergen.
- This test is done by treating the Guinea pigs with patch embedded extract of

material and untreated patch as control to the other Guinea pig.

- If the animal is allergic to leachables, erythema (redness) and edema (swelling)

object at regular intervals.

vi. Systemic toxicity
- It is done to evaluate the possible toxicity in living body caused by leachables from devices at sites distant from the implant site.
- Material may be biocompatible but the leached components are toxic in nature.
- Toxicity depends not only on chemistry but also on the quantity released in unit time.
- Every compound has a threshold value above which the toxicity becomes evident.

vii. Blood compatibility

viii. Biofunctionality test
- Material selected for prosthesis construction may be a biomaterial but may not be a biocompatible for life.
- Invivo performance is different from the theoretical point of view.
- Example: shaped material may degenerate under biological attack.
- It is necessary to perform suitable physical and chemical test considering the physiological condition.
- Stimulation test is done to check how prosthesis behave in different and extreme situations.
- It is called as biofunctionality test as they are designed to check the bioperformance of prosthesis during its functioning.

Material Surface Characterization

- Material surface characterization done by following methods:
  i. Electron spectroscopy for chemical analysis (ESCA) or X-ray photospectroscopy
  ii. Infra-red Spectroscopy
  iii. Secondary ion mass spectrometry
  iv. SEM
  v. STM
  vi. AFM

i. ESCA

- ESCA provides unique information about a surface that cannot be absorbed by other technique.
- ESCA is expensive and generally requires experts to perform the measurement.
- ESCA is otherwise called as XPS (X-ray photoelectron spectroscopy).
- X-ray are focused upon specimen. The interaction of X-rays with atom in the specimen causes the emission of your inner shell electrons.

Working

- The sample is introduced into a preparation chamber and pumped down to 10^{-6} torr pressure.
- A gate valve between the introduction chamber and analytical chamber is opened and the specimen is moved into analysis chamber.
- In the analysis chamber, a 10^{-9} torr pressure, the specimen is positioned on contemporary instrument using a microscope or TV camera.
- And the X-ray source is turned ON.
- The ranges of electron energies to be absorbed are controlled by computer with the retardation lens on the spectrometer.
- First a wide scan is made in which the energies of all the emitted electrons are detected.
- The narrow scans are made in which each of the elements detected with a wide scan is examined in higher resolution.

ii. Infra-red Spectroscopy

- Attenuated total reflectance mode (widely used for biomaterial)
- The infra-red light provides information on the vibration of atomic and molecular unit.
- It is a standard analytical method that can reveal information on specific chemistry and orientation of structure.
- By using FTIR spectrometer, great improvement in signal to noise ratio and spectral accuracy can be analyzed.
- This high SN ration, the small absorption signal associate with the extremely small mass of material in a surface region can challenge the sensitivity spectrometer.
- The attenuated total reflectance (ATR) mode of sampling has been used more often in biomaterial studies.
- The penetration depth into the sample is 1 to 5 □m.
- ATR is not surface sensitive but absorbs a broad region near the surface.

PART-A

1. What is the principle behind contact angle method?
2. How are contact lens classified?
3. What are the types of corrosion?
4. Give the block diagram of the philosophy of biological tests for biomaterials and medical devices.
5. How does it standardize a biomaterial?
6. What is ESCA?
7. What are eye shields? Name few polymers used as eye shields.
8. Draw the structure of human eye.
9. How does SEM characterize a material surface?

PART-B

1. Explain in detail about the various biological tests used to determine the toxicity of biomaterials.
2. Explain about the European standards on biomaterials.
3. How is material surfaces characterized? Briefly describe any two methods for the same.
4. Write about the nature of materials used in ophthalmology, namely contact lenses, artificial tears and eye shields
5. What is corrosion? Describe the nature and types of corrosion that are responsible for failure of implant materials
6. What is a contact lens used for? Explain the types, composition and properties in detail.

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1. RS Khandpur, Hand Book of Biomedical Instrumentation, Tata McGraw Hill, 2nd Edition, 2003.
2. Joon B Park, Biomaterials – An Introduction, Plenum press, New York, 2nd Edition 2012.

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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – IV - BIOMATERIALS AND ARTIFICIAL ORGANS– SBMA7001

IV BLOOD INTERFACING IMPLANTS

NEURAL AND NEUROMUSCULAR IMPLANTS

Brain implants, often referred to as neural implants, are technological devices that connect directly to a biological subject's brain – usually placed on the surface of the brain, or attached to the brain's cortex. A common purpose of modern brain implants and the focus of much current research is establishing a biomedical prosthesis circumventing areas in the brain that have become dysfunctional after a stroke or other head injuries. This includes sensory substitution, e.g., in vision. Other brain implants are used in animal experiments simply to record brain activity for scientific reasons. Some brain implants involve creating interfaces between neural systems and computer chips. This work is part of a wider research field called brain-computer interfaces. (Brain-computer interface research also includes technology such as EEG arrays that allow interface between mind and machine but do not require direct implantation of a device.) Neural implants such as deep brain stimulation and Vagus nerve stimulation are increasingly becoming routine for patients with Parkinson's disease and clinical depression respectively, proving themselves a boon for people with diseases which were previously regarded as incurable.

Brain implants electrically stimulate, block or record signals from singleneurons or groups of neurons (biological neural networks) in the brain. The blocking technique is called intra-abdominal vagal blocking. This can only be done where the functional associations of these neurons are approximately known. Because of the complexity of neural processing and the lack of access to action potential related signals using neuroimagingtechniques, the application of brain implants has been seriously limited until recent advances in neurophysiology and computer processing power.
The neuromuscular junction, the connection between nerve cells (neurons) and muscle fibres in the peripheral nervous system, is an important target for prosthetics. Increasingly high-resolution, low-noise interfaces exploiting nanotechnology show promise for treatment of a wide range of dysfunctions due to neurodegenerative disorder or trauma. The interfaces have enabled recording or stimulation at unprecedented resolution and signal-to- noise ratio. Striated muscle can therefore act as a bio-amplifier to outgoing motor central nervous system impulses that can be used in brain control prosthetics.

The nanocrystalline diamond coatings that cover the 3D mushroom-shaped electrodes impart exceptional electrochemical properties, excellent mechanical and chemical stability, and biocompatibility. The diamond electrodes were tested in vivo in extraneural and intraneural devices. Surface functionalisation with peptides promoted engulfment by neurons. The electrodes were combined into microelectrode arrays and processed to enable flexible implants.

Tests have been performed on intraneural self-opening intrafascicular neural interface (referred to as SELINE) electrodes implanted into the sciatic nerve of rats. Intraneural electrodes were used to deliver sensory feedback through neural stimulation in a below-elbow amputee. Moreover, chronic or long-term validation of a new micro-fabricated design of three-

dimensional intraneural electrode showed potential for stimulation of chronic implants.

MERIDIAN has also developed a planar regenerative electrode. It was inserted into tailored nerve guides, which, after being implanted, allowed the axons to regenerate through the channel over the electrode. The use of thin-film technology and novel technologies for delivering growth and neurotrophic factors via microspheres allowed construction of a device suitable for peripheral nerve applications.

Novel electrodes for in vivo implants will be showcased in bi-directional and real-time bionic devices to treat urinary incontinence and to function in prosthetic hands. Nerve regeneration strategies will boost the impact of these prosthetics even more.

Another type of now-common implant, used by thousands of Parkinson's patients around the world, sends electrical pulses deep into the brain proper, activating some of the pathways involved in motor control. A thin electrode is inserted into the brain through a small opening in the skull; it is connected by a wire that runs to a battery pack underneath the skin. The effect is to reduce or even eliminate the tremors and rigid movement that are such prominent symptoms of Parkinson's (though, unfortunately, the device doesn't halt the progression of the disease itself). Experimental trials are now under way to test the efficacy of such "deep brain stimulation" for treating other disorders as well.

Vascular implants

A vascular implant is a long-term implantation of a patented medical device used in the treatment of an abnormality in the vein or an artery. Currently, it is being used to treat various diseases in the vascular region from aneurysms, ruptures, dissections to blood clots. Vascular implants comes in various forms, whether it is a stent or a graft or a combination of both.

Stents

A vascular stent is a medical device used to hold open a section of blood vessel where there is some restriction of blood flow. It is an artificial tube-like apparatus inserted into the vascular area needed for assistance. Vascular stents or metallic endroprotheses are designed to aid in vascular diseases such as vascular *stenosis*, where a narrowing of the blood vessels is causing restriction of blood flow. They are designed to be self-expanding to facilitate their placement in the vessel endoscopically. By aiding the vessel to return to its homeostatic condition the stent prevents further vascular diseases within the abnormal area. Stents are usually made of a metal component or a thermoplastic material with a polymer coating, one of which is polyurethane. This coating has some form of shape memory and shape recovery temperature within the physiological range (35°C to 50°C), which is essential in the function of stent use in vascular regions. (See Implant Biomaterials for further discussion on materials used for vascular stents). The material used to coat the stent wall is significant in the functioning of the stent in the body. The primary function of this coating is to discourage the formation of a blood clot or prevent a clot from attaching to the stent wall.

Grafts

Vascular grafts are used in the same way as stents, in which a synthetic or biological material is used to patch up an injured or abnormal portion of a blood vessel. Grafts can be made of an artificial material or an implantation of healthy tissue taken from a healthy portion of another vessel and placed onto the damaged area. A stent graft is commonly used in blood vessels,

which consists of a rigid metal mesh-like structure (stent) covered with a synthetic material (graft).

Vascular grafts are used when a portion of a blood vessel is in need of repair or when entire

sections of vessels needs to be replaced due to vascular diseases such as an aneurysm or atherosclerosis. They can be made from a variety of materials either synthetic or biological. Synthetic grafts can be made with various polymers such as Dacron, Teflon, polyester, PTFE (Polytetrafluroethylene), polypropylene, etc. Artificial grafts are usually made with a mesh-like woven material and pre-clotted and coated with protein (either collagen or albumin) prior to insertion to reduce blood loss. Most commonly used grafts for aortic prosthesis are knitted and woven Dacron and Teflon. These materials are durable and less likely to become infected, with durability of 80% to 90% within 5 to 10 years. In some cases biological grafts are used, the most common of which being the AVS (autogenous saphenous veins) graft. Biological grafts are made using vascular tissue taken from another vascular site, with a durability of 70% to 85% within 5 years of implantation. If this type of graft is unavailable a prosthetic graft must be used.

Implant Failure

Although stents and grafts are used to aid blood flow in response to blood restriction the reverse process can occur. This can be due to blood clot formation resulting from protein fouling or an adverse response to the implant by the native tissue.

HEART VALVE IMPLANTS

The introduction of valve replacement surgery in the early 1960s has dramatically improved the outcome of patients with valvular heart disease. Approximately 90 000 valve substitutes are now implanted in the United States and 280 000 worldwide each year; approximately half are mechanical valves and half are bioprosthetic valves. Despite the marked improvements in prosthetic valve design and surgical procedures over the past decades, valve replacement does not provide a definitive cure to the patient. Instead, native valve disease is traded for "prosthetic valve disease," and the outcome of patients undergoing valve replacement is affected by prosthetic valve hemodynamics, durability, and thrombogenicity. Nonetheless, many of the prosthesis-related complications can be prevented or their impact minimized through optimal prosthesis selection in the individual patient and careful medical management and follow-up after implantation. The purpose of this article is to provide an overview of the current state of knowledge and future perspectives with regard to optimal prosthesis selection and clinical management after valve implantation.

Types of prosthetic heart valve devices

The ideal valve substitute should mimic the characteristics of a normal native valve. In particular, it should have excellent hemodynamics, long durability, high thromboresistance, and excellent implantability. Unfortunately, this ideal valve substitute does not exist, and each of the currently available prosthetic valves has inherent limitations.

Mechanical Valves

Three basic types of mechanical valve design exist: bileaflet, monoleaflet, and caged ball valves.

Caged Ball Valves

Caged ball valves, which consist of a silastic ball with a circular sewing ring and a cage formed by 3 metal arches, are no longer implanted. However, several thousands of patients still have caged ball valves, and these patients require follow-up.

Monoleaflet Valves

Monoleaflet valves are composed of a single disk secured by lateral or central metal struts. The opening angle of the disk relative to valve annulus ranges from 60° to 80°, resulting in 2 distinct orifices of different sizes.

Bileaflet Valves

Bileaflet valves are made of 2 semilunar disks attached to a rigid valve ring by small hinges. The opening angle of the leaflets relative to the annulus plane ranges from 75° to 90°, and the open valve consists of 3 orifices: a small, slit-like central orifice between the 2 open leaflets and 2 larger semicircular orifices laterally.

Bioprosthetic Valves

Stented Bioprostheses

The design of bioprostheses purports to mimic the anatomy of the native aortic valve . Porcine bioprosthetic valves consist of 3 porcine aortic valve leaflets cross-linked with glutaraldehyde and mounted on a metallic or polymer supporting stent. Pericardial valves are fabricated from sheets of bovine pericardium mounted inside or outside a supporting stent.

StentlessBioprostheses

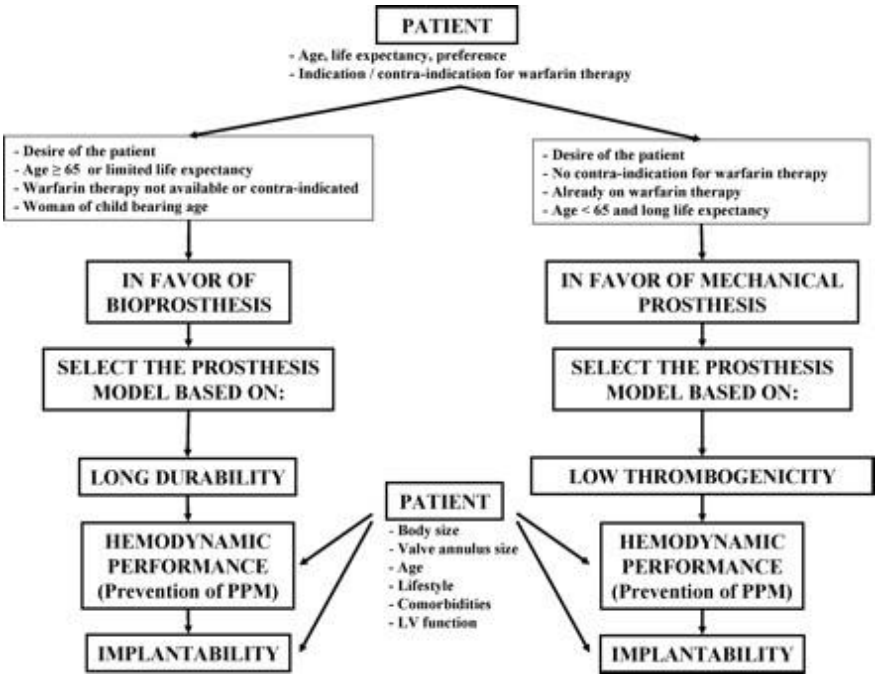
In an effort to improve valve hemodynamics and durability, several types of stentless bioprosthetic valves have been developed. Stentlessbioprostheses are manufactured from whole porcine aortic valves or fabricated from bovine pericardium.

Percutaneous Bioprostheses

Percutaneous aortic valve implantation is emerging as an alternative to standard aortic valve replacement (AVR) in patients with symptomatic aortic stenosis considered to be at high or prohibitive operative risk . The valves are usually implanted using a percutaneous transfemoralapproach.To reduce the problems of vascular access and associated complications, a transapical approach through a small thoracotomy may also be used. At present, the procedure appears promising, but it remains experimental and is currently undergoing further investigation.

Selecting the Optimal Prosthesis in the Individual Patient

Bioprosthetic Versus Mechanical Valve


PATIENT
- Age, life expectancy, preference
- Indication / contra-indication for warfarin therapy
- Desire of the patient
- Age ≥ 65 or limited life expectancy
- Warfarin therapy not available or contra-indicated
- Woman of child bearing age
- Desire of the patient
- No contra-indication for warfarin therapy
- Already on warfarin therapy
- Age < 65 and long life expectancy
IN FAVOR OF BIOPROSTHESIS
IN FAVOR OF MECHANICAL PROSTHESIS
SELECT THE PROSTHESIS MODEL BASED ON:
SELECT THE PROSTHESIS MODEL BASED ON:
LONG DURABILITY
LOW THROMBOGENICITY
PATIENT
- Body size
- Valve annulus size
- Age
- Lifestyle
- Comorbidities
- LV function
HEMODYNAMIC PERFORMANCE (Prevention of PPM)
HEMODYNAMIC PERFORMANCE (Prevention of PPM)
IMPLANTABILITY
IMPLANTABILITY

Prosthesis-Patient Mismatch

The term valve PPM was first proposed in 1978 by Rahimtoola.PPM occurs when the EOA of a normally functioning prosthesis is too small in relation to the patient's body size (and therefore cardiac output requirements), resulting in abnormally high postoperative gradients. The most widely accepted and validated parameter for identifying PPM is the indexed EOA, ie, the EOA of the prosthesis divided by the patient's body surface area. the threshold values of indexed EOA generally used to identify PPM and to quantify its severity. Moderate PPM may be quite frequent in both the aortic (20% to 70%) and mitral (30% to 70%) positions, whereas the prevalence of severe PPM ranges from 2% to 10% in both positions.

Long term Management Antithrombotic Therapy

Patients with prosthetic valves are at risk of thromboembolic complications, including systemic embolization, most commonly cerebral, and prosthetic thrombosis causing valve obstruction and/or regurgitation. The risk of thromboembolic events is higher with mechanical than with bioprosthetic valves, higher with mitral than with aortic prosthetic valves, and higher in the early (<3 months) versus late postoperative phase.[6,7,43] The risk also is increased in the presence of concomitant risk factors for thromboembolism, including atrial fibrillation, LV dysfunction, left atrial dilation, previous thromboembolism, and hypercoagulable condition. Table 4 summarizes the general recommendations for antithrombotic therapy based on the prosthesis type and position and the presence of risk factors.[6,43,44] Patients with mechanical prostheses require lifelong anticoagulation with warfarin. The choice of optimum international normalized ratio (INR) target for oral anticoagulation should also take into account the thrombogenicity of the individual prosthesis

Identifying Indirect Signs of Dysfunction

The size and function of the LV and atrial chambers and the level of systolic pulmonary arterial pressure can be used to corroborate prosthesis dysfunction severity. In particular, these measurements can be compared with previous measurements and often are the first sign to alert attention when the regurgitation is difficult to visualize.

Additional Diagnostic Tests

Exercise testing and plasma natriuretic peptides are additional tests that can be used to further document decreased functional capacity and/or early heart failure resulting from prosthesis dysfunction or PPM.

Previous SectionNext Section

Long-Term Complications: Identification and Management

Mechanical valves have a substantial risk of thromboemboli and thrombotic obstruction and therefore require long-term anticoagulation therapy, which in turn is associated with an increased risk of hemorrhagic complications. Nonetheless, contemporary mechanical valves have excellent durability. In contrast, bioprosthetic valves have a low risk of thromboembolism without anticoagulation, but their durability is limited by calcific or noncalcific tissue deterioration.

Thromboembolic and Bleeding Complications

Thromboembolic complications are an important cause of morbidity and mortality in patients with a prosthetic heart valve, with an estimated incidence of clinical events ranging from 0.6% to 2.3% per patient-year.[6,50] The risk of thromboembolic complications is similar for patients

with mechanical valves on warfarin therapy and bioprosthetic valves without warfarin therapy. The risk of thromboembolism depends not only on prosthesis type but also on valve position and thrombogenicity, patient risk factors, and antithrombotic treatment.

Systemic Emboli

In patients with a prosthetic valve, thromboembolic events are presumed to be related to the valve unless proven otherwise. The presence of a thrombus on the prosthesis may not be confirmed by echocardiography because the thrombus is no longer present, is too small to be detected, or is occulted by the shadowing caused by the valve components. The first step in the management of a patient with a prosthetic valve and a systemic embolic event is to carefully assess the adequacy of anticoagulation control. If it is inadequate, therapy is adjusted or reinstituted to achieve and maintain a therapeutic effect. If anticoagulation has been adequate, warfarin therapy should be increased to achieve a higher INR target, and notwithstanding bleeding risk assessment and the results of the investigation, aspirin may also may be added or increased.[6] Moreover, in patients with recent cerebral embolism who are at high risk for hemorrhagic transformation of the cerebral infarct (infarct size >35% of the cerebral hemisphere and/or uncontrolled hypertension), it is preferable to withhold oral anticoagulation for at least 5 days and use intravenous heparin in the meantime.

Prosthesis Thrombosis

Obstruction of prosthetic valves may be caused by thrombus formation , pannus ingrowth , or their combination. Pannus ingrowth alone may be encountered in both bioprosthesis and mechanical valves. It may present as a slowly progressive obstruction caused by a subvalvular annulus, in which case it may be difficult to visualize and thus distinguish from progressive structural valve deterioration (SVD). Valve thrombosis is most often encountered in patients with mechanical valves and inadequate antithrombotic therapy. Thrombosis also may be seen in bioprosthetic valves where it most often occurs in the early postoperative period. Pannus and thrombosis may be present alone or in combination and cause acute or subacute valve obstruction. The incidence of obstructive valve thrombosis varies between 0.3% and 1.3% per patient-year in patients with mechanical valves.

Design challenges of heart valve prostheses

Mechanisms:

Forward and backward flow shear

Static leakage shear

Presence of foreign material (i.e. intrinsic coagulation cascade)

Cellular maceration

Valve-tissue interaction

Dynamic responsiveness

Failure safety

Valve orifice to anatomical orifice ratio Trans-valvular pressure gradient Minimal leakages

Detachable and Replaceable Models of Heart Valve Prostheses

Many prosthesis-related complications can be prevented or their impact minimized by individualized selection of the optimal prosthesis at the time of valve replacement and by careful

medical management and periodic monitoring of valve function after operation. Prompt recognition of valve dysfunction allows early treatment, often with repeat surgical intervention. Several recent developments, including the rapidly evolving field of percutaneous valve

implantation, lifestyle and/or pharmacological interventions for the prevention of bioprosthetic valve degeneration, and patient self-management of oral anticoagulation, may change the face of the current practice for the surgical management of valve disease in the near future.

HEART AND LUNG ASSISTIVE DEVICE

A ventricular assist device (VAD) is a mechanical pump that's used to support heart function and blood flow in people who have weakened hearts.

The device takes blood from a lower chamber of the heart and helps pump it to the body and vital organs, just as a healthy heart would.

You may benefit from a VAD if one or both of your ventricles (VEN-trih-kuls) don't work well because of heart disease. Ventricles are the lower chambers of your heart.

A VAD can help support your heart:

- During or after surgery, until your heart recovers.
- While you're waiting for a heart transplant.
- If you're not eligible for a heart transplant.

- A VAD has several basic parts. A small tube carries blood out of your heart into a pump. Another tube carries blood from the pump to your blood vessels, which deliver the blood to your body.

- A VAD also has a power source that connects to a control unit. This unit monitors the VAD's functions. It gives warnings, or alarms, if the power is low or the device isn't working well.
- Some VADs pump blood like the heart does, with a pumping action. Other VADs keep up a continuous flow of blood. With a continuous flow VAD, you might not have a normal pulse, but your body is getting the blood it needs.
- Research has shown that, compared with other VADs, continuous flow VADs may decrease hospital stays and complications and improve survival. However, more research is needed.
- ***Types of Ventricular Assist Devices***
- The two basic types of VADs are a left ventricular assist device (LVAD) and a right ventricular assist device (RVAD). If both types are used at the same time, they're called a biventricular assist device (BIVAD).
- The LVAD is the most common type of VAD. It helps the left ventricle pump blood to the aorta. The aorta is the main artery that carries oxygen-rich blood from your heart to your body.
- RVADs usually are used only for short-term support of the right ventricle after LVAD surgery or other heart surgery. An RVAD helps the right ventricle pump blood to the pulmonary (PULL-mun-ary) artery. This is the artery that carries blood from the heart to the lungs to pick up oxygen.
- A BIVAD might be used if both ventricles don't work well enough to meet the body's needs. Another treatment option for this condition is a total artificial heart (TAH). A TAH is a device that replaces the ventricles.
- VADs have two basic designs. A transcutaneous (tranz-ku-TA-ne-us) VAD has its pump

An implantable VAD has its pump located inside of the body and its power source located outside of the body. A cable connects the pump to the power source through a small hole in the abdomen.

Implantable VADs are used mainly for people who are waiting for heart transplants or as a long-term solution for people who can't have heart transplants.

Until recently, VADs were too big to fit in many people's chests, especially women and children. Only people who had large chests could get them.
However, recent advances have resulted in smaller, more reliable devices. This now makes treatment with VADs an option for more people.

Researchers also have made advances in how well VADs work and how much they improve people's quality of life. In the past, VADs mostly were used for people who had end-stage heart failure. Now VADs also can help people who have earlier stages of heart failure.
Children who have heart failure also can be treated with VADs. VADs approved for use in adults sometimes are used in children if the children are large enough for the device. Also, the Food and Drug Administration recently approved a VAD designed for smaller children.

LUNG ASSISTING DEVICES:

Introduction

The Novalung Interventional Lung Assist (ILA) device is a membrane ventilator that allows for oxygen and carbon dioxide gas exchange to occur by simple diffusion. It has been used in patients with severe acute lung failure due to ARDS, inhalation injury, severe pneumonia, chest injury, foreign body aspiration, and after thoracic surgical interventions. The concept of "protective ventilation" was described decades ago, but with the introduction of extracorporeal ventilation devices such as the Novalung it may reach new dimensions. It potentially helps to avoid or reduce ventilator associated lung injury and remote secondary organ failure, which is related to injurious mechanical ventilation.

Technical aspects of the equipment

The ILA consists of a plastic gas exchange module with diffusion membranes made from polymethylpentene (PMP). These PMP fibers are woven into a complex configuration of hollow fibers. The PMP material is woven to bundles in a low resistance configuration mat arranged in well defined stacks, which provides maximum blood/gas mixing. Gas transfer takes place without the direct contact with blood. In addition, the PMP membrane surface in contact with blood is treated with a heparin coating to provide a biocompatible and non-thrombogenic surface. Blood flows over the exterior surface of the device's fibers; the ventilating gas (commonly O2) flows inside these fibers. In this way the Novalung iLA mimics the native lung. This allows for the blood exiting the device to have the normal amount of oxygen and carbon dioxide that exits the normal lung. In the arterio-venous portion of this pumpless shunt carbon dioxide exchange is the primary function due to arterial inflow blood, while a veno- venous attachment, which requires the support of a mechanical pump, additionally allows full oxygenation support.

Clinical use and results

The Novalung has been used in over 1200 patients in Europe to enable advanced protective ventilation . We have recently reported on the successful use of the Novalung iLA as a bridge to lung transplantation in patients with severe ventilation-refractory respiratory acidosis and hypercapnea. The use of the device allows for a safer form of ventilation ('protective ventilation'), because the patients' carbon dioxide levels and pH can be adjusted to normal levels with the device. Extracorporeal life support with the Novalung iLA has been applied up to 32

days at the Hannover Thoracic Transplant and Cardiac Assist Program.
The driving force for this mode is the left ventricular output. In other situations, which include low cardiac output or hypoxic lung failure, a blood pump is required to divert a relatively larger amount of blood from the venous system through the Novalung, which can be returned into the

systemic arterial circulation (veno-arterial mode) or the central veins (veno-venous mode), respectively. The optimal extracorporeal circuit design and configuration for circulatory support is determined by the underlying disease state and the treating physician's choice.

ARTIFICIAL HEART

An artificial heart is a mechanical device, about the size of an orange, that is connected toyour heart or implanted in your chest to help or replace a failing heart. It may have several valves, a mechanism to propel blood forward, and one or more chambers. Sometimes an artificial heart may help your heart temporarily, until yours recovers. If this is the case, the artificial heart will be removed when it is no longer needed. More commonly, when there is irreversible heart muscle damage and your heart can t recover, the artificial heart stays until you can have a hearttransplant. If no other options are available, an artificial heart may completely and permanently replace your heart.

There are two types of artificial heart:-

1) An artificial heart that provides an extra ventricle (pumping chamber in your heart) to help to pump blood around your body. This is called a ventricular assist device (VAD). A VAD is made from metal and plastic, and has a small pumping chamber lined by a special material that stops blood clots forming. It may be put into your body or lie outside your body, depending on what type of artificial heart is being used.
2) Total artificial hearts (TAH) are a mechanical substitute for your entire heart. They are put into your body after your heart has been removed.

Heart is a muscle that pumps blood around your body. It has four chambers:

the left and right atria (blood receiving chambers)
the left and right ventricles (the blood pumping chambers).

Blood in the right ventricle (right heart) is pumped into the pulmonary artery and on to your lungs. Blood in the left ventricle (left heart) is pumped into the aorta and through to your body.

Blood from your body is received via the superior vena cava (SVC) and the inferior vena cava (IVC) into the right atrium (RA). It then passes from the right atrium into the right ventricle (RV) and is subsequently pumped via the pulmonary artery (PA) into your lungs. In the lungs, blood is enriched with oxygen and carbon dioxide is removed from it.

Blood from your lungs is received by the left atrium (LA) and passes into the left ventricle (LV) from where it is pumped via the aorta into your body. It supplies oxygen and nutrients to the different cells in your body. When your heart is not pumping enough blood around your body because your heart is severely failing, you may need an artificial heart

WORKING OF ARTIFICIAL HEART

Blood enters an artificial heart from the left or right atrium (blood receiving chamber). It is then pumped into the aorta (artery to your body) or pulmonary artery (artery to your lungs), depending on which side of your heart is being supported.

An artificial heart is powered by either compressed air or electricity. A thin cable connects the pumping chamber to a control console that regulates the pump function. The control console can be a large box on wheels that stays beside you, moving with you when you walk around the hospital. It can also be much smaller, with attachable batteries, and worn on a belt or vest.

The smaller console gives you more freedom and mobility than the large console, and may make it possible for you to leave hospital.

NEED OF ARTIFICIAL HEART

If you have severe heart failure and your heart can t pump enough blood around your body to keep it working, you may need an artificial heart.

Your heart may fail because:

- your heart muscle is diseased (cardiomyopathy)
- you have coronary heart disease (disease of the arteries to your heart), which has caused
- a very large heart attack, or more than one heart attack
- you have a severe viral infection of your heart (myocarditis)
- you have another less common disease that affects your heart.

If you have severe heart failure, your cardiologist might recommend that you use an artificial heart until a donor heart becomes available. When a suitable donor heart becomes available and you are well enough, the artificial heart will be removed during the transplant operation. Between 20 and 30 people are given artificial hearts each year in Australia. Most artificial hearts are used until a donor heart becomes available. However, a small number are used permanently in people who aren t suitable for a heart transplant.

LASTING OF ARTIFICIAL HEART

If you are just using an artificial heart until you have a heart transplant, your artificial heart will usually function until you have the transplant. This can range from a few weeks to more than one year.

If you need a total artificial heart permanently because you are not suitable for a hearttransplant, an artificial heart may last for several years.

COMPONENTS OF AN ARTIFICIAL HEART

- Energy source
- Control and driving system
- Energy conversion system
- Pump actuator
- Blood handling parts

COMPLICATIONS WITH ARTIFICIAL HEART

Artificial hearts are very reliable and mechanical failure is extremely rare.

Complications that may occur if you have an artificial heart include bleeding and infection. Major organs, such as the kidneys, liver or lungs may also fail, but these organs may have started failing before you received the artificial heart. Everyone who has an artificial heart must take medicine to thin their blood (anticoagulants). This helps to stop blood clots forming and potentially causing a stroke if the blood clot moves to the brain.

Not everyone who has an artificial heart will recover enough to have a donor heart transplant. Some people will die of the complications mentioned above.

It is very rare for someone to recover enough to have their artificial heart removed and not have a donor heart transplant.

PACEMAKER

A pacemaker is a small device that helps your heart beat more regularly. It does this with a small electric stimulation that helps control your heartbeat. Your doctor puts the pacemaker under the skin on your chest, just under your collarbone. It’s hooked up to your heart with tiny wires. You may need a pacemaker to keep your heart beating properly. This helps your body get the blood

and oxygen it needs. Some people just need a pacemaker for a short time (like after a heart attack) and may use a kind that's outside the skin. The battery unit for this type can be worn on a belt.

A pacemaker is implanted under the skin, just under the collarbone. It should help your heart pump almost as well as it did before. Today many people with pacemakers lead full, active lives.

REASON FOR USAGE OF A PACEMAKER:

Pacemakers may be prescribed for a number of conditions, including:

• **Bradycardia** – a condition in which the heart beats too slowly, causing symptoms such as fatigue, dizziness or fainting spells. Bradycardia may be caused by the wear and tear of age or by conditions such as sick sinus syndrome (SSS) or heart block.

• **Atrial fibrillation** – a common heart rhythm disorder in which the upper chambers of the heart beat rapidly and chaotically. Sometimes people with atrial fibrillation can also have slow rhythms. Medicines used to control atrial fibrillation may result in slow rhythms which are treated by pacemakers.

• **Heart failure** – a condition in which the heartbeat is not sufficient to supply a normal volume of blood and oxygen to the brain and other parts of the body. A special pacemaker can be carefully programmed to increase the force of muscle contractions in the heart. This is called "biventricular pacing" or "resynchronization" therapy.

• **Syncope** – a condition best known as the common faint, is usually not serious. Some patients faint when their heart rhythm becomes very slow. For a small percentage of people who experience severe and frequent fainting spells, a pacemaker may prevent the heart rate from slowing to the point of fainting.

WORKING:

• A pacemaker uses batteries to send electric signals to your heart to help it pump the right way.

• The pacemaker is connected to your heart by one or more wires. Tiny electric charges that you can't feel move through the wire to your heart.

• Pacemakers work only when needed. They go on when your heartbeat is too slow, too fast or irregular.

ADVANCMENT OF PACEMAKER:

A major step forward in pacemaker function has been to attempt to mimic nature by utilizing various inputs to produce a rate-responsive pacemaker using parameters such as the QT interval, $pO_2 – pCO_2$ (dissolved oxygen or carbon dioxide levels) in the arterial-venous system, physical activity as determined by an accelerometer, body temperature, ATP levels, adrenaline, etc. Instead of producing a static, predetermined heart rate, or intermittent control, such a pacemaker, a 'Dynamic Pacemaker', could compensate for both actual respiratory loading and potentially anticipated respiratory loading. Many advancements have been made to improve the control of the pacemaker once implanted. Many of these have been made possible by the transition to microprocessor controlled pacemakers. Pacemakers that control not only the ventricles but the atria as well have become common. Pacemakers that control both the atria and ventricles are called dual-chamber pacemakers. Although these dual-chamber models are usually more expensive, timing the contractions of the atria to precede that of the ventricles improves the pumping efficiency of the heart and can be useful in congestive heart failure.

Rate responsive pacing allows the device to sense the physical activity of the patient and respond appropriately by increasing or decreasing the base pacing rate via rate response

algorithms.

TYPES OF PACEMAKER:

Thee basic types exist to serve different purposes:

• **Single-Chamber Pacemakers** – In a single-chamber pacemaker, only one wire (pacing lead) is placed into a chamber of the heart. Sometimes it is the upper chamber, or atrium. Other times it is the lower chamber, or ventricle.

• **Dual-Chamber Pacemakers** – In dual chamber pacemakers, wires are placed in two chambers of the heart. One lead paces the atrium and one paces the ventricle. This approach more closely matches the natural pacing of the heart. This type of pacemaker can coordinate function between the atria and ventricles.

• **Rate-Responsive Pacemakers** – These have sensors that automatically adjust to changes in a person's physical activity.

• **Other devices** – Some devices, such as implantable cardioverter defibrillators (ICDs), designed primarily for other purposes, can function as pacemakers in certain situations.

COMPONENTS OF A CARDIAC PACEMAKER:

Permanent pacemaker or ICD has three main components:

- A pulse generator which has a sealed lithium battery and an electronic circuitry package. The pulse generator produces the electrical signals that make the heart beat. Most pulse generators also have the capability to receive and respond to signals that are sent by the heart itself.
- One or more wires (also called leads). Leads are insulated flexible wires that conduct electrical signals to the heart from the pulse generator. The leads also relay signals from the heart to the pulse generator. One end of the lead is attached to the pulse generator and the electrode end of the lead is positioned in the atrium (the upper chamber of the heart) or in the right ventricle (the lower chamber of the heart). In the case of a biventricular pacemaker, leads are placed in both ventricles.
- Electrodes, which are found on each lead.

Pacemakers can "sense" when the heart's natural rate falls below the rate that has been programmed into the pacemaker's circuitry.

Pacemaker leads may be positioned in the right atrium, right ventricle, or positioned to pace both ventricles, depending on the condition requiring the pacemaker to be inserted. An atrial arrhythmia (an arrhythmia caused by a dysfunction of the sinus node or the development of another atrial pacemaker within the heart tissue that takes over the function of the sinus node) may be treated with an atrial permanent pacemaker whose lead wire is located in the atrium.

When the ventricles are not stimulated normally by the sinus node or another natural atrial pacemaker site, a ventricular pacemaker whose lead wire is located in the ventricle is placed/used. It is possible to have both atrial and ventricular arrhythmias, and there are pacemakers which have lead wires positioned in both the atrium and the ventricle.

An ICD has a lead wire that is positioned in the ventricle, as it is used for treating fast ventricular arrhythmias. Commonly, ICDs will have an atrial lead and ventricular lead.

Pacemakers that pace either the right atrium or the right ventricle are called "single-chamber" pacemakers. Pacemakers that pace both the right atrium and right ventricle of the heart and require two pacing leads are called "dual-chamber" pacemakers. Pacemakers that pace the right atrium and right and left ventricles are called "biventricular" pacemakers.

CARDIAC DEFIBRILLATORS

An implantable cardioverter defibrillator (ICD) is a small device that's placed in the chest or abdomen. Doctors use the device to help treat irregular heartbeats called arrhythmias (ah-RITH-

me-ahs).

An ICD uses electrical pulses or shocks to help control life-threatening arrhythmias, especially those that can cause sudden cardiac arrest (SCA).

SCA is a condition in which the heart suddenly stops beating. If the heart stops beating, blood stops flowing to the brain and other vital organs. SCA usually causes death if it's not treated within minutes.

Understanding the Heart's Electrical System

Your heart has its own internal electrical system that controls the rate and rhythm of your heartbeat. With each heartbeat, an electrical signal spreads from the top of your heart to the bottom. As the signal travels, it causes the heart to contract and pump blood.

Each electrical signal normally begins in a group of cells called the sinus node or sinoatrial (SA) node. As a signal spreads from the top of the heart to the bottom, it coordinates the timing of heart cell activity.

First, the heart's two upper chambers, the atria (AY-tree-uh), contract. This contraction pumps blood into the heart's two lower chambers, the ventricles (VEN-trih-kuls). The ventricles then contract and pump blood to the rest of the body. The combined contraction of the atria and ventricles is a heartbeat.

For more information about the heart's electrical system (including detailed animations), go to the Health Topics How the Heart Works article.

Overview

A problem with any part of the heart's electrical system can cause an arrhythmia. Most arrhythmias are harmless, but some can be serious.

ICDs use electrical pulses or shocks to treat life-threatening arrhythmias that occur in the ventricles (the heart's lower chambers).

When ventricular arrhythmias occur, the heart can't pump blood well. You can pass out within seconds and die within minutes if not treated.

To prevent death, the arrhythmia must be treated right away with an electric shock to the heart. This treatment is called defibrillation (de-fib-ri-LA-shun).

An ICD has wires with electrodes on the ends that connect to your heart chambers. The ICD will monitor your heart rhythm. If the device detects an irregular rhythm in your ventricles, it will use low-energy electrical pulses to restore a normal rhythm.

If the low-energy pulses don't restore your normal heart rhythm, the ICD will switch to high-energy pulses for defibrillation. The device also will switch to high-energy pulses if your ventricles start to quiver rather than contract strongly. The high-energy pulses last only a fraction of a second, but they can be painful.

Doctors also treat arrhythmias with another device called a pacemaker. An ICD is similar to a pacemaker, but has some differences.

Pacemakers give off only low-energy electrical pulses. They're often used to treat less dangerous heart rhythms, such as those that occur in the upper chambers of your heart. Most new ICDs can act as both pacemakers and defibrillators.

ARTIFIAL KIDNEY

Artificial kidney is often a synonym for hemodialysis, but may also, more generally, refer to renal replacement therapies(with exclusion of kidney transplantation) that are in use and/or in

development. This article deals with bioengineeredkidneys/bioartificial kidneys that are grown from renal cell lines/renal tissue.

Kidney failure:

Kidneys are paired vital organs located behind the abdominal cavity, at about the level of the bottom of the ribcage, corresponding to the levels T12-L3 of the spine vertebrae. They perform about a dozen physiologic functions, and are fairly easily damaged. Some of these functions include: filtration and excretion of metabolic waste products; regulation of necessary electrolytes, fluids, stimulation of red blood cell-production. These organs routinely filter about 120 to 150 quarts of blood a day to produce about 1 to 2 quarts of urine, composed of wastes and extra fluid.

Kidney failure results in the slow accumulation of nitrogenous wastes, salts, water, and disruption of the body's normal pH balance. This failure commonly occurs over a long period of time and is commonly known as end stage renal disease (ESRD). Detecting kidney disease before the kidney's start to shut down is uncommon, with high blood pressure and decreased appetite being the sort of symptoms that indicate a problem. Until the Second World War, kidney failure generally meant death for the patient. Several insights into kidney function and acute kidney failure were made during the war, not least of which would be Bywaters and Beall's descriptions of pigment-induced nephropathy drawn from their clinical experiences during the London Blitz.

Need for a bioartificial kidney

Over 300,000 Americans are dependent on hemodialysis as treatment for kidney failure, but according to data from the 2005 USRDS 452,000 Americans have end-stage kidney disease (ESKD).[5] Intriguing investigations from groups in London, Ontario and Toronto, Ontario have suggested that dialysis treatments lasting two to three times as long as, and delivered more frequently than, conventional thrice weekly treatments may be associated with improved clinical outcomes. Implementing six-times weekly, all-night dialysis would overwhelm existing resources in most countries. This, as well as scarcity of donor organs for kidney transplantation has prompted research in developing alternative therapies, including the development of a wearable or implantable device.

Artificial Kidney

Dialyser used in hemodialysis

Hemodialysis is a method for removing waste products such as creatinine and urea,as well as free water from the blood when the kidneys are in kidney failure. The mechanical device used to clean the patients blood is called a dialyser, also known as an artificial kidney. The other name for artificial kidney is also called a dialysis machine. Modern dialysers typically consist of a cylindrical rigid casing enclosing hollow fibers cast or extruded from a polymer or copolymer, which is usually a proprietary formulation. The combined area of the hollow fibers is typically between 1-2 square meters. Intensive research has been conducted by many groups to optimize blood and dialysate flows within the dialyser, in order to achieve efficient transfer of wastes from blood to dialysate.

Wearable artificial kidney[

A wearable artificial kidney is a wearable dialysis machine that a person with end- stage kidney disease could use daily or even continuously. Until November 2008, no wearable kidney was widely available, but many research teams were in the process of developing such devices.

Now the scientists have built an artificial device which can be fitted in the failed kidney. The FDA has approved the first human clinical trials in the United States for a wearable artificial kidney designed by Blood Purification Technologies Inc. of Beverly Hills, California. It is a tube- like structure which allows the impure blood to be passed through it and the inserted fluids

purify the blood which is not pure and the byproducts are allowed to pass through the ureter and out of the body.

Implantable Renal Assist Device (IRAD)

Currently, no viable bioengineered kidneys exist. Although a great deal of research is underway, numerous barriers exist to their creation.

However, manufacturing a membrane that mimics the kidney's ability to filter blood and subsequently excrete toxins while reabsorbing water and salt would allow for a wearable and/or implantable artificial kidney. Developing a membrane using microelectromechanical systems (MEMS) technology is a limiting step in creating an implantable, bioartificial kidney.

The BioMEMS and Renal Nanotechnology Laboratories at the Cleveland Clinic's Lerner Research Institute have focused on advancing membrane technology to develop an implantable or wearable therapy for end-stage kidney disease (ESKD). Current dialysis cartridges are too large and require superphysiologic pressures for blood circulation, and pores in current polymer membranes have too broad of a size distribution and irregular features. Manufacturing a silicon, nanoporous membrane with narrow pore size distributions improves the membrane's ability to discriminate between filtered and retained molecules. It also increases hydraulic permeability by allowing the mean pore size to approach the desired cutoff of the membrane. Using a batch-fabrication process allows for strict control over pore size distribution and geometry.

In recent studies, human kidney cells were harvested from donated organs unsuitable for transplantation, and grown on these membranes. The cultured cells covered the membranes and appear to retain features of adult kidney cells. The differentiated growth of renal epithelial cells on MEMS materials suggests that a miniaturized device suitable for implantation may be feasible.

A UCSF-led effort to create an implantable artificial kidney for dialysis patients has been selected as one of the first projects to undergo more timely and collaborative review at the Food and Drug Administration.

The FDA announced on April 9, 2012 that it had chosen three renal device projects to pilot a new regulatory approval program called Innovation Pathway 2.0, intended to bring breakthrough medical device technologies to patients faster and more efficiently.

The artificial kidney project, which is targeted for clinical trials in 2017, was selected for its transformative potential in treating end stage kidney disease and for its potential to benefit from early interactions with the FDA in the approval process.

The FDA effort will involve close contact between the federal agency and device developers early in the development process to identify and address potential scientific and regulatory hurdles and create a roadmap for project approval. The goal is to improve the projects' overall chance of success, while reducing the time and cost of FDA review and maintaining safety. Lessons, the agency said, will inform approvals in other areas.

Dialysis

In medicine, dialysis is a process for removing waste and excess water from the blood and is used primarily as an artificial replacement for lost kidney function in people withkidney failure. Dialysis may be used for those with an acute disturbance in kidney function (acute kidney injury, previously acute renal failure) or progressive but chronically worsening kidney function—a state known aschronic kidney disease stage 5 (previously chronic renal failure or end-stage renal disease). The latter form may develop over months or years, but in contrast to

acute kidney injury is not usually reversible and dialysis is regarded as a "holding measure" until a kidney transplant can be performed or sometimes as the only supportive measure in those for whom a transplant would be inappropriate. The kidneys have important roles in maintaining

health. When healthy, the kidneys maintain the body's internal equilibrium of water and minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulfate). The acidic metabolism end-products that the body cannot get rid of via respiration are also excreted through the kidneys. The kidneys also function as a part of the endocrine system, producing erythropoietin, calcitriol and renin. Erythropoietin is involved in the production of red blood cells and calcitriol plays a role in bone formation. Dialysis is an imperfect treatment to replace kidney function because it does not correct the compromised endocrine functions of the kidney. Dialysis treatments replace some of these functions through diffusion(waste removal) and ultrafiltration (fluid removal).

Principles of Dialysis

Dialysis works on the principles of the diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane. Diffusion is a property of substances in water; substances in water tend to move from an area of high concentration to an area of low concentration. Blood flows by one side of a semi-permeable membrane, and a dialysate, or special dialysis fluid, flows by the opposite side. A semipermeable membrane is a thin layer of material that contains holes of various sizes, or pores. Smaller solutes and fluid pass through the membrane, but the membrane blocks the passage of larger substances. This replicates the filtering process that takes place in the kidneys, when the blood enters the kidneys and the larger substances are separated from the smaller ones in the glomerulus.

The two main types of dialysis, hemodialysis and peritoneal dialysis, remove wastes and excess water from the blood in different ways. Hemodialysis removes wastes and water by circulating blood outside the body through an external filter, called adialyzer, that contains a semipermeable membrane. The blood flows in one direction and the dialysate flows in the opposite. The counter-current flow of the blood and dialysate maximizes the concentration gradient of solutes between the blood and dialysate, which helps to remove more urea and creatinine from the blood. The concentrations of solutes are undesirably high in the blood, but low or absent in the dialysis solution, and constant replacement of the dialysate ensures that the concentration of undesired solutes is kept low on this side of the membrane. The dialysis solution has levels of minerals like potassium and calcium that are similar to their natural concentration in healthy blood. For another solute, bicarbonate, dialysis solution level is set at a slightly higher level than in normal blood, to encourage diffusion of bicarbonate into the blood, to act as a pH buffer to neutralize the metabolic acidosis that is often present in these patients. The levels of the components of dialysate are typically prescribed by a nephrologist according to the needs of the individual patient.

In peritoneal dialysis, wastes and water are removed from the blood inside the body using the peritoneum as a natural semipermeable membrane. Wastes and excess water move from the blood, across the peritoneal membrane, and into a special dialysis solution, called dialysate, in the abdominal cavity.

Types of Dialysis

There are three primary and two secondary types of dialysis: hemodialysis (primary), peritoneal dialysis (primary),hemofiltration (primary), hemodiafiltration (secondary),and intestinal dialysis (secondary).

In hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a partially permeable membrane. The dialyzer is composed of thousands of tiny

hollow synthetic fibers. The fiber wall acts as the semipermeable membrane. Blood flows through the fibers, dialysis solution flows around the outside of the fibers, and water and wastes move between these two solutions. The cleansed blood is then returned via the circuit back to the body. Ultrafiltration occurs by increasing the hydrostatic pressure across the dialyzer membrane. This usually is done by applying a negative pressure to the dialysate compartment of the dialyzer. This pressure gradient causes water and dissolved solutes to move from blood to dialysate, and allows the removal of several litres of excess fluid during a typical 4-hour treatment. In the United States, hemodialysis treatments are typically given in a dialysis center three times per week (due in the United States to Medicare reimbursement rules); however, as of 2005 over 2,500 people in the United States are dialyzing at home more frequently for various treatment lengths. Studies have demonstrated the clinical benefits of dialyzing 5 to 7 times a week, for 6 to 8 hours. This type of hemodialysis is usually called "nocturnal daily hemodialysis", which a study has shown a significant improvement in both small and large molecular weight clearance and decrease the requirement of takingphosphate binders. These frequent long treatments are often done at home while sleeping, but home dialysis is a flexible modality and schedules can be changed day to day, week to week. In general, studies have shown that both increased treatment length and frequency are clinically beneficial

ARTIFICIAL BLOOD

A blood substitute also called artificial blood or blood surrogates is a substance used to mimic and fulfill some functions of biological blood. It aims to provide an alternative to blood transfusion, which is transferring blood or blood-based products from one person into another. Thus far, there are no well-accepted *oxygen-carrying* blood substitutes, which is the typical objective of a red blood cell transfusion; however, there are widely available non-blood volume expanders for cases where only volume restoration is required. These are helping doctors and surgeons avoid the risks of disease transmission and immune suppression, address the chronic blood donor shortage, and address the concerns of Jehovah's Witnesses and others who have religious objections to receiving transfused blood. The main categories of 'oxygen-carrying' blood substitutes being pursued are hemoglobin- based oxygen carriers (HBOC) and perfluorocarbon-based oxygen carriers (PFBOC).[1][2] Oxygen therapeutics are in clinical trials in the U.S. and Europe, and Hemopure is available in South Africa.

Oxygen carrying substitute

An *oxygen-carrying blood substitute*, sometimes called *artificial haemoglobin*, is an artificially made red blood cell substitute whose main function is to carry oxygen, as does natural hemoglobin. The use of oxygen-carrying blood substitutes is often called oxygen therapeutics to differentiate from true blood substitutes. The initial goal of oxygen carrying blood substitutes is merely to mimic blood's oxygen transport capacity. There is additional longer range research on true artificial red and white blood cells which could theoretically compose a blood substitute with higher fidelity to human blood. Unfortunately, oxygen transport, one function that distinguishes real blood from other volume expanders, has been very difficult to reproduce.

There are two basic approaches to constructing an oxygen therapeutic. The first is perfluorocarbons (PFC), chemical compounds which can carry and release oxygen. The specific PFC usually used is perfluorodecalin. The second is haemoglobin derived from humans,

animals, or artificially via recombinant technology, or via stem cell production of red blood cells in vitro.

Advantages over human blood

Oxygen therapeutics, even if widely available, would not eliminate the use of human blood, which performs various functions besides oxygen transport. However oxygen therapeutics have major advantages over human blood in various situations, especially trauma.

Blood substitutes are useful for the following reasons:

1. Donations are increasing by about 2–3% annually in the United States, but demand is climbing by between 6–8% as an aging population requires more operations that often involve blood transfusion.
2. Although the blood supply in many countries is very safe, this is not the case for all regions of the world. Blood transfusion is the second largest source of new HIV infections in Nigeria. In certain regions of southern Africa, it is believed that as much as 40% of the population has HIV/AIDS, although testing is not financially feasible. A disease-free source of blood substitutes would be incredibly beneficial in these regions.
3. In battlefield scenarios, it is often impossible to administer rapid blood transfusions. Medical care in the armed services would benefit from a safe, easy way to manage blood supply.
4. Great benefit could be derived from the rapid treatment of patients in trauma situations. Because these blood substitutes do not contain any of the antigens that determine blood type, they can be used across all types without immunologic reactions.
5. While it is true that receiving a unit of transfused blood in the US does not carry many risks, with only 10 to 20 deaths per million units, blood substitutes could eventually improve on this. There is no practical way to test for prion-transmitted diseases in donated blood, such as mad cow and Creutzfeld-Jacob disease, and other disease could emerge as problems for the blood supply, including smallpox and SARS.
6. Transfused blood is currently more cost effective, but there are reasons to believe this may change. For example, the cost of blood substitutes may fall as manufacturing becomes refined.
7. Blood substitutes can be stored for much longer than transfusable blood, and can be kept at room temperature. Most haemoglobin-based oxygen carriers in trials today carry a shelf life of between 1 and 3 years, compared to 42 days for donated blood, which needs to be kept refrigerated.
8. Blood substitutes allow for immediate full capacity oxygen transport, as opposed to transfused blood which can require about 24 hours to reach full oxygen transport capacity due to 2,3-diphosphoglycerate depletion. Also, in comparison, natural replenishment of lost red blood cells usually takes months, so an oxygen-carrying blood substitute can perform this function until blood is naturally replenished.
9. Oxygen-carrying blood substitutes also would become an alternative for those patients that refuse blood transfusions for religious or cultural reasons, such as Jehovah's Witnesses.
10. Synthetic oxygen carriers may also show potential for cancer treatment, as their reduced size allows them to diffuse more effectively through poorly vasculated tumour tissue, increasing the effectiveness of treatments like photodynamic therapy and chemotherapy.

The U.S. military is one of the greatest proponents of oxygen therapeutics, mainly because of the vital need and benefits in a combat scenario. Since oxygen therapeutics are not yet widely available, the United States Army is experimenting with varieties of dried blood, which take up

less room, weigh less and can be used much longer than blood plasma.Saline has to be added prior to use. These properties make it better for first aid during combat than whole blood or packed red cells.

Risks of artificial blood

Haemoglobin-based blood substitutes may increase the odds of deaths and heart attacks. According to studies of outcomes of transfusions given to trauma patients in 2008,[15] blood substitutes yielded a 30% increase in the risk of death and about a threefold increase in the chance of having a heart attack for the recipients. More than 3,711 patients were tested in sixteen studies using five types of artificial blood. Public Citizen sued the U.S. Food and Drug Administration (FDA) to attain information on the duration of these studies which were found to have been conducted from 1998 until 2007. The FDA permits artificial blood transfusions in the US without informed consent under a special exemption from requirements of informed consent during traumatic care.

PART-A

1. What is transplantation?
2. Highlight few basic engineering concerns related to design heart valve.
3. What is cardiac pacemaker?
4. Mention the function of SA node
5. List the composition of Dialysate.
6. Write the importance of cardiac pacemaker.
7. Brief the implantation procedure of pacemaker.
8. Schematically represent the surgical removal of kidney from a living donor.
9. Define dialysis.
10. Mention the principle of Dialysis
11. Dialysis. 14 What is artificial kidney?
12. What is artificial kidney?

PART-B

1. Compare the salient features and drawbacks of mechanical versus tissue heart valves with examples.
2. What are the characteristics an ideal heart valve should possess?
3. Narrate the design requirements of prosthetic cardiac valves. What are the problems associated with different types of valves?
4. What is artificial heart? Explain the procedures involved in cardiac pacemakers

5. What is artificial heart? Explain the procedures involved in cardiac pacemakers
6. Explain in detail about the kidney dialysis procedure and add a note on reuse of cartridge
7. Describe how the dialysis procedure takes place during dialysis.

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2. Joon B Park, Biomaterials – An Introduction, Plenum press, New York, 2nd Edition 2012.

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DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – V - BIOMATERIALS AND ARTIFICIAL ORGANS– SBMA7001

V TRANSPLANTS

TRANSPLANTS

OVERVIEW OF TRANSPLANTS

An organ transplant replaces a failing organ with a healthy organ. A transplant surgeon will remove an organ from another person and place it in your body. This may be done when your organ has stopped working or stopped working well because of disease or injury.

Not all organs can be transplanted. Organs most often transplanted include:

- The kidney , because of diabetes, polycystic kidney disease,lupus, or otherproblems.
- The liver , because of cirrhosis, which has manycauses.
- The heart , because of coronary artery disease, cardiomyopathy, heart failure, and other heart problems.
- The pancreas , because of diabetes.
- The lung , because of cystic fibrosis, COPD, and otherproblems.
- The small intestine , because of short bowel syndrome caused by necrotizing enterocolitis, Crohn's disease, and other problems. An intestine transplant is sometimes an option if you have problems with total parenteral nutrition (TPN).

More than one organ can be transplanted at one time. For example, a heart/lung combined transplant is possible. Not everyone is a good candidate for an organ transplant. The transplant centre will do tests to see if you are. Once the transplant team sees you and completes all the investigations, tests and consults and your tests all show you are a good candidate, you are put on a waiting list. It may be days, months, or years before a transplant takes place.

SUCCESS OF AN ORGAN TRANSPLANT:-

Organ transplants have been done in Canada since the 1950s. The procedure is always improving, and transplants are more successful today than ever before. Organ transplant success depends on:

- Which organ is transplanted.
- How many organs are transplanted. For example, you could have a heart transplant or a heart and lung transplant.
- The disease that has caused your organ to

fail. PROCEDURE FOR ORGAN TRANSPLANT:-

First, you'll need to have blood and tissue tests done that will be used to match you with a donor. This is because your immune system may see the new organ as foreign and reject it. A match with both blood type and some antibodies in the blood is important.

Need to take care of patien health. Continue to take your medicines as prescribed and get regular blood tests. Follow your doctor's directions for eating and exercising. You also may want to talk with a

psychiatrist, psychologist, or counsellor about your transplant. To learn more about what happens, talk to someone who has had a transplant. Your transplant centre or doctor can give you the name of someone who is willing to share his or her experience with you. You may have to wait days, months, or years for your transplant. Be patient, and ask your doctor what you can do while you're waiting.

AFTER TRANSPLANT:-

After a transplant, many people say they feel better than they have in years. What you can and can't do will depend on the type of transplant you had, other health problems you have, and how your body

reacts to the new organ. You will have to take daily medicines for the rest of your life to prevent your immune system from rejecting the new organ. You will also have regular checkups and blood tests to see how well your new organ is working. These will be frequent and directed by the transplant centre. Some people feel depressed after an organ transplant. If you think you may be depressed, get help. The earlier depression is treated, the more quickly you will feel better.

You may need to make lifestyle changes to keep your new organ healthy and strong. This can include eating healthy foods, getting regular exercise, and getting enough sleep. Your doctor can help you plan any needed changes. Keeping in touch with your transplant coordinator and your local primary doctor, taking your medicines, going to your doctor appointments, and making lifestyle changes are all important.

ORGAN DONAR:-

Most people can be organ donors. If you are interested in donating an organ, add your name to the Alberta Organ and Tissue Donation Registry. Many people choose to donate an organ upon their death. But a person can donate certain organs while he or she is still living. These people are called "living donors."

IMMUNOLOGICAL CONSIDERATIONS

Rejection: The Allogeneic Immune Response

Transplantation of organs or tissues between genetically nonidentical individuals of the same species is plagued by rejection and its associated problems. "Foreignness" is equated with the presence on transplanted tissue membrane of antigens that the host does not have and therefore recognizes as foreign or nonself. If all other factors are optimal the major reason for transplant failure is rejection.

The transplanted organ represents a continuous source of HLA alloantigens capable of inducing a rejection response at any time posttransplantation. Because it cannot be eliminated, the allograft continuously activates the immune system, resulting in lifelong overproduction of cytokines, constant cytotoxic activity, and sustained alteration in the graft vasculature. Therefore, lifelong immunosuppression is required to ensure allograft survival.

Transplanted organs express donor MHC molecules, resulting in 2 pathways of antigen recognition (allorecognition) by T cells: direct and indirect. Allorecognition refers to T cell recognition of genetically encoded polymorphisms between members of the same species. The primary targets of the immune response to allogeneic tissues are MHC molecules on donor cells.

Direct and indirect pathways of T-cell allorecognition are mediated by different APCs, and their cellular mechanisms are different *direct pathway* requires that

recipient T cells recognize intact donor MHC molecules complexed with peptide and expressed on donor cells. Allograft rejection via the *indirect pathway* requires that recipient APCs process the donor-MHC antigen before presenting it to recipient T cells. Both pathways are important in mechanisms of allograft rejection. It is thought that the direct pathway is responsible for acute rejection and that the indirect pathway is responsible for chronic rejection.

Hyper acute Graft Rejection

Hyperacute rejection occurs immediately, within minutes to hours of vascularization of the transplanted graft, and is caused by a humoral immune response. Hyperacute rejection is an antibody-mediated cytotoxic response to the fixation of antibodies to specific class I antigens on vascular endothelium, followed by entrapment of formed blood elements and clotting factors in the microvasculature of the graft, resulting in complement activation, massive intravascular coagulation, lack of tissue perfusion, and graft necrosis. Hyperacute rejection results in immediate thrombotic occlusion and loss of the allograft.

Antibodies responsible for hyperacute rejection include antibodies to ABO blood group antigens and those produced against vascular endothelial antigens and histocompatibility antigens. For example, if an ABO blood group O recipient receives a kidney from an ABO blood group A donor, once blood circulates through the transplanted kidney, antibody to the A antigen will combine with antigens on the endothelial cells of the kidney and activate the complement system. The activated complement system causes chemotaxis for phagocytes and induces fibrin deposition. Recruited phagocytes degranulate and release hydrolytic enzymes that cause tissue destruction and rapid rejection of the kidney. Hyperacute rejection most commonly occurs while the patient is still in the operating room; the kidney frequently turns black before the surgical team's eyes.Antibody-to-transplant antigens can develop in recipients who have received multiple blood transfusions or prior transplants or who have had multiple pregnancies. Transfusion exposes the potential transplant recipient to foreign HLA proteins, which naturally stimulate the production of anti-HLA antibodies. Ensuring ABO blood group compatibility and avoiding positive lymphocyte cross-matches are universally accepted methods for prevention of hyperacute rejection.

Initially, hyperacute rejection was thought to occur only in transplanted kidneys. However, all solid organs are susceptible. Liver grafts in particular, however, are more tolerant of ABO and HLA incompatibility than are renal and heart grafts.[15] Retrospective histocompatibility antigen typing and lymphocyte cross- matching have not shown these factors to be relevant to liver graft survival. Although the reason that hyperacute rejection does not occur in liver grafts is not fully understood, it is speculated that the enormous cell mass of the liver is capable of absorbing circulating antibody. Another reason may be differences in microvascular structures. The

major complication associated with ABO- incompatible liver transplantation is hemolysis. A form of graft-vs-host reaction is caused by B lymphocytes in lymphoid tissue transplanted with the graft. Donor B lymphocytes produce antibodies to ABO antigens on recipient RBCs, resulting in lysis or hemolysis.

Acute Graft Rejection

Acute rejection occurs within a week to approximately 4 months after transplantation; the risk is greatest during the first 6 months and few episodes occur after the first year posttransplantation. The vast majority of acute rejection episodes do not lead to graft loss because they are diagnosed and treated promptly andaggressively**.**

Acute rejection is a cellular immune response involving mononuclear, cytotoxic and Th cells, monokines, and lymphokines. Acute rejection occurs when antigen is trapped within recipient macrophages and cannot be cleared by the RE system. Quiescent, nonactivated Th cells encounter specific class II antigens displayed on the donor organ, become activated, and synthesize receptors for lymphokines that are simultaneously released from monocytes. Activated monocytes release the lymphokine IL-1, which causes clonal expansion of activated Th cells. Monocytes also release the lymphokine IL-2, which activates and causes the clonal expansion of CTLs. Clinical signs of rejection are nonspecific and vary depending on the organ transplanted. A biopsy is required to make a definitive diagnosis of acute rejection.

Chronic Graft Rejection

Chronic rejection probably begins at the time of transplantation, but may take months or years to manifest clinically. While the clinical and biochemical signs are organ-specific, the result of chronic rejection is the same for all solid organ allografts. Slowly deteriorating graft function caused by fibrosis of the graft parenchyma and widespread arteriopathy are the hallmarks of chronic rejection that lead to loss of function and eventual graft loss. A comprehensive review of the pathophysiology of chronic allograft rejection has been previously published in Medscape Transplantation.

The cause of chronic rejection is unclear. However, there is evidence that both immune and nonimmune events are responsible. T cells and B cells contribute to the damage characteristic of chronic rejection. Overproduction of cytokines, including TGF-beta and platelet-derived growth factor, contribute to fibrosis. Continuous production of alloantibody by B cells under the influence of T cells contributes to the arteriopathy. Formerly thought to be the product of donor factors including reduced nephron mass, prolonged cold ischemia time, advanced donor kidney age, and donor hypertension, recent evidence suggests that recipient immune reactivity against the allograft also contributes to the development of DGF.Chronic rejection is a prolonged process of declining

allograft function. Thus, it is not surprising that transplant recipients who develop chronic rejection often experience many of the same health problems associated with primary organ failure. In addition, they develop the complications and cumulative adverse effects associated with years of daily administration of immunosuppressive agents. Susceptibility to infection, development of skin cancer, cardiovascular disease, osteoporosis, and mood changes are common in patients who receive substantial doses of corticosteroids.

HEART TRANSPLANT

A heart transplant is surgery to remove a person's diseased heart and replace it with a healthy heart from a deceased donor. Most heart transplants are done on patients who have end-stage heart failure. Heart failure is a condition in which the heart is damaged or weak. As a result, it can't pump enough blood to meet the body's needs. "End-stage" means the condition is so severe that all treatments, other than a heart transplant, have failed.

Overview

Heart transplants are done as a life-saving measure for end-stage heart failure.

Because donor hearts are in short supply, patients who need heart transplants go through a careful selection process. They must be sick enough to need a new heart, yet healthy enough to receive it.

Survival rates for people receiving heart transplants have improved, especially in the first year after the transplant. About 88 percent of patients survive the first year after transplant surgery, and 75 percent survive for 5 years. The 10-year survival rate is about 56 percent. After the surgery, most heart transplant patients can return to their normal levels of activity. However, less than 30 percent return to work for many different reasons.

The Heart Transplant Process

The heart transplant process starts when doctors refer a patient who has end-stage heart failure to a heart transplant center. Staff members at the center assess whether the patient is eligible for the surgery. If the patient is eligible, he or she is placed on a waiting list for a donor heart. Heart transplant surgery is done in a hospital when a suitable donor heart is found. After the transplant, the patient is started on a lifelong health care plan. The plan involves multiple medicines and frequent medicalcheckups.

While there are many people with "end-stage" heart disease with inadequate function of the heart, not all qualify for a heart transplant. All the other important organs in the body must be in pretty good shape. Transplants cannot be performed in patients with active infection, cancer, or bad diabetes mellitus; patients who smoke or abuse alcohol are also not good candidates. It's not easy to be a transplant recipient. These patients need to change their lifestyle and take numerous medications. Hence, all potential transplants patients must undergo psychological testing to identify social and behavioral factors that could interfere with recovery, compliance with medications, and lifestyle changes required after transplantation.

LUNG TRANSPLANT

A lung transplant is surgery to remove a person's diseased lung and replace it with a healthy lung from a deceased donor. Lung transplants are used for people who are likely to die from lung disease within 1 to 2 years. Their conditions are so severe that other treatments, such as medicines or breathing devices, no longer work.

Overview

Lung transplants aren't very common because of the small number of donor organs available. About 1,800 lung transplants were done in the United States in 2010. More donor lungs would mean a larger number of suitable lungs available for transplant. Most people who have lung transplants are between the ages of 18 and 65. The surgery sometimes is used for children and older adults. This chapter focuses on lung transplants in adults.

Each patient must go through a careful screening process to make sure he or she is a good candidate for a lung transplant. Donor lungs also are carefully screened to make sure they're healthy enough to be used for a transplant. The Organ Procurement and Transplantation Network (OPTN) manages the nationwide organ-sharing process. OPTN also maintains the waiting lists for all organ donations. The number of people on the lung transplant waiting list changes often. About half of the people on the list receive a lung in any given year.

Some people get one lung during a transplant. This is called a single-lung transplant. Other people get two lungs, which is called a double-lung transplant. The number of double-lung transplants has gone up over the years. More double-lung transplants are done now than single-lung transplants. Some people who have severe heart disease and lung disease get a heart and lung(s). This is called a heart–lung transplant. A rare kind of lung transplant is a living donor lobar lung transplant. For this surgery, a healthy adult donates a segment, or lobe, of one lung to another person. This type of transplant usually is done in children.

Outlook

Lung transplants are a "last resort" treatment for people who have severe disease and no other medical options. A lung transplant can improve a person's quality of life. For people who have certain lung problems, a transplant also may help them live longer than they would without the surgery. Lung transplants have serious risks. Your body may reject the new lung, or you may get infections. The short- and long-term complications of a lung transplant can be life threatening.

Lung transplantation, or **pulmonary transplantation** is a surgical procedure in which a patient's diseased lungs are partially or totally replaced by lungs which come from a donor. Donor lungs can be retrieved from a living donor or a deceased donor. A living donor can only donate one lung lobe. With some lung diseases a recipient may only need to receive a single lung. With other lung diseases such as cystic fibrosis it is imperative that a recipient receive two lungs. While lung transplants carry certain associated risks, they can also extend life expectancy and enhance the quality of life for end-stage pulmonary patients.

Requirements for potential donors

There are certain requirements for potential lung donors, due to the needs of the potential

recipient. In the case of living donors, this is also in consideration of how the surgery will affect the donor:

- healthy;
- size match; the donated lung or lungs must be large enough to adequately oxygenate the patient, but small enough to fit within the recipient's chest cavity;
- age;
- blood type.

While a transplant center is free to set its own criteria for transplant candidates, certain requirements are generally agreed upon

- end-stage lung disease;
- has exhausted other available therapies without success;
- no other chronic medical conditions (e.g., heart, kidney, liver);
- no current infections or recent cancer. There are certain cases where pre-existing infection is unavoidable, as with many patients with cystic fibrosis
- no HIV or hepatitis;
- no alcohol, smoking, or drug abuse;within an acceptable weight range (marked undernourishment or obesity are both associated with increased mortality);
- age (single vs. double tx);
- acceptable psychological profile;
- has social support system;
- financially able to pay for expenses
- able to comply with post-transplant regimen. A lung transplant is a major operation, and following the transplant, the patient must be willing to adhere to a lifetime regimen

BONE MARROW

Bone marrow is the flexible tissue in the interior of bones. In humans, red blood cells are produced by cores of bone marrow in the heads of long bonesin a process known as hematopoiesis. On average, bone marrow constitutes 4% of the total body mass of humans; in an adult having 65 kilograms of mass (143 lbs), bone marrow typically accounts for approximately 2.6 kilograms (5.7 lb). The hematopoietic component of bone marrow produces approximately 500 billion blood cells per day, which use the bone marrowvasculature as a conduit to the body's systemic circulation. Bone marrow is also a key component of the lymphatic system, producing the lymphocytes that support the body's immunesystem.

BONE MARROW TRANSPLANTS

Bone marrow transplants can be conducted to treat severe diseases of the bone marrow, including certain forms of cancer such as leukemia. Additionally, bone marrow stem cells have been

successfully transformed into functionalneural cells,[4] and can also potentially be used to treat illnesses such asinflammatory bowel disease.[5] A bone marrow transplant is a procedure to replace damaged or destroyed bone marrow with healthy bone marrow stem cells. Bone marrow is the soft, fatty tissue inside your bones. The bone marrow produces blood cells. Stem cells are immature cells in the bone marrow that give rise to all of your different blood cells.

Description

Before the transplant, chemotherapy, radiation, or both may be given. This may be done in two ways:

- Ablative (myeloablative) treatment: High-dose chemotherapy, radiation, or both are given to kill any cancer cells. This also kills all healthy bone marrow that remains, and allows new stem cells to grow in the bonemarrow.
- Reduced intensity treatment, also called a mini transplant: People receive lower doses of chemotherapy and radiation before a transplant. This allows older people, and those with other health problems to have a transplant.

There are 3 kinds of bone marrow transplants:

- Autologous bone marrow transplant: The term auto means self. Stem cells are removed from you before you receive high-dose chemotherapy or radiation treatment. The stem cells are stored in a freezer. After high-dose chemotherapy or radiation treatments, your stems cells are put back in your body to make normal blood cells. This is called a rescue transplant.

- Allogeneic bone marrow transplant: The term allo means other. Stem cells are removed from another person, called a donor. Most times, the donor's genes must at least partly match your genes. Special tests are done to see if a donor is a good match for you. A brother or sister is most likely to be a good match. Sometimes parents, children, and other relatives are good matches. Donors who are not related to you, yet still match, may be found through national bone marrow registries.

- Umbilical cord blood transplant: This is a type of allogeneic transplant. Stem cells are removed from a newborn baby's umbilical cord right after birth. The stem cells are frozen and stored until they are needed for a transplant. Umbilical cord blood cells are very immature so there is less of a need for perfect matching. Due to the smaller number of stem cells, blood counts take much longer torecover.A stem cell transplant is usually done after chemotherapy and radiation is complete. The stem cells are delivered into your bloodstream usually through a tube called a central venous catheter. The process is similar to getting a blood transfusion. The stem cells travel through the blood into the bone marrow. Most times, no surgery isneeded.

Risks

A bone marrow transplant may cause the following symptoms:

- Chest pain

- Drop in blood pressure
- Fever, chills, flushing
- Funny taste in the mouth
- Headache
- Hives
- Nausea
- Pain
- Shortness ofbreath

Possible complications of a bone marrow transplant depend on many things, including:

- The disease you are being treated for
- Whether you had chemotherapy or radiation before the bone marrow transplant and the dosages of such treatments
- Your age
- Your overall health
- How good of a match your donor was
- The type of bone marrow transplant you received (autologous, allogeneic, or umbilical cord blood)

Complications may include:

- Anemia
- Bleeding in the lungs, intestines, brain, and other areas of the body
- Cataracts
- Clotting in the small veins of theliver
- Damage to the kidneys, liver, lungs, andheart
- Delayed growth in children who receive a bone marrowtransplant
- Early menopause
- Graft failure, which means that the new cells do not settle into the body and start producing stemcells
- Graft-versus-host disease (GVHD), a condition in which the donor cells attack your own body
- Infections, which can be veryserious
- Inflammation and soreness in the mouth, throat, esophagus, and stomach, called mucositis
- Pain
- Stomach problems, including diarrhea, nausea, and vomiting

CORNEA TRANSPLANT

A cornea transplant, also called keratoplasty, is a surgical procedure to replace part of your cornea with corneal tissue from a donor. Your cornea is the transparent, dome- shaped surface of your eye that accounts for a large part of your eye's focusing power.A cornea transplant can restore vision, reduce pain and improve the appearance of a damaged or diseased cornea. Most cornea transplant procedures are successful. But cornea transplant carries a small risk of complications, such as rejection of the donor cornea. A cornea transplant is most often used to restore vision to a person who has a damaged cornea. A cornea transplant may also relieve pain or other signs and symptoms associated with diseases of the cornea.

- A cornea that bulges outward(keratoconus)
- Fuchs' dystrophy
- Thinning of the cornea
- Cornea scarring, caused by infection or injury
- Clouding of thecornea
- Swelling of the cornea
- Corneal ulcers, including those caused by infection
- Complications caused by previous eye surgery

Cornea transplant is a relatively safe procedure. Still, a cornea transplant does carry a small risk of serious complications, such as:

- Eye infection
- Increased risk of clouding of the eye's lens (cataracts)
- Pressure increase within the eyeball (glaucoma)
- Problems with the stitches used to secure the donor cornea
- Rejection of the donorcornea
- Swelling of the cornea

Signs and symptoms of cornea rejection

In some cases, your body's immune system may mistakenly attack the donor cornea. This is called rejection, and it may require medical treatment or another cornea transplant. Make an appointment with your eye doctor if you notice any signs and symptoms of rejection, such as:

- Loss of vision
- Pain
- Redness
- Sensitivity to light

Rejection occurs in about 20 percent of cornea transplants. Before cornea transplant surgery the patient should undergo:

- **A thorough eye exam.** Your eye doctor looks for conditions that may cause complications after surgery.
- **Measurements of your eye.** Your eye doctor determines what size donor cornea you need.
- **A review of all medications and supplements you're taking.** You may need to stop taking certain medications or supplements before or after cornea transplant.
- **Treatment for other eye problems.** Unrelated eye problems, such as infection or inflammation, may reduce your chances of successful cornea transplant. Your eye doctor will work to treat those problems before your surgery.

The doctor will discuss what to expect during the procedure and explain the risks of the procedure.

Finding a donor cornea

Most corneas used in cornea transplants come from deceased donors. Unlike with other organs, such as livers and kidneys, people needing cornea transplants generally will not need to endure long waits. That's because many people specifically request that their corneas be available for donation

after they die, unless they have had certain conditions, so more corneas are available for transplantation compared with other organs.Corneas may not be used from donors who had several

conditions, such as certain central nervous system conditions, infections, and prior eye surgery or eye conditions, or from people who died from an unknown cause.

During your cornea transplant

On the day of your cornea transplant, you'll be given a sedative to help you relax and a local anesthetic to numb your eye. You won't be asleep during the surgery, but you shouldn't feel any pain.

During the most common type of cornea transplant, your surgeon cuts through the entire thickness of the abnormal or diseased cornea to remove a small button-sized disc of corneal tissue. An instrument that acts like a cookie cutter (trephine) is used to make this precise circular cut. The donor cornea, cut to fit, is placed in the opening. Your surgeon then uses a fine thread to stitch the new cornea into place. The stitches may be removed at a later visit when you see your eyedoctor.

Procedures to transplant a portion of the cornea

With some types of cornea problems, a full-thickness cornea transplant isn't always the best treatment. Partial-thickness (lamellar) transplants may be used in certain situations. These types of proceduresinclude:

- **Replacing the inner layer of the cornea.** This procedure, called a deep lamellar transplant, replaces only the innermost layer of your cornea's five layers. A small incision is made in the side of your eyeball to allow for removal of your cornea's inner layer without damaging the outer layers. A donor graft replaces theremoved portion.
- **Replacing the surface layers of the cornea.** The outer layers of the cornea that have been damaged by certain diseases and conditions can be replaced using a procedure called surface lamellar transplant. These surface layers, too, can be removed and replaced with a donor graft.

After care of cornea transplant

Once your cornea transplant is completed, you can expect to:

- **Receive several medications.** Eyedrops and, occasionally, oral medications immediately after cornea transplant and continuing during your recovery will help control infection, swelling and pain.

Wear an eye patch. An eye patch may protect your eye as it heals after yoursurgery.

- **Protect your eye from injury.** Plan to take it easy after your cornea transplant, and slowly work your way up to your normal activities, including exercise. For the rest of your life, you'll need to take extra precautions to avoid harming youreye.
- **Return for frequent follow-up exams.** Expect frequent eye exams in which your doctor looks for complications in the first year after surgery.Most people who receive a cornea transplant will have their vision at least partially restored. What you can expect after your cornea transplant depends on the reason for your surgery and your health.

this reason, expect to see your eye doctor annually. Cornea rejection can often be managed with medications.

SKIN TRANSPLANTATION

Skin graft

A skin graft is a patch of skin that is removed by surgery from one area of the body and transplanted, or attached, to another area.

Description

This surgery is usually done while you are under general anesthesia. That means you will be asleep and pain-free. Healthy skin is taken from a place on your body called the donor site. Most people who are having a skin graft have a split-thickness skin graft. This takes the two top layers of skin from the donor site and the layer under the epidermis.

The donor site can be any area of the body. Most times, it is an area that is hidden by clothes, such as the buttock or inner thigh. The graft is carefully spread on the bare area where it is being transplanted. It is held in place either by gentle pressure from a well-padded dressing that covers it, or by staples or a few small stitches. The donor-site area is covered with a sterile dressing for 3 to 5 days.

People with deeper tissue loss may need a full-thickness skin graft. This requires an entire thickness of skin from the donor site, not just the top two layers. A full-thickness skin graft is a more complicated procedure. Common donor sites for full- thickness skin grafts include the chest wall, back, or abdominal wall.

Skin grafts may be recommended for:

- Areas where there has been infection that caused a large amount of skin loss
- Burns
- Cosmetic reasons or reconstructive surgeries where there has been skin damage or skin loss
- Skin cancer surgery
- Surgeries that need skin grafts to heal
- Venous ulcers, pressure ulcers, or diabetic ulcers that do not heal
- Very large wounds
- A wound that the surgeon has not been able to close properly

  Full-thickness grafts are done when a lot of tissue is lost. This can happen with open fractures of the lower leg, or after severe infections.

Risks of skin graft

Risks for anesthesia are:

- Reactions tomedicines
- Problems with breathing Risks
- Bleeding
- Chronic pain (rarely)
- Infection

- Loss of grafted skin (the graft not healing, or the graft healing slowly)
- Reduced or lost skin sensation, or increased sensitivity

- Scarring
- Skin discoloration
- Uneven skin surface

Before the Procedure

- What medicines you are taking, even drugs or herbs you bought without a prescription.
- If you have been drinking a lot of alcohol. During the days before surgery:
- You may be asked to stop taking medicines that make it hard for your blood to clot. These include aspirin, ibuprofen, warfarin (Coumadin), and others.
- Ask your surgeon which drugs you should still take on the day of yoursurgery.
- If you smoke, try to stop. Smoking increases your chance of problems such as slow healing. Ask your doctor or nurse for help quitting.

On the day of the surgery:

- Follow instructions about when to stop eating and drinking.
- Take the drugs your surgeon told you to take with a small sip of water.

After the Procedure

You should recover quickly after split-thickness skin grafting. Full-thickness grafts need a longer recovery time. If you received this kind of graft, you may need to stay in the hospital for 1 to 2 weeks.

After you are discharged from the hospital, follow instructions on how to care for your skin graft, including:

- Wearing a dressing for 1 to 2 weeks. Ask your provider how you should care for the dressing, such as protecting it from getting wet.
- Protecting the graft from trauma for 3 to 4 weeks. This includes avoiding being hit or doing any exercise that might injure or stretch the graft.
- Getting physical therapy, if your surgeon recommendsit.

PANCREAS TRANSPLANTATION

A **pancreas transplant** is an organ transplant that involves implanting a healthy pancreas into a person who usually has diabetes.

Because the pancreas is a vital organ, performing functions necessary in the digestion process, the recipient's native pancreas is left in place, and the donated pancreas is attached in a different location. In the event of rejection of the new pancreas which would quickly cause life-threatening diabetes, the recipient could not survive without the native pancreas still in place. The healthy pancreas comes from a donor who has just died or it may be a partial pancreas from a living donor. At present, pancreas transplants are usually performed in persons with insulin-dependent diabetes, who can develop severe complications. Patients with the most common- and deadliest- form of pancreatic cancer are usually not eligible for valuable pancreatic transplantations, since the condition usually has a very high mortality rate and the disease, which is usually highly malignant and detected too late to treat, could and probably would soon return.

In most cases, pancreas transplantation is performed on individuals with type 1 diabetes with end-stage renal disease, brittle diabetes and hypoglycaemia unawareness. The majority of

pancreas transplantation (>90%) are simultaneous pancreas-kidney transplantation. It may also be performed as part of a kidney- pancreas transplantation.

Complications

Complications immediately after surgery include thrombosis, pancreatitis, infection, bleeding and rejection. Rejection may occur immediately or at any time during the patient's life. This is because the transplanted pancreas comes from another organism, thus the recipient's immune system will consider it as an aggression and try to combat it. Organ rejection is a serious condition and ought to be treated immediately. In order to prevent it, patients must take a regimen ofimmunosuppressive drugs. Drugs are taken in combination consisting normally of ciclosporin, azathioprine andcorticosteroids. But as episodes of rejection may reoccur throughout a patient's life, the exact choices and dosages of immunosuppressants may have to be modified over time. Sometimes tacrolimus is given instead of ciclosporin andmycophenolate mofetil instead of azathioprine.

Types

There are four main types of pancreas transplantation:

- Pancreas transplant alone, for the patient with type 1 diabetes who usually has severe, frequent hypoglycemia, but adequate kidney function.
- Simultaneous pancreas-kidney transplant (SPK), when the pancreas and kidney are transplanted simultaneously from the same deceaseddonor.
- Pancreas-after-kidney transplant (PAK), when a cadaveric, or deceased, donor pancreas transplant is performed after a previous, and different, living or deceased donor kidney transplant.
- Simultaneous deceased donor pancreas and live donor kidney (SPLK) has the benefit of lower rate of delayed graft function than SPK and significantly reduced waiting times, resulting in improved outcomes.

Preservation until implantation

Standard practice is to replace the donor's blood in the pancreatic tissue with an ice- cold organ storage solution, such as UW (Viaspan) or HTK until the allograft pancreatic tissue is implanted.
The prognosis after pancreas transplantation is very good. Over the recent years, long- term success has improved and risks have decreased. One year after transplantation more than 95% of all patients are still alive and 80-85% of all pancreases are still functional. After transplantation patients need lifelong immunosuppression. Immunosuppression increases the risk for a number of different kinds of infection and cancer. It is unclear if steroids, which are often used as immunosuppressant, can be replaced with something els.

Hair transplantation

Hair transplantation is a surgical technique that removes hair follicles from one part of the body, called the 'donor site', to a bald or balding part of the body known as the 'recipient site'. The technique is primarily used to treat male pattern baldness. In this minimally invasive procedure, grafts containing hair follicles that are genetically resistant to balding are transplanted to the bald scalp. Hair transplantation can also be used to restore eyelashes, eyebrows, beard hair, chest hair, pubic hair and to fill in scars caused by accidents or surgery such as face-lifts and previous hair

transplants. Hair transplantation differs from skin grafting in that grafts contain almost all of the epidermis and dermis surrounding the hair follicle, and many tiny grafts are transplanted rather than a single strip of skin.

Since hair naturally grows in groupings of 1 to 4 hairs, current techniques harvest and transplant hair "follicular units" in their natural groupings. Thus modern hair transplantation can achieve a natural appearance by mimicking original hair orientation. This hair transplant procedure is called follicular unit transplantation (FUT). Donor hair can be harvested in two different ways: strip harvesting, and follicular unit extraction (FUE).

Procedure

Pre-operative assessment and planning

The surgeon analyzes the patient's scalp, discusses their preferences and expectations, and advises them on the best approach and what results might reasonably be expected. Pre-operative folliscopy will help to know the actual existing density of hair, so that postoperative results of newly transplanted hair grafts can be accurately assessed. Some patients may benefit with preoperative topical minoxidil application and vitamins.

For several days prior to surgery the patient refrains from using any medicines which might result in intraoperative bleeding and resultant poor grafting. Post operative antibiotics are commonly prescribed to prevent wound or graft infections.

Harvesting methods

There are several different techniques for harvesting hair follicles, each with their own advantages and disadvantages. There are two main ways in which donor grafts are extracted today: strip excision harvesting, and follicular unit extraction.

Strip harvesting

Strip harvesting (also known as follicular unit transplantation or FUT) is the most common technique for removing hair and follicles from a donor site. The surgeon harvests a strip of skin from the posterior scalp, in an area of good hair growth. A single-, double-, or triple-bladed scalpel is used to remove strips of hair-bearing tissue from the donor site. Each incision is planned so that intact hair follicles are removed. The excised strip is about 1–1.5 x 15–30 cm in size. While closing the resulting wound, assistants begin to dissect individual follicular unit grafts, which are small, naturally formed groupings of hair follicles, from the strip. Working with binocular Stereo-microscopes, they carefully remove excess fibrous and fatty tissue while trying to avoid damage to the follicular cells that will be used for grafting. The latest method of closure is called 'Trichophytic closure' which results in much finer scars at the donor area.

The surgeon then uses very small micro blades or fine needles to puncture the sites for receiving the grafts, placing them in a predetermined density and pattern, and angling the wounds in a consistent fashion to promote a realistic hair pattern. The technicians generally do the final part of the procedure, inserting the individual grafts in place.

Follicular unit extraction (FUE)

With Follicular Unit Extraction or FUE harvesting, individual follicular units containing 1 to 4 hairs are removed under local anesthesia; this micro removal typically uses tiny punches of

between 0.6mm and 1.0mm in diameter. The surgeon then uses very small micro blades or fine needles to puncture the sites for receiving the grafts, placing them in a predetermined density and pattern, and angling the wounds in a consistent fashion to promote a realistic hair pattern. The technicians generally do the final part of the procedure, inserting the individual grafts in place.

FUE takes place in a single long session or multiple small sessions. The FUE procedure is more time-consuming than strip surgery. An FUE surgery time varies according to the surgeons experience, speed in harvesting and patient characteristics. The procedure can take anywhere from a couple hours to extract 200 grafts for a scar correction to a surgery over two consecutive days for a mega session of 2,500 to 3,000 grafts. With the FUE Hair Transplant procedure there are restrictions on patient candidacy. Clients are selected for FUE based on a fox test,[5] though there is some debate about the usefulness of this in screening clients for FUE.

FUE can give very natural results. The advantage over strip harvesting is that FUE harvesting negates the need for large areas of scalp tissue to be harvested, so there is no linear incision on the back of the head and it doesn't leave a linear scar. Because individual follicles are removed, only small, punctate scars remain which are virtually not visible and any post-surgical pain and discomfort is minimized.

Disadvantages include increased surgical times and higher cost to the patient. It is challenging for new surgeons because the procedure is physically demanding and the learning curve to acquire the skills necessary is lengthy and tough. Some surgeons note that FUE can lead to a lower ratio of successfully transplanted follicles as compared to strip harvesting.

Follicular unit transplant

Follicular unit transplant (FUT) is the traditional hair transplant method which involves extracting a linear strip of hair bearing skin from the back or the side of the scalp. The strip is then dissected to separate individual grafts.

Types of surgery

There are a number of applications for hair transplant surgery, including:

- Androgenetic alopecia
- Eyebrow transplant
- Frontal hair line lowering or reconstruction

Post-operative care

Advances in wound care allow for semi-permeable dressing, which allow seepage of blood and tissue fluid, to be applied and changed at least daily. The vulnerable recipient area must be shielded from the sun, and shampooing is started two days after the surgery. Some surgeons will have the patient shampoo the day after surgery. During the first ten days, some of the transplanted hairs, inevitably traumatized by their relocation, may fall out. This is referred to as "shock loss". After two to three months new hair will begin to grow from the moved follicles. The patient's hair will grow normally, and continue to thicken through the next six to nine months. Some patients elect to use medications to retard such loss, while others plan a subsequent transplant procedure to deal with this eventuality.

Side effectsHair thinning, known as "shock loss", is a common side effect that is usually temporary. Bald patches are also common, as fifty to a hundred hairs can be lost each day.

Post-operative hiccups have also been seen in around 4% of transplant patients.

Expectations and Recovery

After the surgery, your scalp may be very tender. You may need to take pain medications for several days. Your surgeon will have you wear bandages over your scalp for at least a day or two. He may also prescribe an antibiotic or an anti-inflammatory drug for you to take for several days. Most people are able to return to work 2 to 5 days after the operation. Within 2 to 3 weeks after surgery, the transplanted hair will fall out, but you should start to notice new growth within a few months. Most people will see 60% of new hair growth after 6 to 9 months.

Risks and Costs of Treatment

The cost of a hair transplant will depend largely on the amount of hair you're moving, but it generally ranges from $4,000 to $15,000. Transplants have some risks, including bleeding and infection. There's also the chance for scarring and unnatural-looking new hair growth.

Some people have inflammation or an infection of the hair follicles, called folliculitis. Antibiotics and compresses can relieve the problem. It's also possible to suddenly lose some of the original hair in the area where you got the new strands, called shock loss.

Ethical considerations in organ transplant

Organ transplant has been hailed as one of the greatest achievements of modern surgery. There are however, many ethical dilemmas and controversies associated with this procedure. Among the questions raised were; who gets priority? Will priority be based on the severity of a person's illness or his age or other factors? The role of the committee was to ensure that all Transplant Specialists adhere to this set of guidelines.

Another factor that needs to be considered was the cost of organ transplant, as all organ transplants are very expensive, as it includes the surgical process and later on, the continuing rehabilitation process. A third factor to be considered was the question of consent and incentive. Currently, someone had to agree directly for transplantation in order for organs to be removed. The organ procurement process could also pose problems. This was mainly due to the different definitions of 'death'. Should death be defined as when the heart and lungs stop, or when the entire brain ceased to have activity, or just when the higher functions stop?

There is currently shortage of donor organs worldwide; the ageing population and increase in incidence of diabetes will worsen this shortage. Therefore there is a demand for donor organs in the developed world. This problem is compounded by the general reluctance of Asians in cadaveric organ donation despite legal sanction for cadaveric donations and support from the major religious groups.

Law and regulations regarding living-unrelated transplantation in many countries are either non-existence or loosely regulated. Physician and Transplant Specialist should also consider values such as patient-doctor trust, respect for human dignity and presence of conflict of interest. Ethically and legally, a person should not be killed to provide organs for another, and that organ retrieval can only begin until the donor had been declared dead. This determination of the correct interval between death and organ harvests is a continuous issue.

Social and religious considerations regarding organ transplantation

The shortage of organs for transplantation makes it important to understand why some oppose organ donation. There are many reasons why certain populations are less likely to consent to organ donations. Among these reasons, both social and religious issues play an important role, especially in a multiethnic, multicultural and multireligious community.

a. Social issues

Many social issues need to be considered when promoting organ transplant in the community. Some of these issues are misconceptions that need to be addressed individually.

The first misconception that needs to be corrected is the perception that the body of the donor would be mutilated and treated badly.

The second misconception is the worry that even if the person wanted to donate one organ, that other organs would also be taken.

The third misconception is the worry that if a person was involved in an accident, that the doctors would not save his life if they knew that he was a donor.

The fourth misconception is the worry that a person's religion do not approve donation.

The fifth misconception reported was whether a person was the right age for donation.

Religious considerations

In this report, the author wishes to discuss the religious perspective of the 3 main religion; Islamic view, Confucianism and Christianity

(i) Islamic perspective

There is a striking variability in attitudes towards transplantation throughout the Muslim world. Almost half of Arab Bedouins believe that Islam prohibits organ donation. Majority of Muslim scholars (both Sunni and Shia) promote the importance of saving human life, based on the teachings of Prophet Muhammad who encouraged his followers to seek medical attention when ill, and hence allow organ transplantation.

It was reported that Muslims who argue against organ donation believed that Islam forbids organ donation as it was not mentioned in the Quran and traditional Islamic literature.

There were also those who believed that organ transplantation extended a patient's life and his suffering. In order to respond to these misperceptions, it would be important to recognize the importance of authoritative religious figures and involve them in the decision process for organ transplant.

(ii). Confucianism, Buddhist and Taoist perspective

In particular, in Confucianism, the concept of ‘filial piety’ dictated that individuals should return their bodies in the same condition that they received from their parents, out of respect for their ancestors However, if they do decide to donate their organs after their death, the priority is to close relatives, and then in descending order, distant relatives, people from their home country

and then only to strangers. This 'negotiable' willingness to donate has enormous implications, where transplant specialist can use it as a strategy to increase organ donation rates among Chinese community. As for the Buddhist, they believe that the dying process takes several hours, and the Taoist believes that organs have one to one relationship with nature.

(iii). Christianity perspective

As for Christianity, the main branches of Christianity; i.e. Catholics and Protestants support and encourage organ transplant. Christians look at Jesus Christ, whose life was one of self-giving as guidance. Pope John Paul II, the recently deceased Pope had repeatedly advocated organ donation and organ transplant as a 'service of life'

Implications of ethical, social and religious aspect of organ transplants

Understanding the ethical, social, cultural and religious beliefs of a multiethnic population is important, as this could be used to explore negotiable limits of those beliefs and values.
Firstly, a physician involved in the procurement process should explore issues based on the effect of procurement on the donor's body, where, in a patient who may be reluctant to donate because the organ procurement process seemed to violate their religious and spiritual beliefs, a physician who understands this belief, may change the procurement protocol to allow a patient to donate their organs without violating their values.

For example, a Buddhist patient who believes that the dying process takes several hours may allow his organs to be removed for donation. Taoist who believed that his major organs have a one-to-one relationship with nature may not allow those particular organs to be removed for donation. A Chinese patient, who declined to donate his organ to an open system, may be willing to donate if he were allowed to specify the recipient.
As for the Muslim community, the same 'negotiation', can be used where, the recipient of the organ from a Muslim should also be a Muslim, as this would be an act of charity in the name of 'Islamic brotherhood'.

Therefore to overcome the aforementioned difficulties, the following are suggested steps to be taken to attain societal acceptance of organ transplantation.

1) Minimizing difficulties of the organ donation process including avoiding delays in funerals

2) Public Awareness of benefit of transplant to society, legal definition of brain death and stress absent of religious objections to transplantation

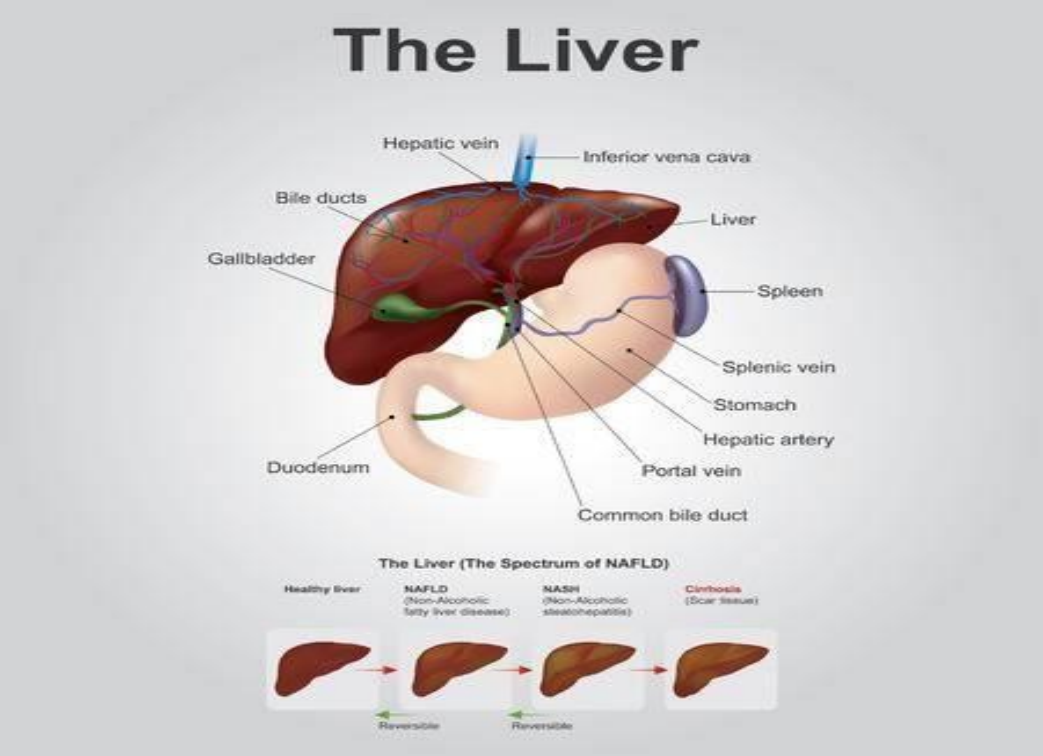
One of the suggested ways to reduce this apparent deficit is by increasing cadaveric transplantation rate.

Organ transplant is a safe procedure that gives new hope and new life to thousands of people. It should not be forgotten that this is a discussion of life and death, where a decision is made on who lives, who dies and why. This issue is also regarding real people who are suffering, and decisions made based on good ethics and proper understanding of social and religious aspects

will facilitate and make the process less painful. Both the community and physicians should therefore approach organ transplant positively and objectively and treat ethical, social and religious issues as negotiable perspectives and not barriers to organ transplant.

Regeneration of tissue and organs

Regeneration means the re-growth of part of the affected or lost organs of the remaining tissue. Animals can regenerate some organs, such as the liver. If a part of the liver is lost due to illness or injury, the liver grows back to its original size, but not in its original form. The liver is the only human internal organ capable of natural regeneration of lost tissue as little as 25% of a liver can regenerate into a whole liver. This is, however, not true regeneration but rather compensatory growth in mammals.



Regeneration in humans is the re-growth of lost tissues or organs in response to injury. This is in contrast to wound healing, which involves closing up the injury site with a scar. Some tissues such as skin and large organs including the liver re-grow quite readily, while others have been thought to have little or no capacity for regeneration. However ongoing research, particularly in the heart and lungs, suggests that there is hope for a variety of tissues and organs to eventually become regeneration-capable.

Naturally regenerating organs

Heart

Cardiomyocyte necrosis activates an inflammatory response that serves to clear the injured myocardium from dead cells, and stimulates repair. Cell types involved in the process play an

important role. Namely monocyte-derived macrophages tend to induce inflammation while inhibiting cardiac regeneration, while tissue resident macrophages may help restoration of tissue structure and function.

Endometrium

The endometrium after the process of breakdown via the menstruation cycle, re-epithelializes swiftly and regenerates. The endometrium is the only human tissue that completely regenerates consistently after a disruption and interruption of the morphology.

Fingers

L.H. McKim in 1932 described that the regeneration of an adult digit-tip following amputation. A house surgeon in the Montreal General Hospital underwent amputation of the distal phalanx to stop the spread of an infection. In less than one month following surgery, x-ray analysis showed the regrowth of bone while macroscopic observation showed the regrowth of nail and skin.

The children up to the age of 10 or so who lose fingertips in accidents can re-grow the tip of the digit within a month provided their wounds are not sealed up with flaps of skin.

In August 2005, Lee Spievack, in his early sixties, accidentally sliced off the tip of his right middle finger just above the first phalanx. His brother, Dr. Alan Spievack, was researching regeneration and provided him with powdered extracellular matrix, developed by Dr. Stephen Badylak of the McGowan Institute of Regenerative Medicine. Mr. Spievack covered the wound with the powder, and the tip of his finger re-grew in four weeks.

A woman named Deepa Kulkarni lost the tip of her little finger. Her personal research and consultation with several specialists including Badylak eventually resulted in her undergoing regenerative therapy and regaining her fingertip.

Kidney

Regenerative capacity of the kidney has been recently explored.

The basic functional and structural unit of the kidney is nephron, which is mainly composed of four components: the glomerulus, tubules, the collecting duct and peritubular capillaries. The regenerative capacity of the mammalian kidney is limited compared to that of lower vertebrates.

In the mammalian kidney, the regeneration of the tubular component following an acute injury is well known. Recently regeneration of the glomerulus has also been documented. Following an acute injury, the proximal tubule is damaged more, and the injured epithelial cells slough off the basement membrane of the nephron. Recently, the presence and participation of kidney stem cells in the tubular regeneration has been shown. However, the concept of kidney stem cells is currently emerging. In addition to the surviving tubular epithelial cells and kidney stem cells, the bone marrow stem cells have also been shown to participate in regeneration of the proximal tubule, however, the mechanisms remain controversial. Recently, studies examining the capacity of bone marrow stem cells to differentiate into renal cells are emerging.

Like other organs, the kidney is also known to regenerate completely in lower vertebrates such as fish. Some of the known fish that show remarkable capacity of kidney regeneration are goldfish, skates, rays, and sharks. In these fish, the entire nephron regenerates following injury or partial removal of the kidney.

Liver

The human liver is particularly known for its ability to regenerate, and is capable of doing so from only one quarter of its tissue, due chiefly to the unipotency of hepatocytes. Resection of liver can induce the proliferation of the remaining hepatocytes until the lost mass is restored, where the intensity of the liver's response is directly proportional to the mass re-sected.

Toes

Toes damaged by gangrene and burns in older people can also re-grow with the nail and toe print returning after medical treatment for gangrene.

Vas deferens

The vas deferens can grow back together after a vasectomy, thus resulting in vasectomy failure. This occurs due to the fact that the epithelium of the vas deferens similar to the epithelium of some other human body parts is capable of regenerating and creating a new tube in the event that the vas deferens is damaged. Even when as much as five centimeters of the vas deferens is removed, the vas deferens can still grow back together and become reattached, thus allowing sperm to once again pass and flow through the vas deferens, restoring one's fertility

IMMUNOSUPPRESIVE DRUGS:

Immunosuppressive drugs or immunosuppressive agents or antirejection medications are drugs that inhibit or prevent activity of the immune system. They are used in immunosuppressive therapy to: Prevent the rejection of transplanted organs and tissues (e.g., bone marrow, heart, kidney, liver)

FOUR MAJOR CLASSES

1. *Corticosteroids*

Prednisone (DELTASONE) and Prednisolone (HYDELTRASOL), Dexamethasone

2. *Cytotoxic Agents*

Cyclophosphamide, Azathioprine (IMURAN), and Mycophenolate Mofetil (CELLCEPT)

3. *T-cell Suppressive Agents*

Cyclosporine (SANDIMMUNE) and Tacrolimus (PROGRAF, FK506)

4. *Antibodies*

Polyclonal: Antilymphocyte globulin (ALG) and Antithymocyte Globulin (ATG), Muromonoab-CD3 (ORTHOCLONE OKT3)

Monoclonal (Antitumor mAbs): Alemtuzumab (anti-CD52), Avastin (anti-VEGF), Rituximab (anti-CD20), anti-TNF-α

1. Corticosteroids:

Prednisone (DELTASONE), Prednisolone (HYDELTRASOL), Dexamethasone

Mechanism of action:

a. Lympholytic (lysis oflymphocytes)
b. Inhibit mitosis oflymphocytes
c. Reduce size and lymphoid content of the lymph node andspleen
d. Inhibit the production of inflammatory mediators, including PAF, leukotrienes, prostaglandins, histamine and bradykinin.

Uses:

a. Autoimmune diseases (e.g., Idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia)
b. Isoimmune disease (e.g., Hemolytic disease of thenewborn)
c. Organ Transplantation (e.g., renal, heart, liver, bone marrow). Given in combination with cyclosporine, azathioprine, methotrexate.
d. Prevention of cell proliferation (e.g., coronary stents, neovascular macular degeneration)
e. Asthma

Side Effects:

Associated with high-dose long-term glucocorticoid therapy can produce

1. Sodium and fluid retention,
2. Muscle weakness,
3. Steroid myopathy,
4. Loss of muscle mass andosteoporosis,
5. Peptic ulcer with possible perforation andhemorrhage;
6. Pancreatitis, impaired wound healing, thin fragileskin,
7. Diabetogenesis.
8. Insomnia

2. Cytotoxic Agents:

Cyclophosphamide, Azathioprine, Leflunomide, Hydroxychloroqui ne, vincristine, methotrexate, etc.,

– **a. Cyclophosphamide** is an alkylating agent. It is a widely used as a cytotoxic agent.
– It is given orally as well as intravenously with efficacy.

Mechanism of action:

suppress bone marrow function

– It is inactive in parent form, and must be activated to cytotoxic form by liver CYT450 liver microsomal system to 4-Hydroxycyclophamide and Aldophosphamide. 4-of DNA synthesis.

Side effects:

Usually large Doses of cyclophosphamide is associated with -

a. Pancytopenia
b. Hemorrhagic cystitis
c. Nausea andvomitting
d. Cardiac toxicity
e. Electrolyte imbalances

b. Azathioprine (is a prodrug of mercaptopurine), must be converted into active antimetabolite.

Mechanism of Action:

a. Interferes with purine nucleic acid metabolism
b. Primarily suppresses T-cell production
c. Inhibit cellular immunity *as well as* primary and secondary serum antibody responses.

Uses:

a. Used for graft rejection
b. Normally used in combination with corticosteroids.

Side effects:

1. Bone marrow suppression (leukopenia, anemia)
2. Skin rashes
3. Fever
4. Nausea and vomiting, diarrhea
5. Hepatic dysfunction

3. Mycophenolate Mofetil

Mechanism of action:

a Inhibits inosine monophosphate a. dehydrogenase; an enzyme required for *de novo* purine synthesis

b. Selective because T and B cells rely on de novo pathway
c. Suppresses lymphocyte proliferation and B-cell antibody productionUses:
Can be used to inhibit transplant rejection

E. T-Cell Suppressor Agents (cyclosporine)

• Oral formulation of cyclosporine that immediately forms a microemulsion in an aqueous environment. It is an 11-amino-acid cyclic peptide drived from *Tolypocladium inflatum*

Mechanism of action:

– Binds to cyclophilin; complex inhibits calcineurin phosphatase and Tcell Activation

Cyclosporine

- **Uses**

– Kidney, liver, heart organ transplantation used in combination with azathioprine and corticosteroids

– Rheumatoid Arthritis used in combination with methotrexate in rheumatoid arthritis patients who do not respond adequately to methotrexate alone

– Psosiasis *nonimmunocompromised patients with severe (i.e.,*extensive and/or disabling), recalcitrant, plaque psoriasis who have failed to respond to at least one systemic therapy (eg., PUVA, retinoids, or methotrexate) or in patients for whom other systemic therapies are contraindicated, or cannot be tolerated

Side effects

– Nephrotoxicity, hemolytic–uremic syndrome, hypertension, neurotoxicity, gum hyperplasia, skin changes, hirsutism, posttransplantation diabetes mellitus, hyperlipidemia; trough monitoring or checking levels two hours after administration required

Antibodies:

Selective antibodies against lymphocytes and thymocytes have been used as immunosuppressants.

1. Antithymocyte Globulin (ATG)

Mechanism of Action:

Polyclonal antibody, binds T-lymphocytes

Use:

Graft rejection during acute phase

Side effects:

a. *A*llergic reactions;

b. consequences of immune suppression

2. Muromonoab-CD3 (ORTHOCLONE OKT3)

Mechanism of Action:

Monoclonal antibody, binds to T-lymphocytes

Use:

Acute graft rejection

Side effects:

a. Cytokine release syndrome (can be fatal);

b. Allergic reactions;

c. Consequences of immune suppression

PART-A

1. What are the donors?

2. Define transplantation.
3. What are the immunological considerations in transplantation?
4. Brief the ethical considerations in transplantation.
5. Define regeneration
6. Define blood transfusion
7. Mention the different types of transplants.
8. What are problems encountered during blood transfusion?
9. State the fundamentals of transplantation
10. What are the immunological factors affecting organ transplants?

PART-B

1. Explain in detail about the transplantation of kidney
2. Explain in detail about the bone, hair and pancreatic transplantation
3. How does the immunological factor affect the organ transplant process? Briefly explain blood transfusion.
4. Discuss the transplantation of liver and bone
5. Define transplantation. Brief about procedure of renal transplantation
6. Brief about the ethical considerations of organ transplantation.
7. Discuss briefly about regeneration and factors involved for the same.
8. Discuss the transplantation of kidney and include the need, technical feasibility, economic and social concepts in your discussion
9. Discuss about biological factors involved in blood transfusion
10. Discuss transplantation of heart, lung and skin. Include question of need, technical, ethical, economic and social aspects in your discussion.

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