SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

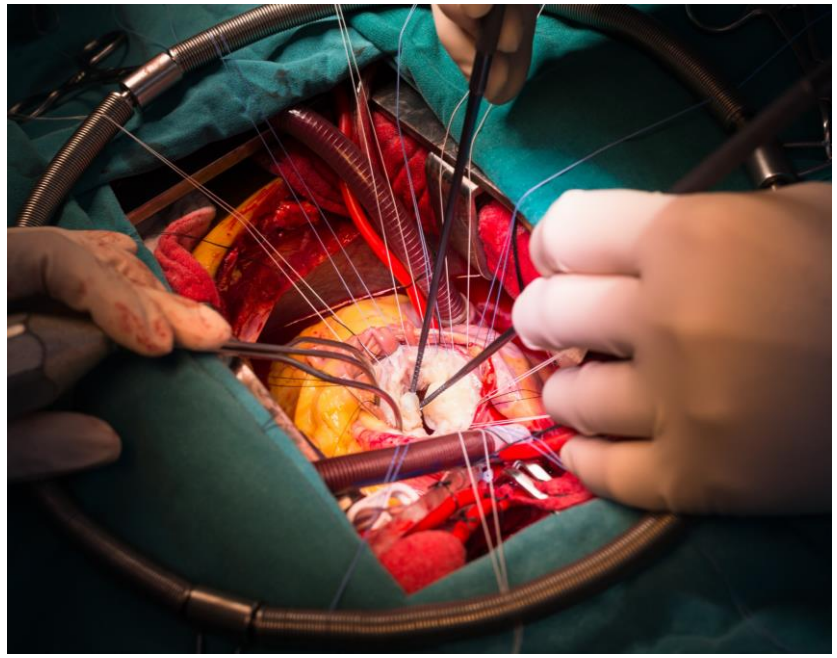
DEPARTMENT OF CARDIOPULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME: CPB and Perfusion Technology

TOPIC : Myocardial Protection

Case Presentation

56 years Male Patient was posted for MVR. The patient had a past history of Hypertension x 10 years. While initiating the case after induction the patient went through slight hypotension. After sternotomy, the procedure was started with cannulation on Aorta, SVC and IVC. What are the measures you will take to preserve myocardium from the surgical insult? What Cardioplegia solution you will prescribe for this case?



Introduction

- Cardiac surgery is performed to **restore cardiac function** in a diseased heart
- By necessity it is accompanied by myocardial injury
- Myocardial protection is required to minimize the harmful effects on heart
- There is no universally accepted strategy for myocardial protection
- Minimize the difference between o2 delivery and utilization

Introduction

Protection of myocardium during bypass is one of the most vital part of cardiac surgery. It provides dry, motionless operative area for surgeon to work with fine ultra thin suture on very small anastomosis in Grafting and other procedures.

Many methods has been proposed for the protection. The techniques are,

- **Anoxic Arrest**
- **Coronary Perfusion**
- **Hypothermic Arrest**
- **Chemical Arrest**
- **Electrical Fibrillation**

Cardiac physiology

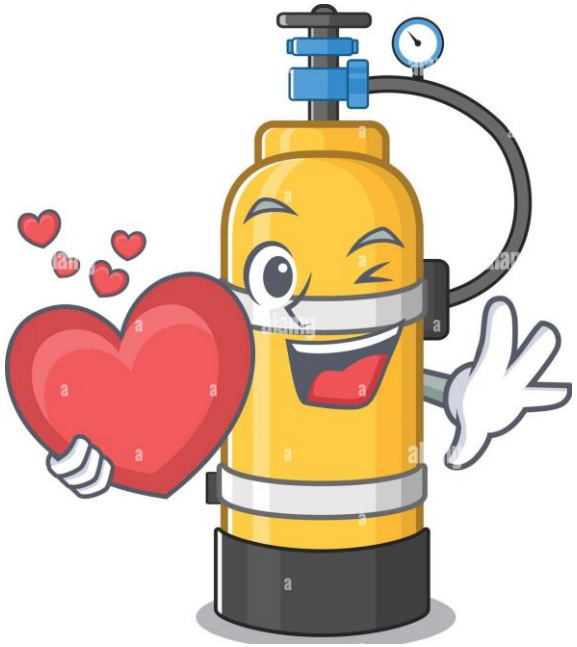
- Myocardium has a high rate of o2 consumption under normal circumstances
- Ischemia occurs when the supply of o2 is exceeded by the demand
- Infarction occurs when ischemia occurs for prolonged period of time

- O2 delivery to myocardium depends on

1 - hemoglobin

2- o2 saturation

3- blood flow



Cardiac physiology

Sub endocardium

- most vulnerable to injury
- flow occurs primarily during diastole
- flow depends upon transmural gradient

Insufficient flow causes systemic hypotension

- And **Insufficient flow** occurs incase of aortic stenosis, CAD, VF, ventricular distension

Physiology – myocardial o2 consumption

- Heart depends on continuous supply of o2 to maintain full function
- In presence of o2 1 mole glucose – 36 moles ATP
- Under anaerobic conditions 1 mole glucose – 2 moles ATP, lactate and hydrogen accumulate in tissues

CONDITION	O2 CONSUMPTION
Normal working ventricular myocardium	8 ml of o2/100g per min
Empty beating heart	5.6 ml of o2/100g per min
Potassium arrested heart	1.1 ml of o2/100g per min
Myocardial cooling	0.3 ml of o2/100g per min

History

Melrose in 1955

- Rapid or elective cardiac arrest using high dose potassium over 200mM (2.5% of K+ Citrate)
- Disadvantage – intracellular calcium overload and reperfusion injury

In 1960's, rapid operations, intermittent aortic cross clamping

Hearse

Concept of cold chemical cardioplegia

Three components - Chemical arrest, Hypothermia, Additional protection- energy substrates, steroid, buffers etc.

- In 1970's, Intracellular and extracellular CP solutions
- **Bretschneider solution-** intracellular
- **St thomas** hospital no2 solution - extracellular

Objectives of the surgeon using cross clamp

- A still , bloodless field
- Motionless field
- The heart is soft and can be retracted more easily for posterior anastomosis
- Microvascular anastomosis can be more accurately constructed
- Cerebral air embolism can be prevented
- Certain cardiac anomalies can only be corrected with prolonged X-clamping of the aorta

Electrical Fibrillatory Arrest

- **One to 6 volts** of 60 cycles of current is sufficient to cause continual ventricular fibrillation.
- It can be done by placing **electrodes** or alligator clips or plates directly on the myocardium
- The technique used along with **moderate hypothermia (32 degree Celsius).**
- Once temperature achieved, the electrical current will be discontinued.
- This technique was withdrawn from usage because of **anoxia**, that **causes ventricular distension, sub endocardial necrosis, ventricular hemorrhage** on continual prolonged electrical fibrillation

Anoxic Arrest

- This is one of the simplest method of arrest, **just by providing aortic cross clamp, to the proximal ascending aorta**, that prevents the blood from reaching the coronary arteries, results in arresting the heart due to anoxia.

- The safe arrest period of **60 minutes** was provided with the **combination of topic hypothermia of myocardium.**

- This technique was withdrawn because of **myocardial mitochondria damage, depression of LV Function and hypertrophy and stone heart syndrome.**

Hypothermic Arrest

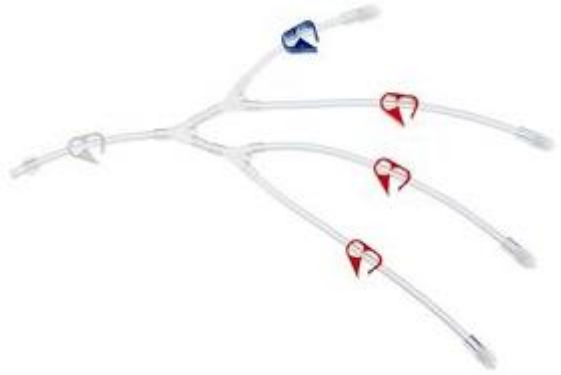
- Hypothermic arrest can be done by reducing the temperature of 10 – 20 degree Celsius.
- During this period, the myocardium inactivity occurs with decreased myocardial oxygen supply and metabolic rate.
- The arrest has been given by, applying cold media to the opened pericardium.

- Ice Chips
- Ice Saline Slush
- Continual Saline slush by placing sump in pericardium 0 to 4 degree Celsius Saline in 100ml/min infusion

This method is withdrawn from usage because of frost bite with isolated myocardial necrosis and constrictive pericarditis

Coronary Perfusion

- Coronary perfusion can be continues or intermittent along with hypothermia
- Normal resting coronary blood flow is approximately 250 ml/min (5% of CO)
- Normal Perfusion pressure of coronary arteries is 80 to 100 mm Hg
- The coronary perfusion cannulas are placed in coronary ostia
- The tip of the cannula may extend beyond the bifurcation of the left main coronary artery.
- This technique is not ideal because of placement of individual cannulas in each coronaries.



Mechanisms of myocardial ischemic injury

Ischemia

↓

Mitochondrial Oxidative Phosphorylation arrest (due to lack of O2)

↓

Decreased ATP Production

↓

To compensate this, Cardiomyocytes conduct anaerobic glycolysis

↓

Accumulation of Photons and Lactate

↓

Intracellular Acidosis

Elevated H+ ions activates Na+/H+ Exchanger

↓

H+ Ions expel out and Influx of Na+

↓

Increased Na+ intracellularly cause Activation of Sarcolemmal Na+/Ca+ exchanger

↓

Build High Ca+ Intracellularly

- Depletion of high energy phosphates
- Intracellular acidosis
- Alterations in the intracellular calcium homeostasis
- Direct myocardial injury from ischemia

Mechanisms of Myocardial ischemia reperfusion injury

Reperfusion

↓

ATP Synthesis, Respiratory Activity and pH comes to normal rapidly

↓

Already deposited Ca+ ions activates protease enzyme to produce Calpain

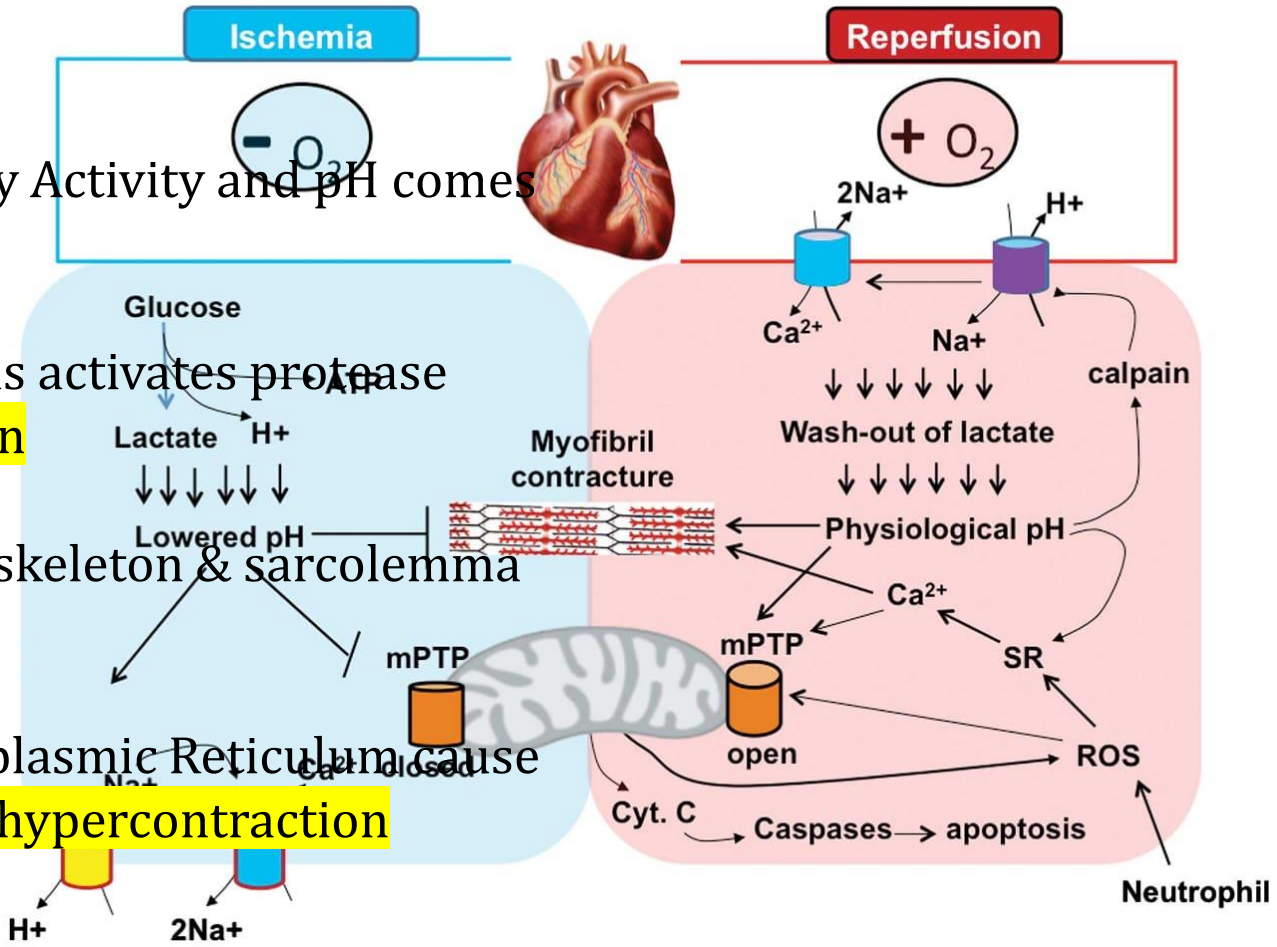
↓

Calpain degrades the cytoskeleton & sarcolemma of myocardium

↓

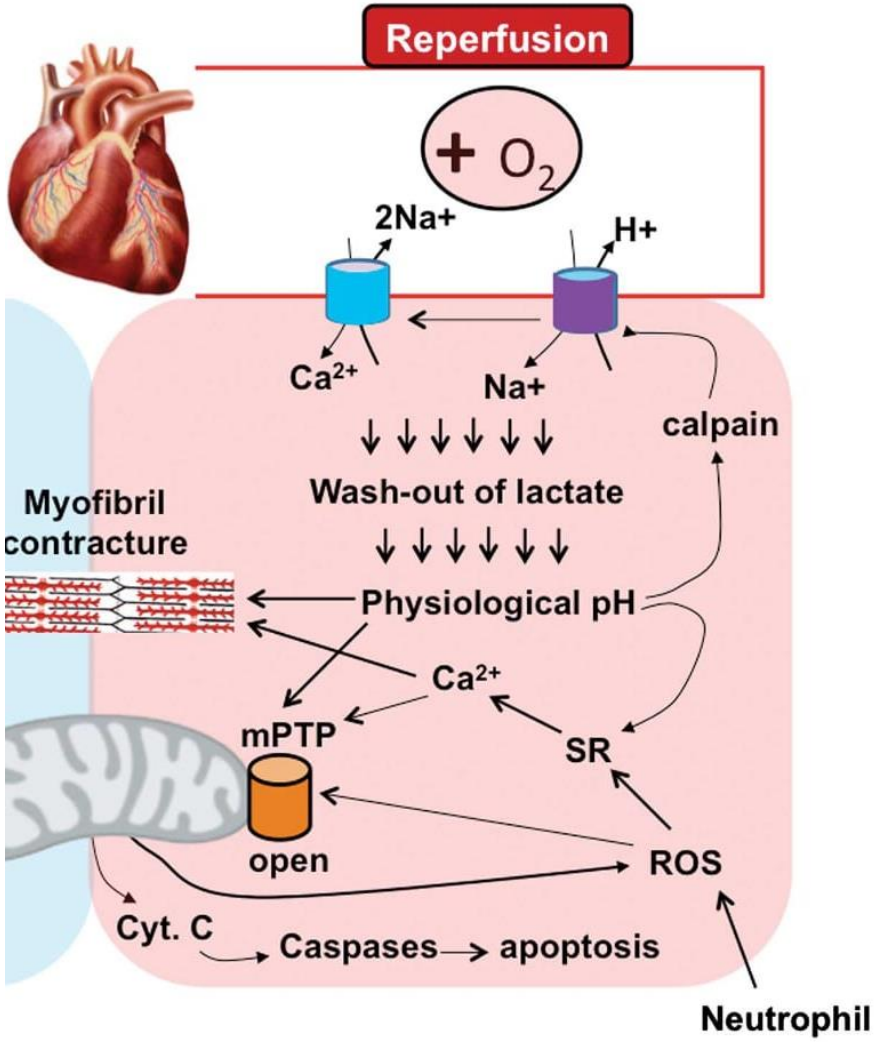
Excessive Ca+ from Sarcoplasmic Reticulum cause uncontrolled myofibrillar hypercontraction

↓



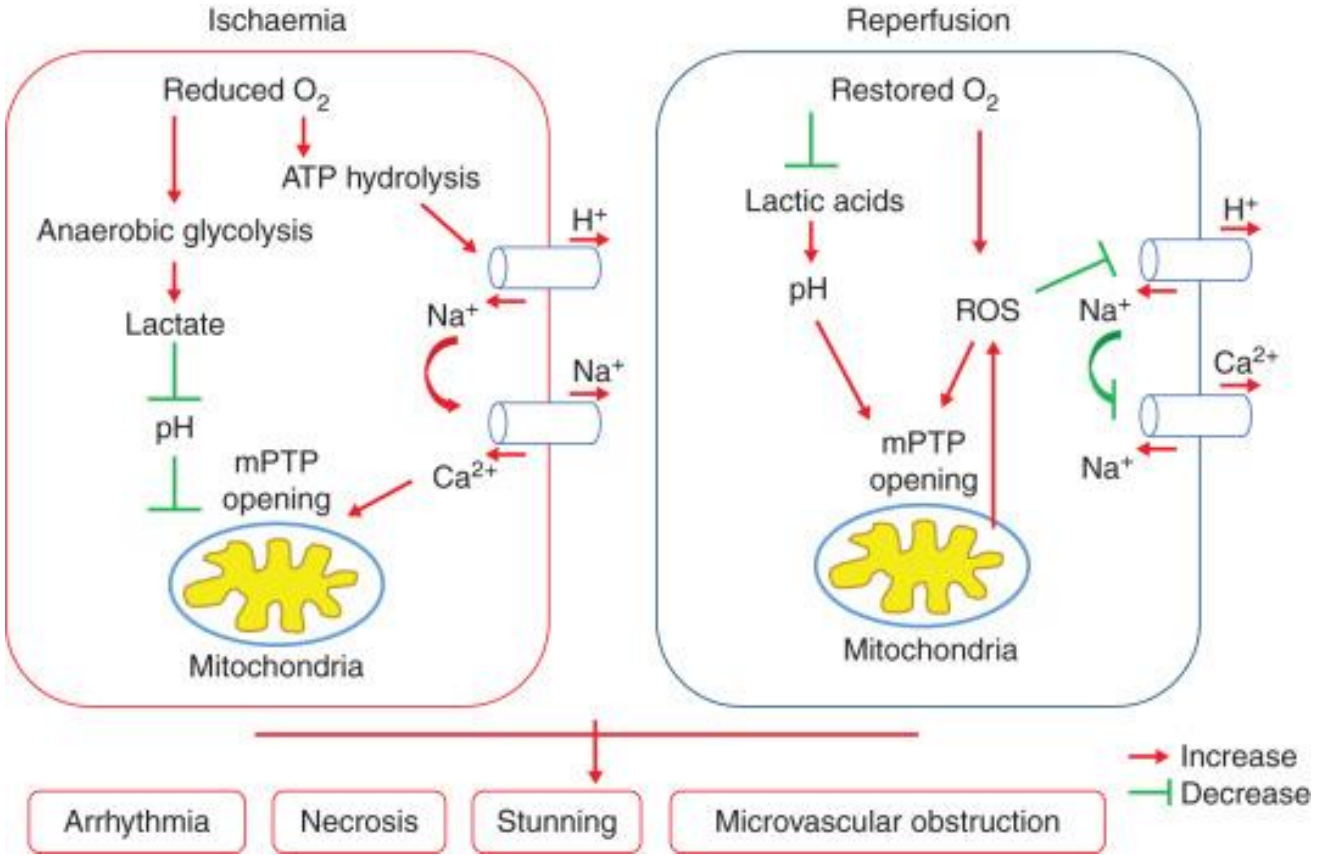
Mechanisms of Myocardial ischemia reperfusion injury

- Opening of mitochondrial permeability pore (mPTP)
- Matrix swelling
- Rupture of mitochondrial outer membrane
- Cytochrome C from mitochondria release into cytosol
- Cytochrome C activates Caspases (promotes programmed cell death)
- Excessive Ca+ produce ROS Reactive Oxygen Species (leads to cell death)



Effects of Ischemia – reperfusion injury

- Calcium overload
- Generation of oxygen derived free radicals
- Complement activation
- Adverse endothelial cell- leucocyte interactions
- Myocellular edema
- Damage to non-myocyte components



Consequence of ischemia –reperfusion injury

Severity depends on length of ischemia, temperature of myocardium, conditions of myocardium before during and after the ischemia

- Functional deficit
- Myocardial stunning **– reversible myocardial contractile dysfunction induced by acute ischemia followed by reperfusion**

- Myocardial necrosis (stone heart) – Ischemic Contracture of heart

Reperfusion injuries can cause atrial and ventricular dysarrhythmias, reversible systolic and diastolic LV dysfunction(stunning), myocardial necrosis.

Protective strategies

Protective strategies before the onset of ischemia

- Minimization of ongoing ischemia
- Rapid revascularization
- Nutritional repletion
- Prevention of ventricular distension
- Myocardial preconditioning

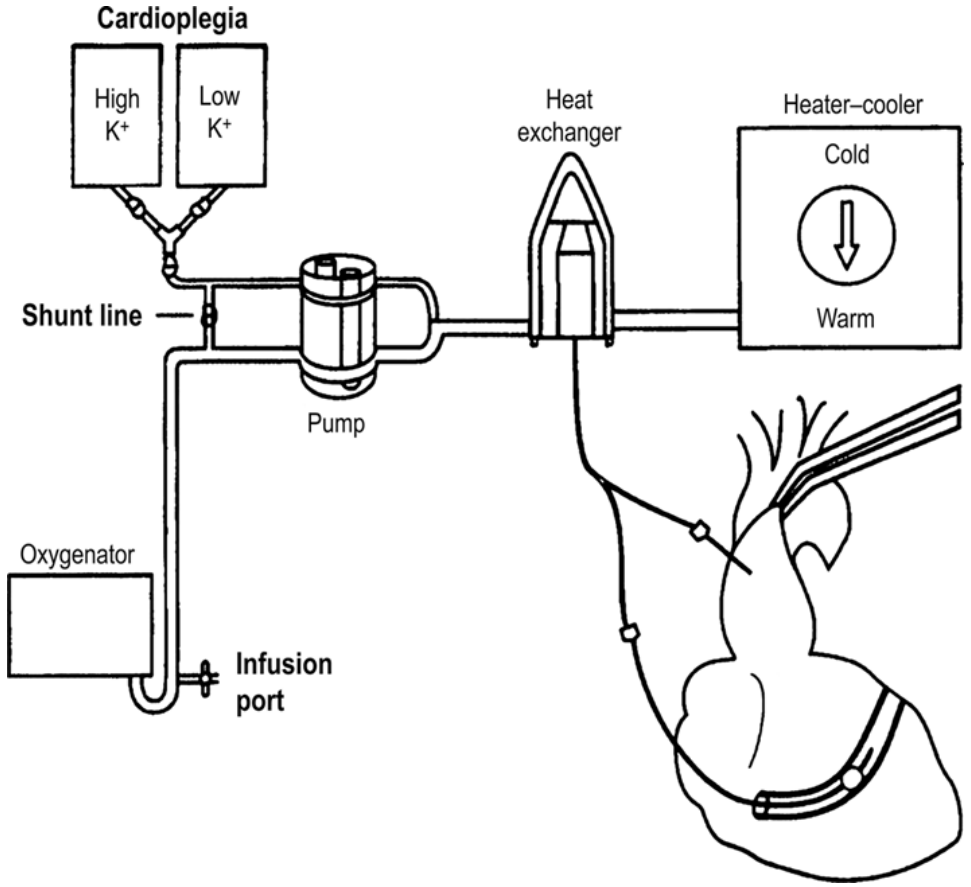
Protective strategies during ischemia

- Numerous interventions are possible
- Not all are required in every circumstances
- Must be individualized to situations

Myocardial Protection strategies

A variety of strategies for myocardial protection have been identified

- **Established strategies**
- **Emerging strategies**
- **Experimental strategies**



Elements of myocardial protection – well established strategies

1. Asystole
2. Hypothermia
3. Avoidance of edema
4. Buffering of acidosis
5. Calcium management

Avoidance of edema
Controlled delivery
pressure
Composition – mannitol and glucose

Asystole - Prevents depletion of ATPs
Good post ischemic functional recovery of myocardium

Hypothermia: Myocardial o2 consumption decreases by 50% for every 10 ‘ C decrease in myocardial temperature **(Q10 effect)**

Advantage : allows the interruption of myocardial blood flow for short period of time enabling the conduct of operation

Disadvantages: alterations in cellular fluidity, transmembrane gradients, myocardial edema

Calcium management
Extreme hypercalcemia and hypocalcemia- suboptimal myocardial protection
Calcium chelation
Drugs

Buffering of acidosis
Episodic reinfusion of solution- washout
Composition-- blood, histidine, bicarbonate, THAM

Cardioplegia

A chemical solution used to arrest the heart and preserve the myocardium from damage.

Types → **Blood Cardioplegia** →

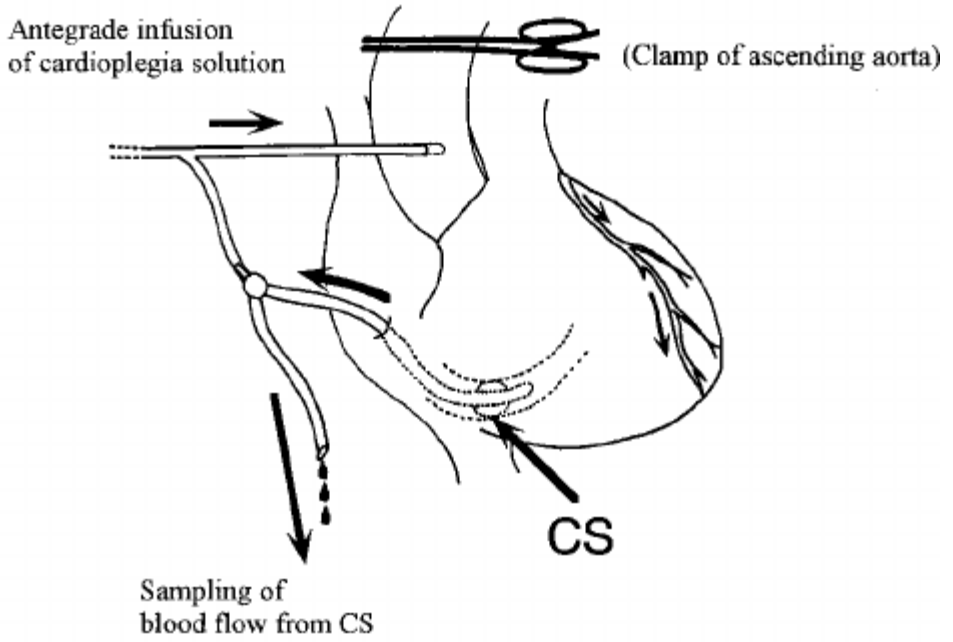
- Proposed by **Buckberg**
- Higher osmotic pressure
- Greater acid base balance capacity
- Mixing blood to crystalloid with a final hematocrit of 16-20%
- **High o2 carrying capacity**
- Contains free radical scavengers, colloids

Crystalloid Cardioplegia

- Uncommonly used in adult patients
- Preservation of donor heart during transplantation
- Do not contain hemoglobin and deliver only dissolved o2

Purpose of cardioplegia

- To provide cardiac quiescence
- Bloodless field, enhances visibility,
- Reduction in myocardial energy consumption, preservation of myocardial function
- Current methods allow rapid resumption of contractile activity at the end of the procedure



Methods of producing myocardial hypothermia

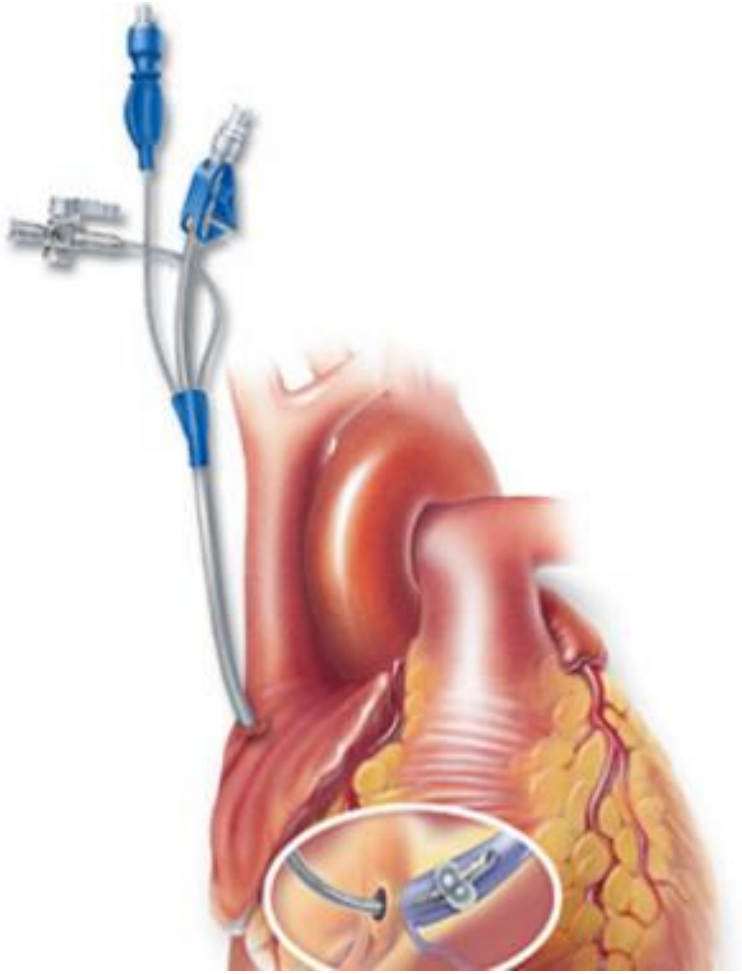
Administration of cardioplegia, given at a temp of 4-10”C will produce myocardial cooling to 15-16”C

Systemic hypothermia

Topical cooling

TABLE 13.2. POSITIVE AND NEGATIVE PHYSIOLOGIC CONSEQUENCES OF HYPOTHERMIA	
Positive	**Negative**
Decreases metabolic rate	Decreases rate of repair
Decreases oxygen requirements	Increases intracellular swelling, Na^+ accumulation
Temporarily decreases cell–cell interactions	Decreases *rate* of contraction; increases energy demands *per beat*
Decreases rate of degradative reactions	Induces ventricular fibrillation, arrhythmias
Increases tolerance to ischemia	Impairs oxygen dissociation
Reduces $[K^+]$ necessary for arrest	Impairs coronary autoregulation
Prolongs electrical silence, cardioplegia	Potential for phrenic nerve damage
Decreases cell deformability	Promotes rouleau formation(?)
Inhibits intracellular Ca^{2+} accumulation	Decreases membrane fluidity; decreases receptor transduction , transmembrane transport
Decreases rate of NF-kB (nuclear factor) translocation	Inhibits sarcoplasmic reticulum Ca^{2+} uptake

Route of delivery & CP Solutions



Route of Delivery

- Antegrade
- Retrograde
- Both Antegrade and retrograde
- Coronary Ostial

CP Solutions

- Del Nido Solution
- Custodial HTK Solution
- Senthoma's CP Solution
- Bioplegia

Antegrade Cardioplegia

- Cardioplegia administration will prevent LV Distension and Rewarming of Heart
- Infusion of cardioplegia between the aortic cross clamp and aortic valve force the cardioplegia solution into the coronary arteries through Ostium.
- **Initial dosage** = 10 ml/kg
- **Preparation ratio** 4:1 (4 part of blood with 1 part of CP)
- **Infusion Pressure** = 125 – 150 mm Hg
- **Temperature** = 10 to 15 degree Celsius
- **Aortic Pressure** = 50 -70 mm Hg

Low perfusion pressure – uneven distribution

High perfusion pressure – endothelial damage
Root perfusion cannot be given in aortic valve regurgitation

Retrograde Cardioplegia

- Placement of cannula in coronary sinus.
- The cannula insertion is done after venous cannulation to prevent dislodgement
- The one end with balloon is placed in coronary sinus and the other end placed in transducer for monitoring line pressure.
- **Pressure** = 30 to 50 mm Hg
- **Flow** = 200 ml/min
- The aorta must be vented to remove the CP and prevent overload

High pressure – damage to coronary sinus

Improper placement – injury to CS

May not adequately protect RV

Advantages: aortic valve procedures, coronary

Ideal CP Solution & Calculation

- D = Diastolic Arrest
- O = Osmolarity
- E = Prevent Edema
- S = Act as a Substrate
- M = Membrane Stabilizer
- A = Prevent Acidosis
- C = Prevent Ca++ Influx
- H = Proper Hypothermia

Adult = Patient weight x 20 ml
Pediatric = Patient weight x 30 ml

Composition of CP and its uses

- **Potassium** = Depolarize and arrest the heart muscle, stops its contraction
- **Sodium Bicarbonate** = Buffer the high K+ Content, maintaining proper pH
- **Magnesium** = stabilize the myocardial cells and reduce the risk of arrhythmias during arrest period
- **Xylocord** = Antiarrhythmic medication
- **Mannitol** = Osmotic Support, prevent cellular edema and protect heart tissue
- **Histidine** = Buffers the acidosis (caused during ischemic period)
- **Ketoglutarate** = Helps in ATP Production during reperfusion
- **Tryptophan** = Stabilizes the cell membrane

DEL NIDO CARDIOPLEGIA

1 liter plasma-lyte solution to which the following are added

1. Mannitol 20%, = 16.3 ml
2. Magnesium sulfate 50%, = 4ml
3. Sodium bicarbonate 8.4%, = 13ml
4. Potassium chloride (2meq/ml), = 13ml
5. Lignocaine 1%, = 13ml

Arrest time =60 -90 minutes

Temp = 4 to 8 degree

Prepared in 50cc syringe

Cardioplegia Solution
Plasma-Lyte A -**1000 mL**
Sodium Bicarbonate 1 mEq/mL -**13 mL**
Mannitol (20%)- **16.3 mL**
Magnesium Sulfate (50%)- **4 mL**
Lidocaine (1%)-**13 mL**
Potassium Chloride 2 mEq/mL -**13 mL**

Final Volume = 1059.3 mL
EXPIRATION DATE: (9 days from current date)
Keep refrigerated - DO NOT FREEZE
Dr. del Nido Formula
CARDIOPLEGIA ADMIXTURE SOLUTION
NOT FOR I.V. ADMINISTRATION
CARDIAC PERFUSION ONLY

Custodial HTK cardioplegia (Bredschnider's solution)

1 L contains

1. Sodium chloride- 15 mmol/L
2. Potassium chloride - 9 mmol/L
3. Magnesium chloride – 4mmol/L
4. Histidine hydrochloride- 18mmol/L
5. Histidine – 180mmol/L
6. Tryptophan – 2mmol/L
7. Mannitol- 30mmol/L
8. Calcium chloride – 0.015mmol/L
9. Potassium hydrogen 2-ketoglutarate- 1mmol/L

Osmolarity- 310mOsm/kg, pH- 7.02-7.20

Arrest time = 3 hours

Temp = 4 to 8 degree

Single Dose given

Senthoma's CP Solution

- Procaine HCL = 13.64 mg
- Potassium Chloride = 59.65 mg
- Magnesium Chloride = 164.65 mg
- Disodium edotate = 0.1 mg
- Sodium Metabisulphiate = 2 mg
- Water for Injection = 1ml

Arrest time = 20 - 30 minutes

Temp = 4 to 8 degree

Need Multiple Dose

Disodium edotate = treat calcium overload, irregular heart beat

Procaine HCL = Anesthetic agent, protect myocardium

Sodium Metabisulphiate = Antioxidant properties

Elements of myocardial protection – emerging strategies

- **Oxygen radical therapy**
- **Amino acid enhancement** *(Arginine helps to promote the production of protein, enhances cell growth, triggers collagen production, strengthens immune function and promotes blood flow.)*
- **Adenosine** *(Rapid intravenous injection of adenosine induces temporary asystole that enables placement of sutures in a motionless surgical field and improved postoperative hemodynamic function)*

Elements of myocardial protection – experimental strategies

- Nitric oxide
- Specific anti neutrophil therapy
- Complement related therapy
- Hyper polarizing agents
- Sodium – hydrogen exchange inhibitors

Moderately Hypothermic Intermittent Global Myocardial Ischemia

- Perfusate Temperature 25 – 30 degree Celsius
- The surgeon works on the heart intermittently for a period of 10 to 15 minutes, and release of cross clamp for 3 to 5 minutes.
- When the technique is used optimally, the heart is made to beat during this interval without fibrillation

Continuous Normothermic Coronary Perfusion

The earliest intracardiac operations were performed on Normothermic, Perfused, Empty Beating Heart.

This method is not ideal for usage.

Water tends to accumulate in the myocardium during CPB and lack of ATP

Key points

- Intraoperative myocardial injury can occur **before, during or after CPB**
- The degree of permanent myocardial injury after ischemia is a function of **severity and duration of ischemia** which can be modified
- **Reperfusion injury** is defined as additional myocardial injury incurred after restoration of blood flow to ischemic myocardium
- Impaired microvascular blood flow (no-reflow response) can result from these injuries
- Cardioplegia administration

THANK YOU

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