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delNido for Myocardial Protection

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No disclosure for this presentation

Top Priority in Protecting the Heart During Induced Ischemia is to:

Decrease Myocardial Oxygen Consumption

- **Hypothermia**-Decrease Temp by 10 degrees, O^2 consumption by 40-50%.

- **Electrical**-Fibrillatory arrest, not used much now

- **Chemical** (depolarizing/polarizing/hyperpolarizing)

Myocardial Oxygen Consumption (ml/100gm/min) avg. heart 310 gms

Temp	37^0 C	32^0 C	28^0C	22^0 C
Vented Beating	5.5	5.0	4.0	2.9
Cardioplegia	1.0	0.8	0.6	0.3
Fibrillating	6.5	3.8	3.0	2.0

Myocardial oxygen consumption (MVO2) is defined by the equation: MVO2 = coronary blood flow x arteriovenous difference in O2 content. The average value for a heart of 300 g is 30 to 35 ml/min.

Cardioplegia arrest remains the GOLD standard

- Cardioprotection with **potassium** rich solutions: depolarized arrest
- Despite its almost universal usage, cardioplegia in its current form is associated with potential downsides rendering those cardioprotective regimens a less than optimal choice in certain clinical situations and certain patient populations.

Cardioplegia History

1950s Whole body hypothermia (Bigelow, Swan, Ross, Lewis)

1960s Topical myocardial hypothermia with aortic cross clamp. (Shumway)

1972 Hyperpolarizing solution (Bretschneider, Kirsch)

1970 Warm aortic cross clamping (Cooley)

1973 Chemical arrest/hypothermia (Gay & Ebert)

1976 Hypothermia, potassium, glucose, calcium (Hearse)

1978 4:1 blood with warm reperfusion (Buckberg)

1978 Retrograde cardiopleiga (Solorzano)

1989 Warm continuous cardioplegia (Panos)

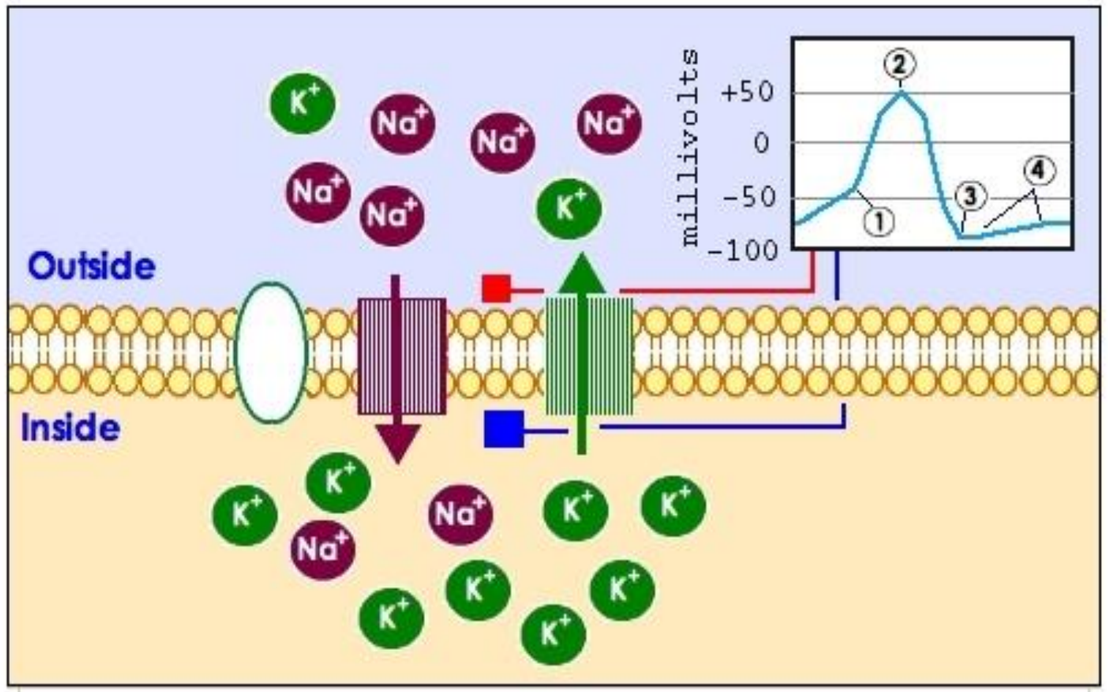
1991 Warm continuous retrograde (Salerno)

1999 Microplegia (Califiore, Weisel)

2003 Single dose cardioplegia (del Nido)

2005 Potassium channel openers (Dobson)

Action Potential



① At -40 mV, Na+ channels open & Na+ ions flood inside
② At +50 mV, Na+ channels close & K+ channels open so that K+ ions flood outside
③ Voltage decreases to -90 mV & K+ channels close
④ Na-K Pump restores potential to -70mV in 1-2 mSec.

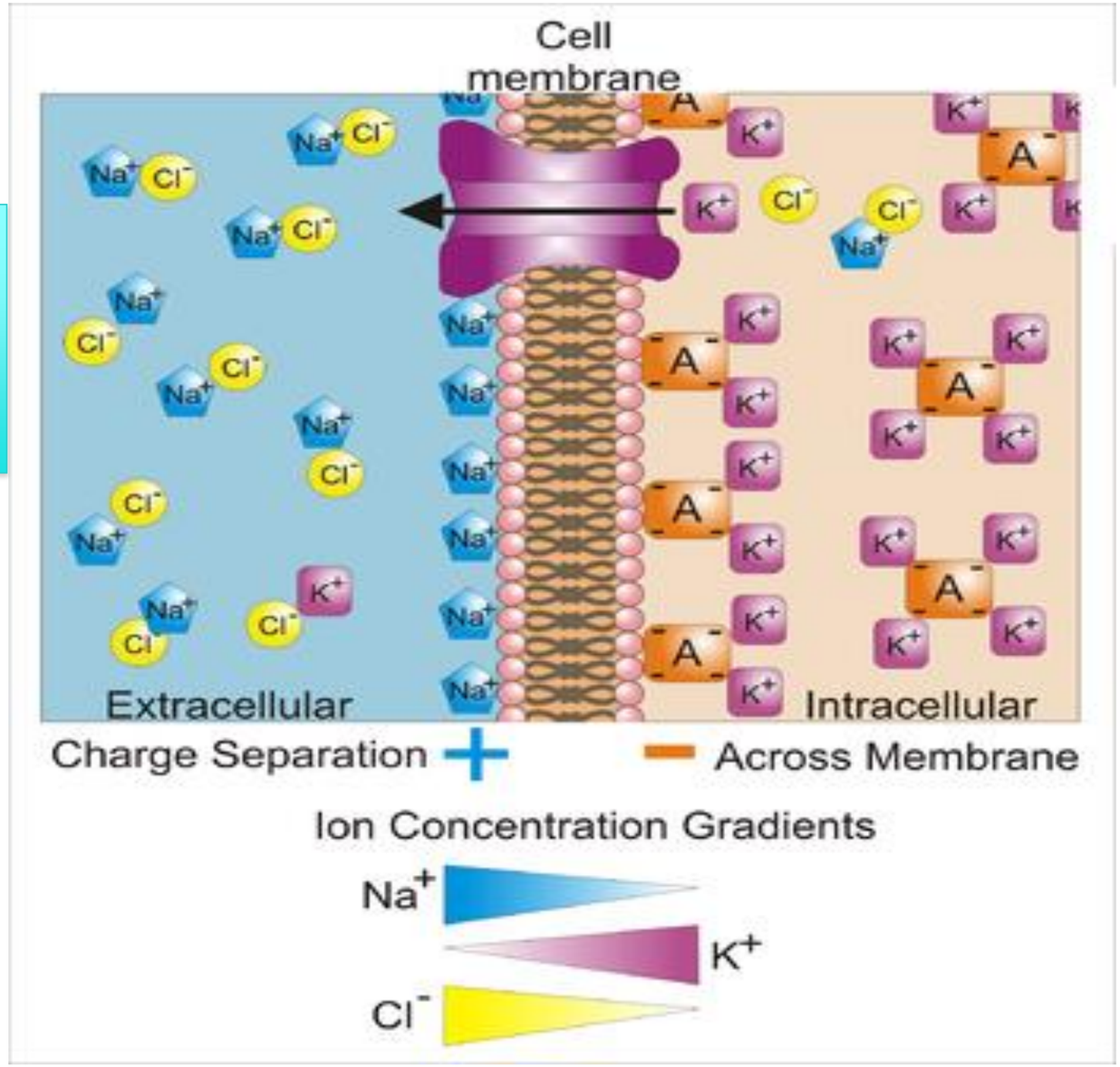
- Na channels open and Na moves in (depolarization)
- (Repolarization) occurs when K channels open and K moves out.
- Very short acting event lasting ~1-2 mSec

Chemical

Diastolic Depolarizing Solutions

- del Nido
- St Thomas
- Buckberg
- Plegisol

Add K^+



With or Without Blood

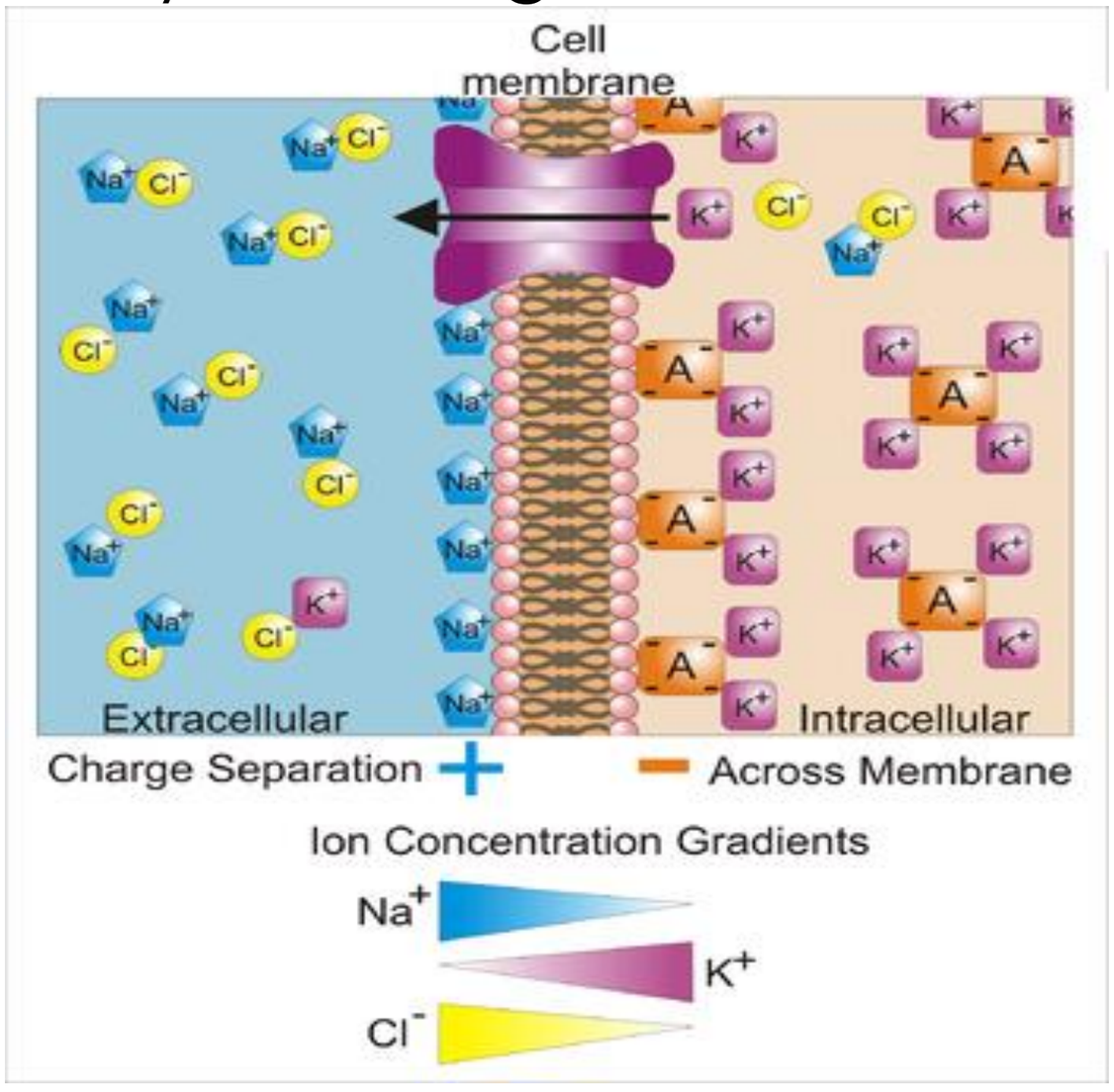
Chemical

- **Polarize** by filling the extracellular space with a sodium poor solution effectively avoiding an action potential.

Remove Na^+

- Bretschneider
- HTK
- Custodial

All the same solution!



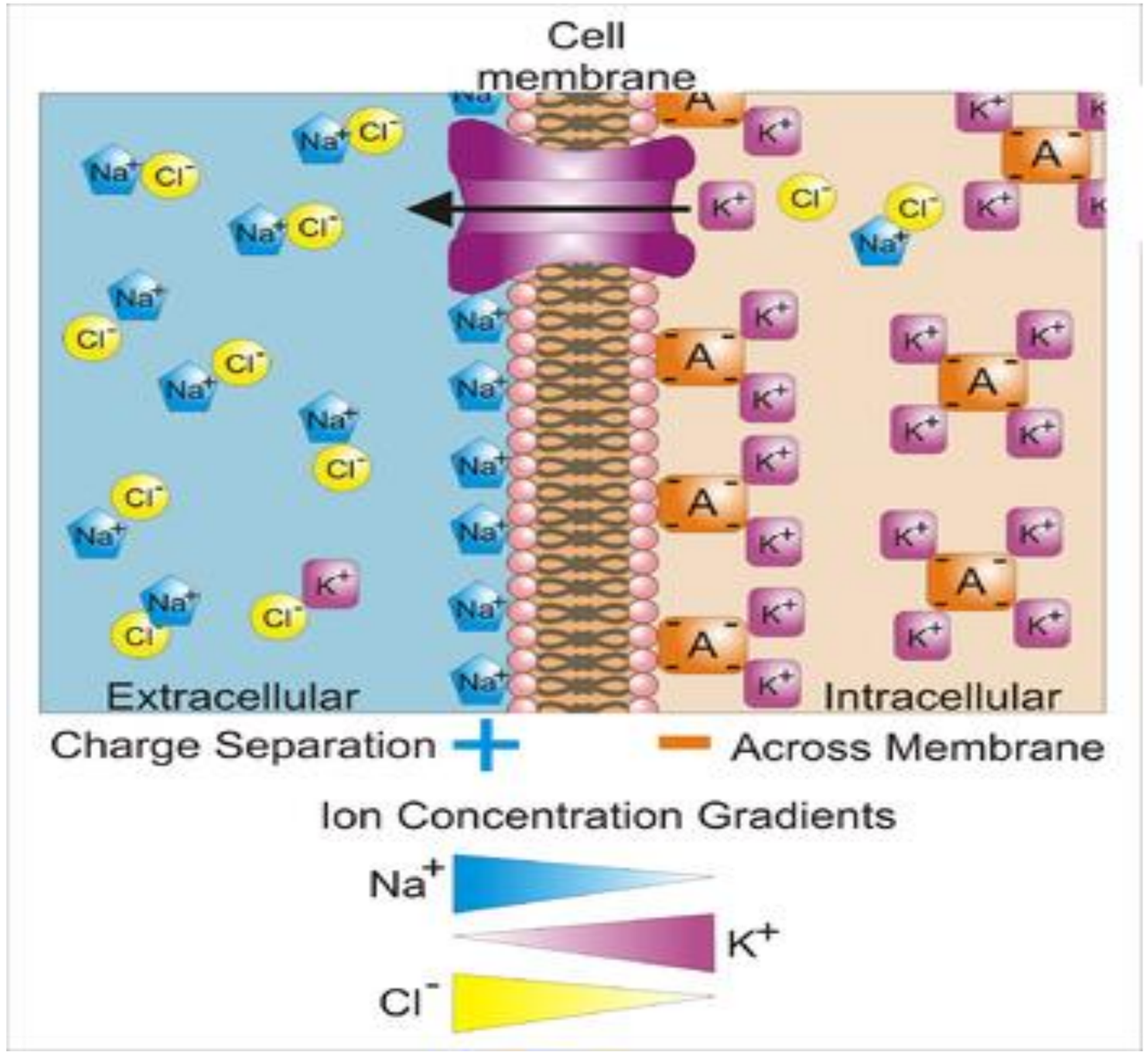
Chemical

- **Hyperpolarize** by filling the extracellular space with K^+ channel openers thereby avoiding an action potential.

Depolarize for rapid arrest with high potassium in the extra-cellular space.

Enhance the arrest with **hypothermia** 6^0– 22^0

Adenosine
Adenocaine
Pinacidil



Elderly

- 25% of the population over 75 years suffers from symptoms of cardiovascular disease.
- as the elderly represent the fastest growing population demographic in industrialized nations, the proportion of elderly patients being evaluated for cardiac surgery is only expected to increase: average age of cardiac surgical patients increased from 55.8 years to 68.8 years over the last decade.

Case complexity + operative risk

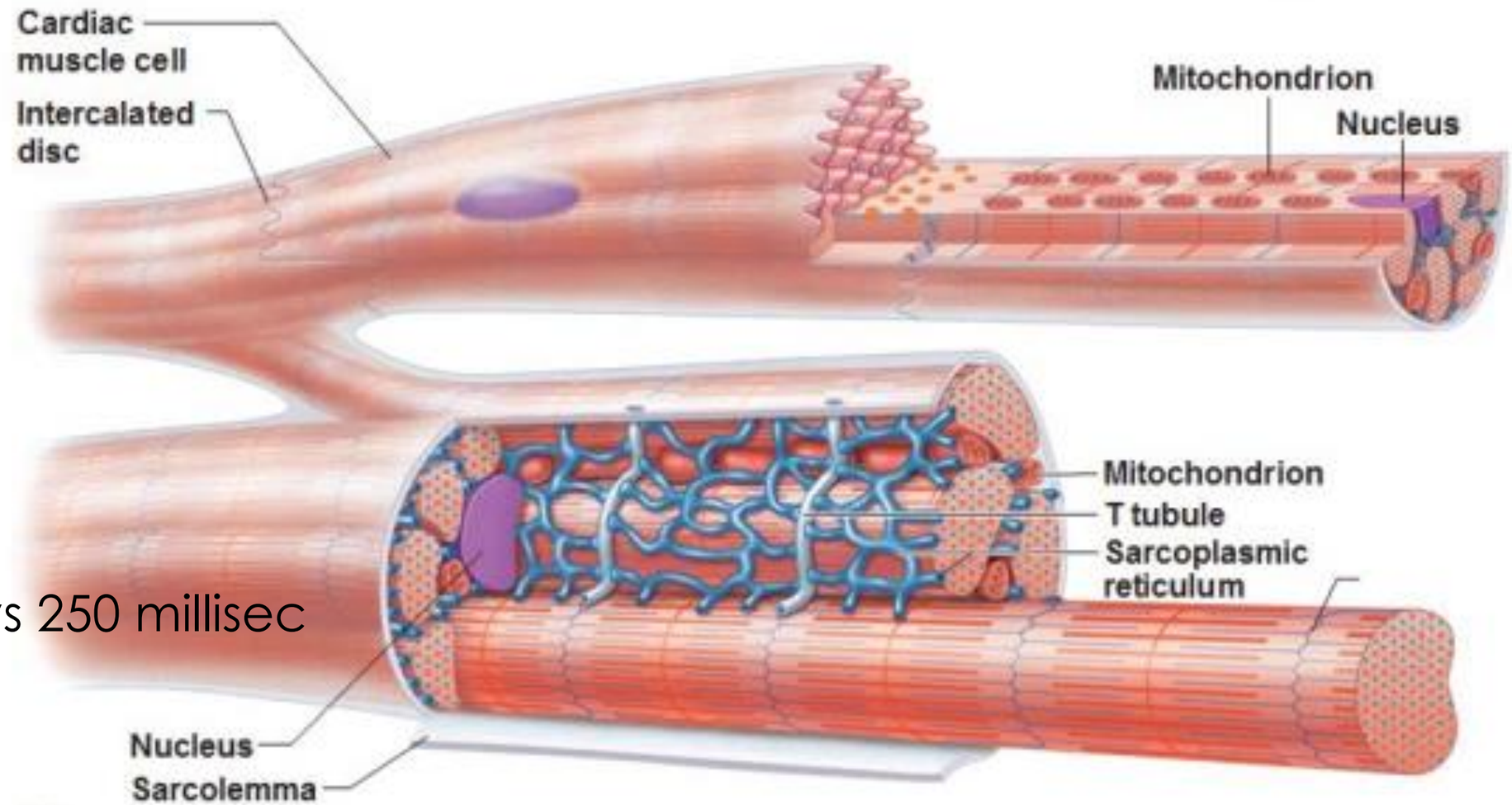
- Hearts more susceptible to ischemic injury
- Impaired ventricles (LVH)
- >70 y, female, renal impairment
- Extracardiac vascular disease (PVD)
- Chronic lung disease, PH, diabetes
- EF < 50%
- NYHA III/IV

Avoid Rapid Ca^{++} Fluxuations
(most cardioplegia solutions contain very low or trace Ca^{++} amounts)

- The sarcoplasmic reticulum of the myocyte acts as a "sponge" by absorbing and releasing Ca^{++} during the appropriate phases of the cardiac cycle.

- Hypercalcemic systolic arrest is known as "stone heart" and is irreversible.

- Pediatric SR is immature and not fully functional, very susceptible to stone heart. (elderly)



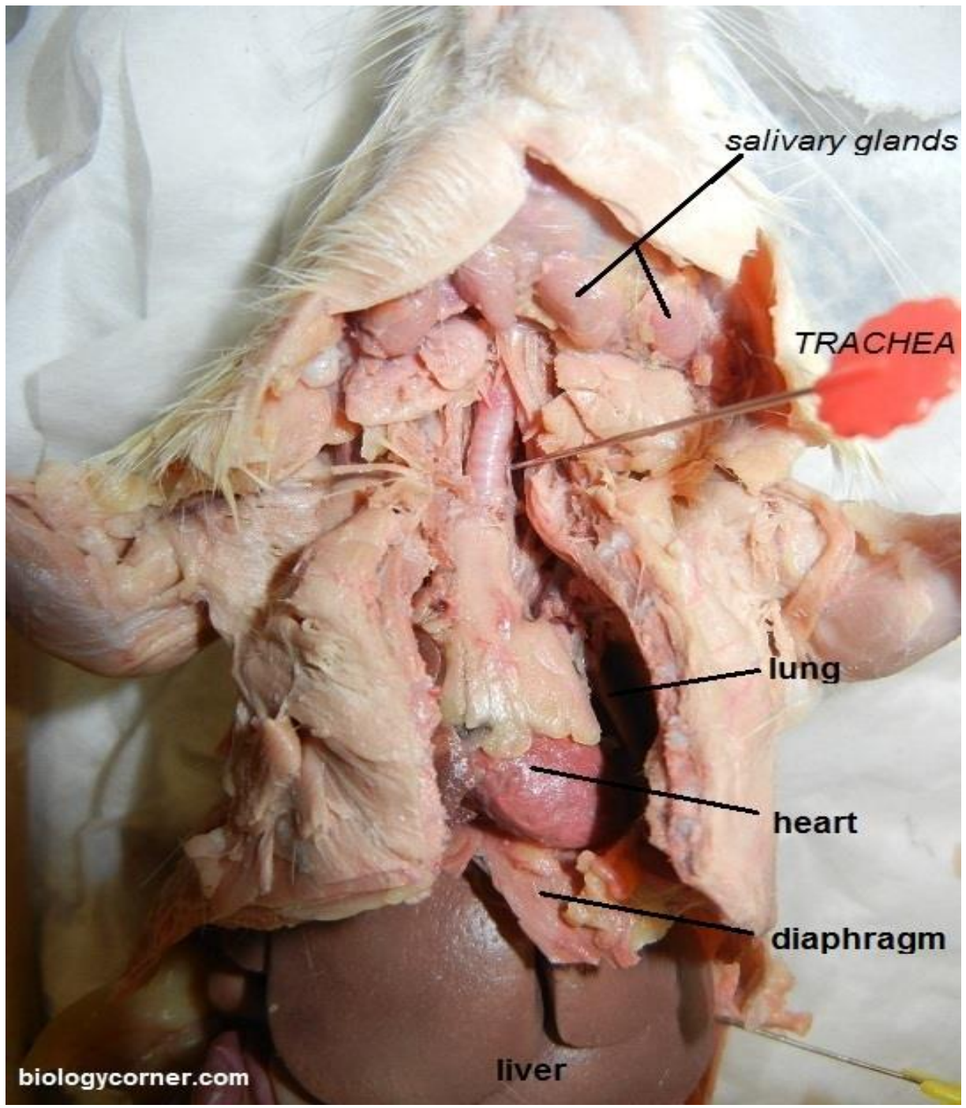
150 millisec vs 250 millisec

The sarcoplasmic reticulum is a specialized type of smooth ER that regulates the calcium ion concentration in the cytoplasm of striated muscle cells.

Protecting the aged heart during cardiac surgery: The potential benefits of del Nido cardioplegia

O'Blenes SB, *Friesen CH, Ali A, Howlett S JTCS 2010*

- Find me an adult publication using del Nido
- Literature search
- Objective: aged hearts
- Methods: isolated cell model of cardioplegic arrest and reperfusion
- Senescent RAT hearts
- =70 yo human heart

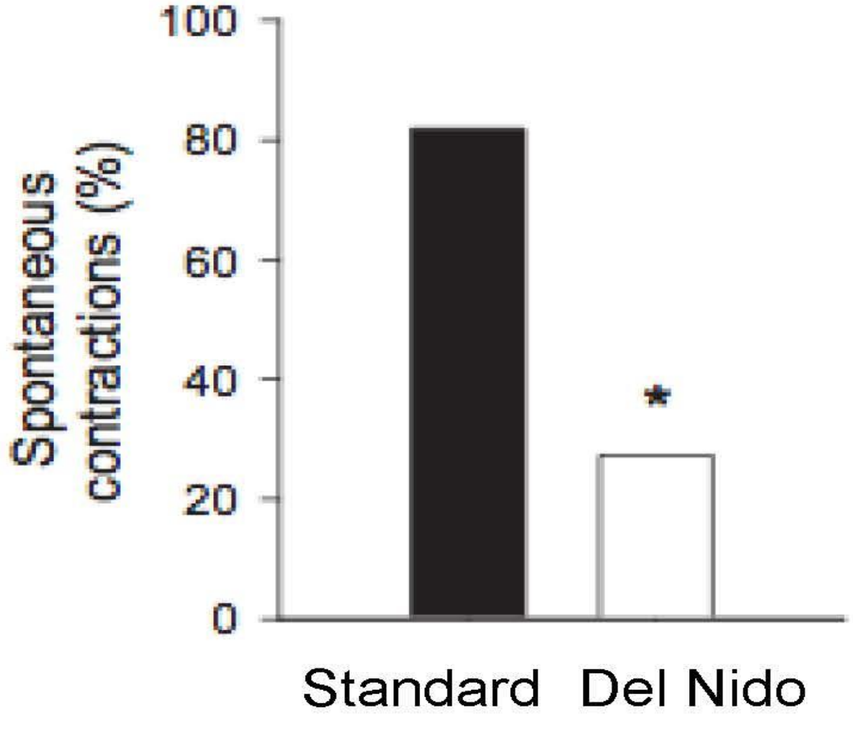


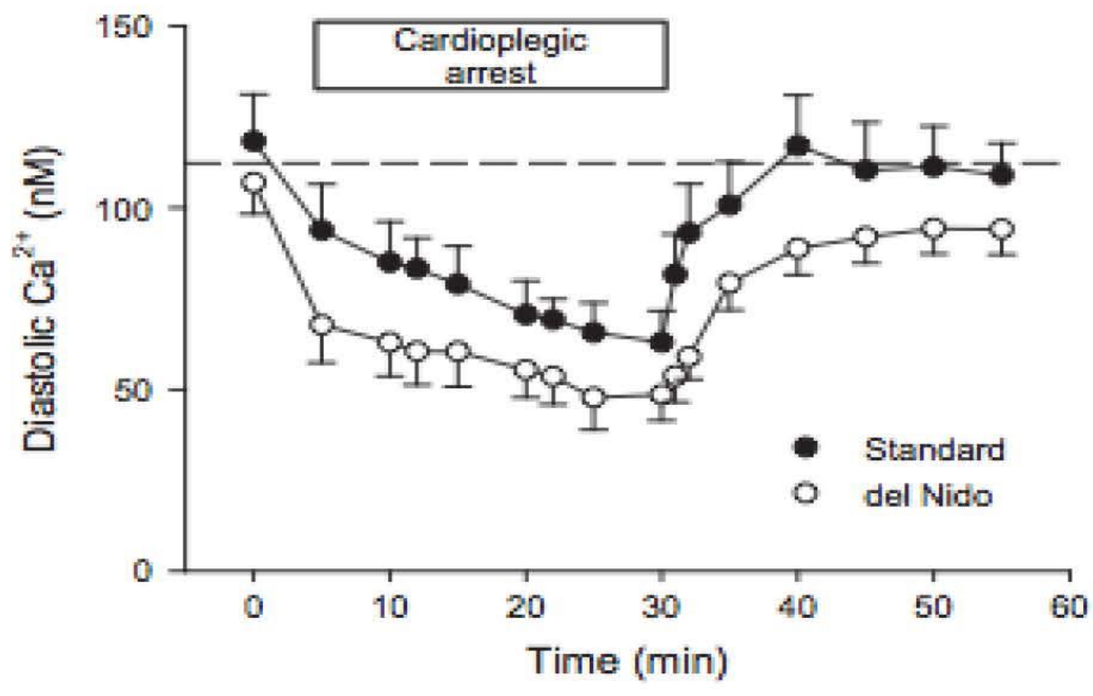
- Elderly hearts are not as well protected by some cardioplegia solutions

- The aged heart is similar to the immature heart
  - more susceptible to ischemia reperfusion injury
  - poorly equipped to handle intracellular calcium overload

- Our hypothesis:
  - A cardioplegia strategy developed for **immature hearts** may also provide superior myocardial protection for **aged hearts**

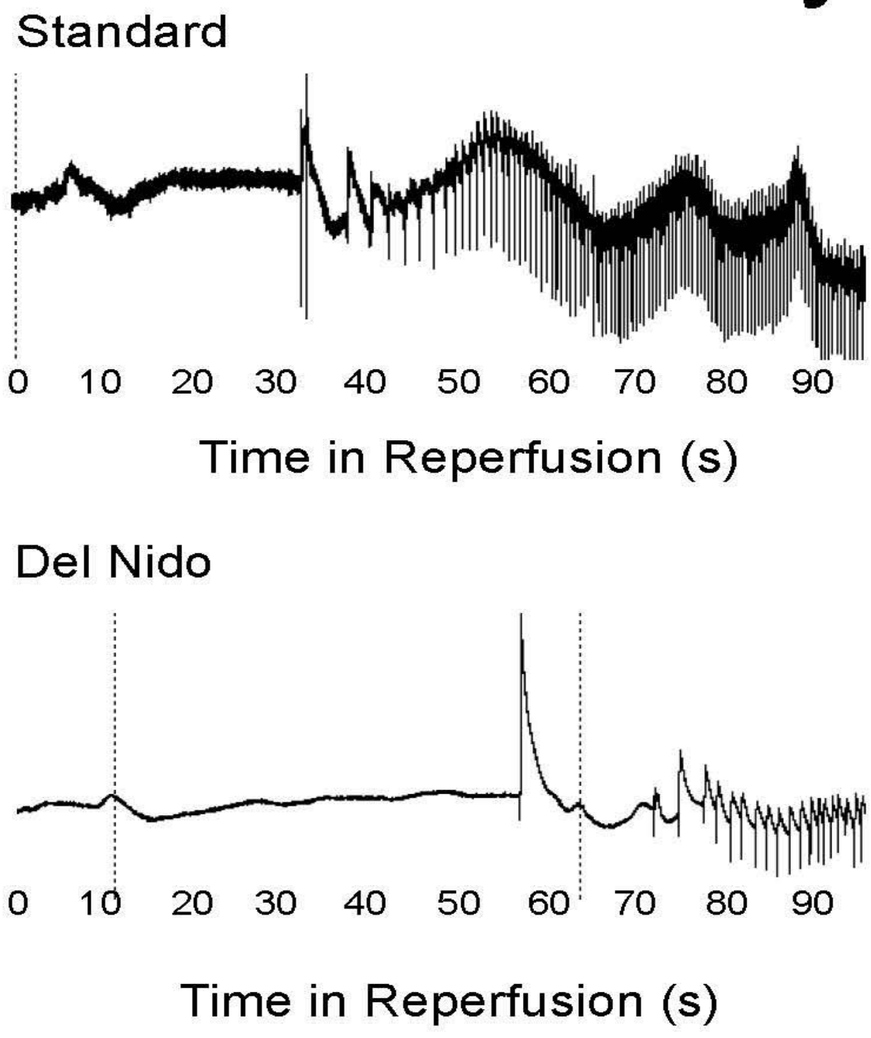
Del Nido cardioplegia is associated with less activity during arrest and lower intracellular Ca^{2+} in aged cardiomyocytes.

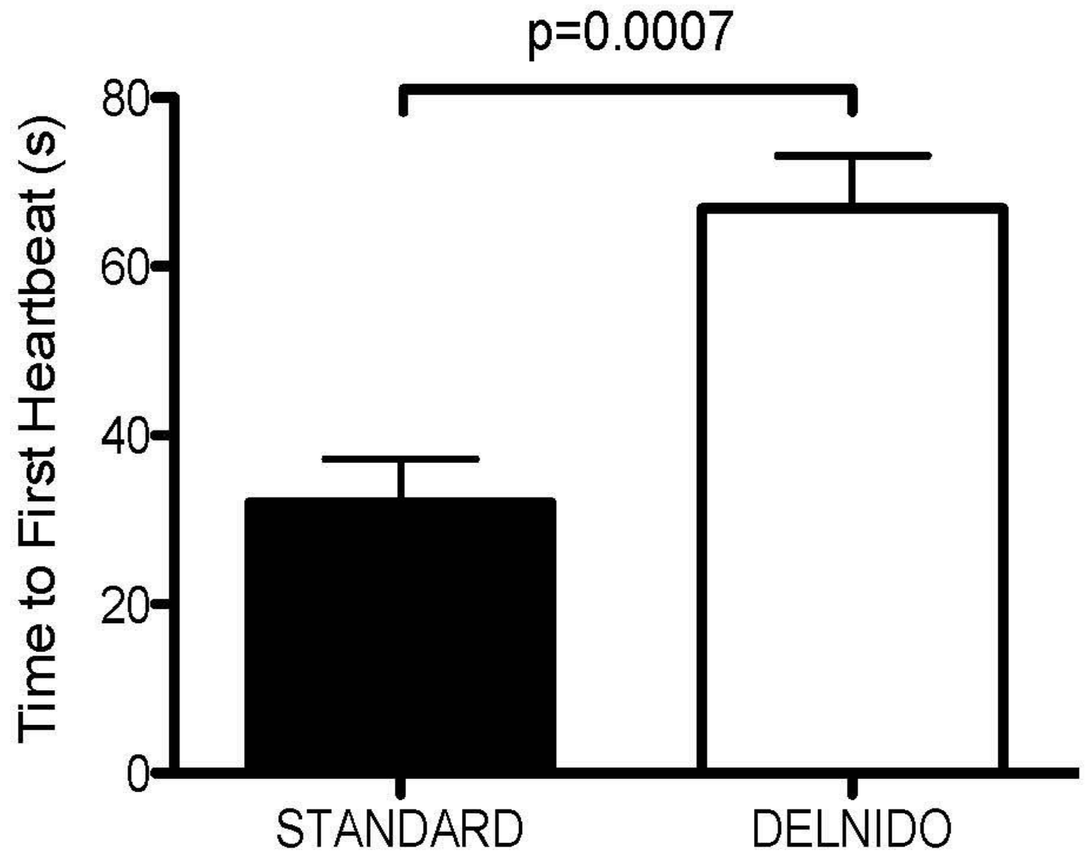




O'Blenes et al., J Thorac Cardiovasc Surg 2011;141:762-70

Return of Rhythm at Reperfusion





Conclusion

- Del Nido cardioplegia prevents spontaneous activity during cardioplegic arrest, reduces myocardial injury, and results in superior myocardial function after reperfusion in aged hearts.
- Del Nido cardioplegia has the potential to provide superior myocardial protection for older patients undergoing cardiac surgery.

del Nido cardioplegia (dN)

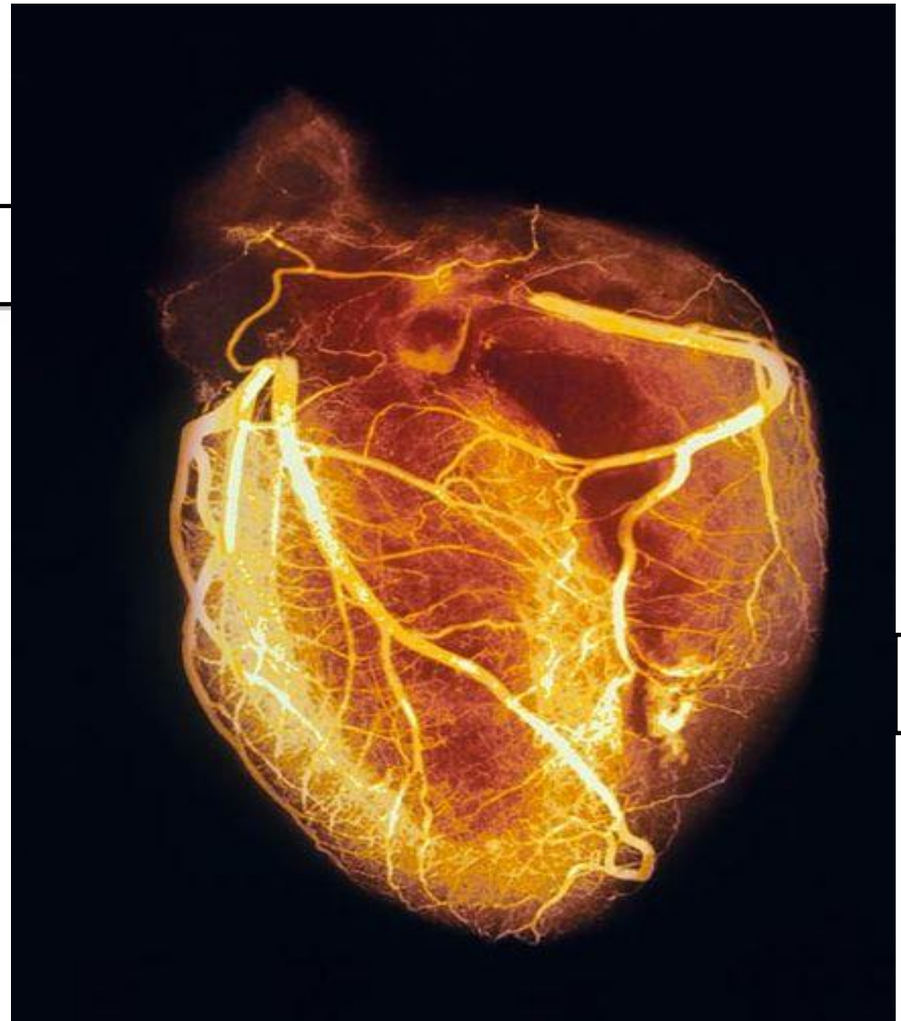
Plasma-Lyte A -1000ml
KCL -26 mEq
Lidocaine 1% -130mg
Mg Sulfate 50% -2g
Mannitol 20% -3.26g

Contains no Glucose

Which Solution is Best?

There are a number of studies which show conflicting results as to which method provides the best protection.

Multi-dose



Single dose

What is the BEST strategy?

Multidose blood

Multidose clear

Adenocaine

Continuous warm

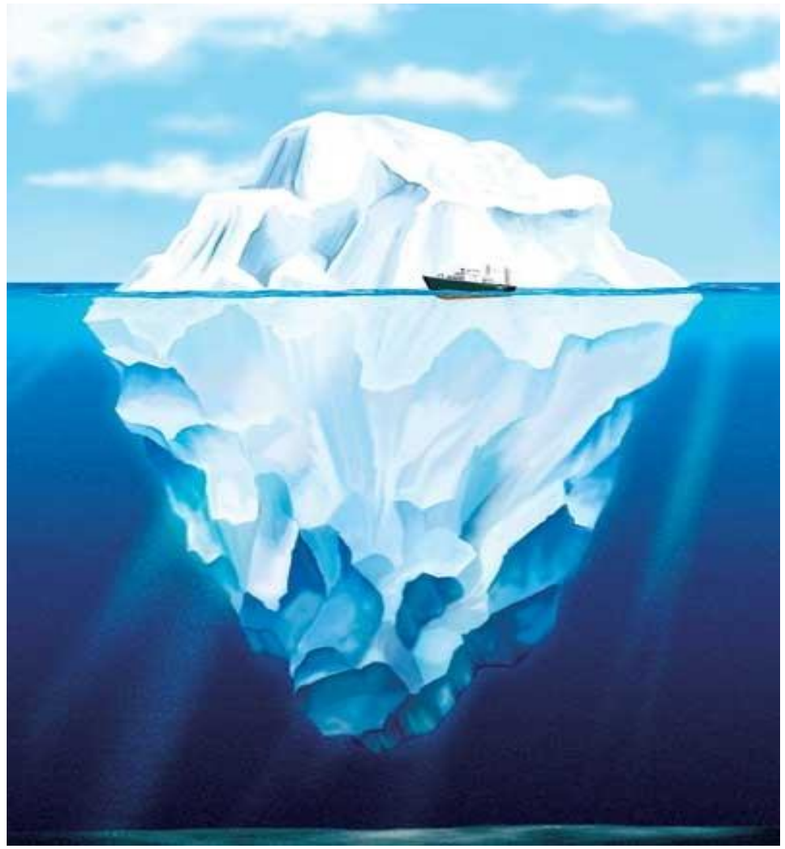
Single dose Bretschneider

Single dose del Nido

Literature ????

Multidose Solutions

- St Thomas
- Adenocaine
- Plegisol
- Buckberg



Need to be replenished every 20-30 minutes.

What if you could just give them once with the same degree of protection?

Single Dose Solutions

- Bretshneider
- del Nido
- Custodial

Only one dose required for up to two hours of cross clamp time.

Hyperpolarizing Good!

SUPERIORITY OF HYPERPOLARIZING TO DEPOLARIZING CARDIOPLEGIA IN PROTECTION OF CORONARY ENDOTHELIAL FUNCTION

Guo-Wei He , MD, PhD, Cheng-Qin Yang , MD, *J Thorac Cardiovasc Surg* 1997;114:643-650

Background:

Depolarizing solutions impair the coronary endothelial function

A clinical comparative study between crystalloid and blood-based St Thomas' hospital cardioplegic solution

Mohamed F. Ibrahim, Graham E. Venn, Christopher P. Young, David J. Chambers*
Cardiac Surgical Research and Cardiothoracic Surgery, The Rayne Institute, St. Thomas' Hospital, London SE1 7EH, UK

Conclusions: In a higher risk (EF <40%) group of patients undergoing elective cardiac surgery, **addition of blood to an established crystalloid cardioplegic solution significantly enhanced myocardial protection**

Blood Not Necessary!

*Is there any difference between **blood and crystalloid** cardioplegia for myocardial protection during cardic surgery? A meta-analysis of **5576 patients from 36 randomized trials.***

Sa, Rueda, Ferraz, et al, Perfusion 27(6) 535-546

Conclusion: We found evidence that argues against any superiority in terms of hard outcomes between blood or crystalloid cardioplegia

Bretschneider Good!

[Single-dose and high-volume Bretschneider cardioplegic solution for congenital heart surgery].

Kyobu Geka. 1999 Jan;52(1):82-6.

Bretschneider cardioplegic solution had preserved the heart the same as blood cardioplegia. This is a very convenient method so that we can use only one time infusion.

Bretschneider Bad!

The effect of cardioplegic solution-induced sodium concentration fluctuation on postoperative seizure in pediatric cardiac patients.

Kim JT, Park YH, Chang YE, Byon HJ, Kim HS, Kim CS, Lim HG, Kim WH, Lee JR, Kim YJ. Ann Thorac Surg. 2011 Jun;91(6):1943-8.

- HTK solution during CPB frequently causes fluctuations of sodium concentration, usually combined with hyponatremia, which is associated with postoperative seizure. Special attention to sodium concentration is required, particularly when HTK solution is used in pediatric cardiac patients

Del Nido Good!

The Effect of Cardioplegic Solution-Induced Sodium Concentration Fluctuation on Postoperative Seizure in Pediatric Cardiac Patients

The Annals of Thoracic Surgery
Volume 91, Issue 6 , Pages 1943-1948, June 2011

Results

•The ΔNa>15 was detected in 63 of 189 patients (33.3%) who received the HTK solution and in 14 of 439 patients (3.2%) who received the del Nido solution ($p < 0.001$). The incidence of ΔNa>15 was strongly associated with postoperative seizure (odds ratio, 6.3; 95% confidence interval, 2.4 to 16.4, $p = 0.001$).

Why use del Nido instead of Custodial?

- Because Custodial Can cause very low intraoperative sodium.
- Introduces a lot of volume to the bypass circuit (30cckg all clear).
- Cost $250 compared to $30.

Pedro del Nido, MD
Boston Childrens' Hospital

- Just got lucky !!!!!
- How long between doses?
- "I will not give another dose until I see activity."
- Why does too frequent dosing cause a "sluggish" heart?
- "It takes the heart a while to metabolize the direct shot of lidocaine."
- Will it work for CABG surgery?
- "My research did not look at this but it should work just as well. Give some retrograde to ensure full coverage and do not be tempted to give too much."

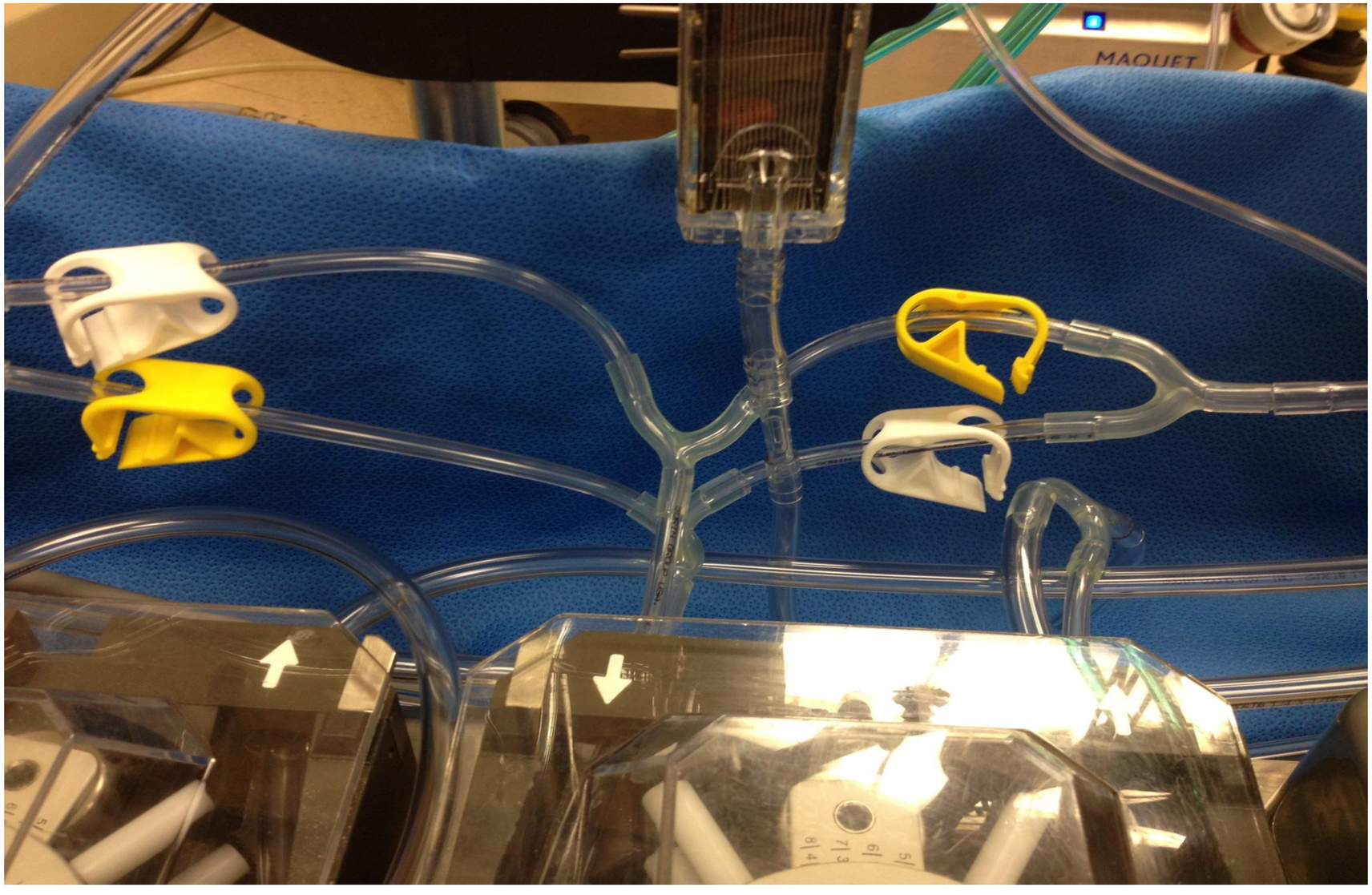
Precaution!

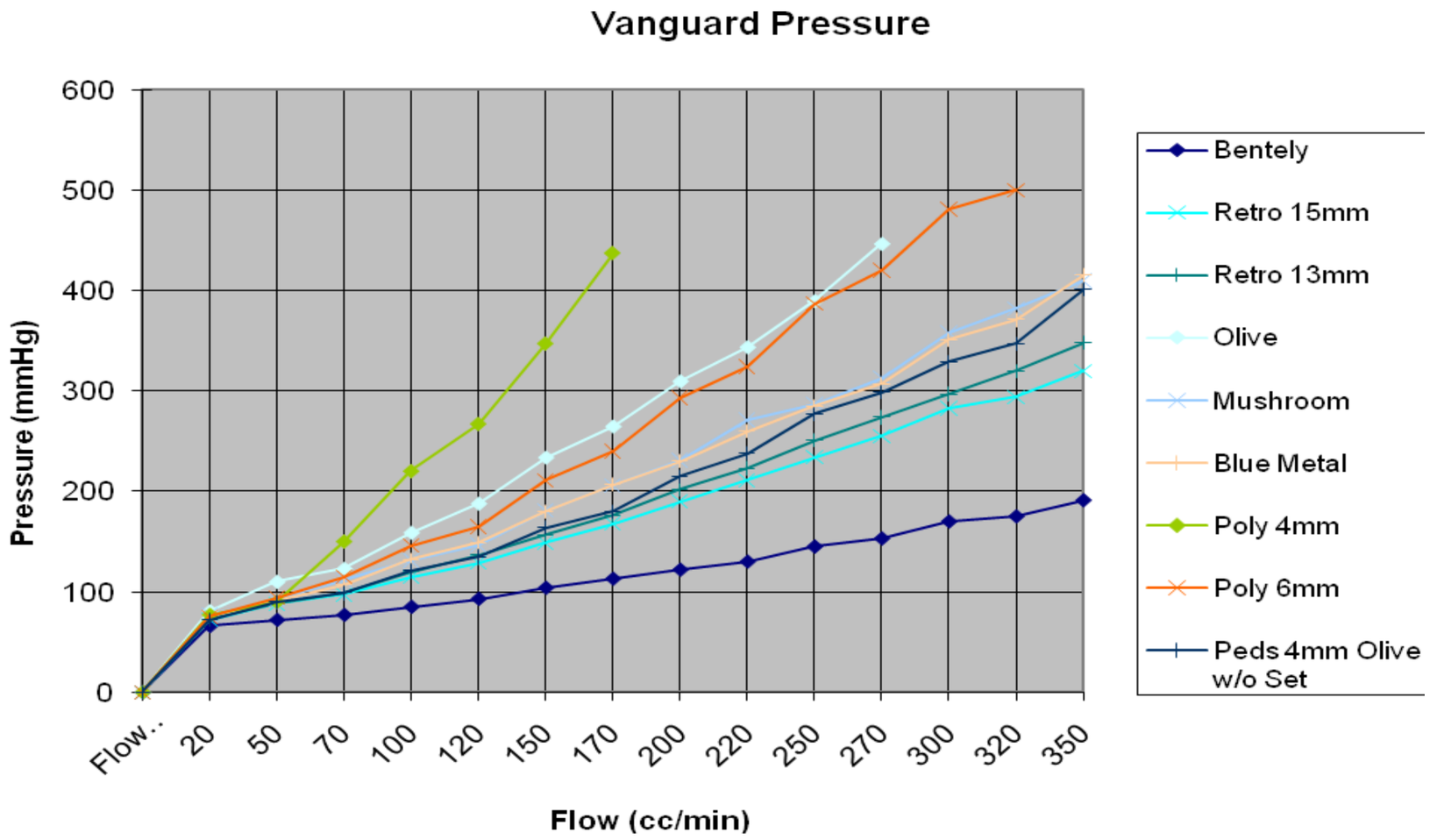
- For short clamp times (such as a secundum ASD repair) only give 10-15ml/kg. (adults)

- Only give 10ml/kg for as a re-dose.
  Otherwise heart will be “sluggish” for a few minutes after clamp removal.

- Attempted defibrillation is usually unnecessary----Just wait!!!!

Delivery of del Nido Cardioplegia custom kit





For DelNido:

Two yellow clamps are in the open position and two white clamps are closed. (Note: Follow lines to make sure 4 parts DelNido and 1 part blood will be delivered. Do not trust color of clamps.)

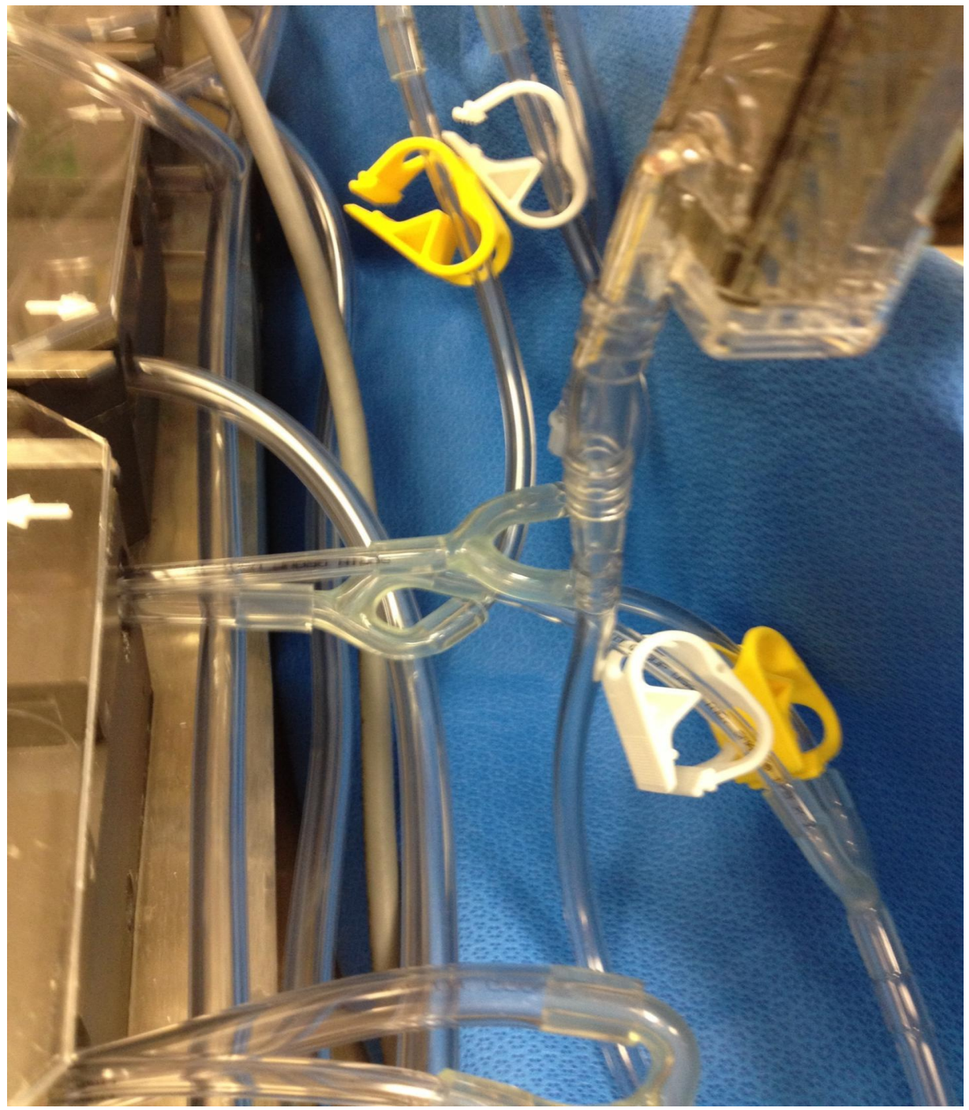
For 4:1 Blood: Cardioplegia

Two white clamps are in the open position and two yellow clamps are closed. (Note: Follow lines to make sure 4 parts blood and 1 part cardioplegia will be delivered. Do not trust the color of clamps.)

Confirm contents of cps bag, High Dose, Low Dose, Continuous or Buckberg.

Continuous Cold delivery

- Contains 5 meq of K+
- Patent mammary artery graft
- Delivered through coronary sinus ~5 ccs/min
- Less than 20 mmHg



del Nido and Adult Hearts

- At NYP used exclusively on over 5000 cases.
- Antegrade single dose technique up to 1L (an extra 500ml is given in cases with a hypertrophied ventricle)
- 90 minute protocol followed unless washout is seen.

STS 2014

Single Dose del Nido Cardioplegia Solution Provides Safe and Efficient Myocardial Protection During Isolated Aortic Valve Replacement in Adult Cardiac Surgery;Propensity Score Matching Study

Ota, Yerebakan, Hwang, Neeley, **Mongero,** et al.

Department of Cardiothoracic Surgery Columbia University, New York, NY

*Compared existing multidose strategy using whole blood cardioplegia delivered with Quest to del Nido single dose.

Matched pairs	P value
CPB time	<0.001
XCLP	0.025
Retrograde	<0.001
Total CP	<0.001
Exogenous	0.021

Conclusions

1. Single dose myocardial protection technique for pediatric congenital heart surgery using del Nido cardioplegia solution is a valuable tool for the cardiac surgeon and provides *at minimum* equivalent protection when compared to more standard cardioplegia solutions.

2. The early evidence suggests that this solution and single dose delivery technique are also effective for protection of the adult myocardium during aortic valve surgery as well. Associated with shortened cross-clamp and may expedite critical portion of surgery by eliminating repeat cardioplegia doses and use of retrograde cannulation. *OTA, et al*

3. DN cardioplegia compared to WB cardioplegia in 88 patients with AMI, provided equivalent protection without negative inotropic or major complications. *George, et al*