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# Routine Post OP care

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# BACKGROUNDS

Failure to Prepare is Preparing to Failure

# BACKGROUNDS

## 6 Alarmings of Post Cardiac Surgury Pts

1. 의식
2. 혈압
3. 소변량
4. 피
5. 리듬
6. 비정상적 통증과 dyspnea

# 의식(Consciousness)

## Altered Mental Status

Defined as impairment of “arousal, cognition, behavior”
환경과 연계된 각성상태의 변화.

1. 의식상태의 변화.
2. Confusion
3. Organic brain syndrome
4. Change in mental status
5. Decreased level of consciousness

*Ulbercht JS et al. Clin Infect Dis. 2004(39);S73-82*

# 의식 (Consciousness)

의식변화에 영향을 주는 인자들 I

- Focal brain lesion E
  - pidural Hematoma S
  - ubdural Hematoma
  - Subarachnoid Hemorrhage (SAH)
  - Intracerebral Hemorrhage (ICH)
  - Stroke
  - Brain stem lesion, Abscess…

# 의식 (Consciousness)

의식변화에 영향을 주는 인자들 2

- Diffuse brain Injury H
  ypoxic brain Injury
  Organ failure
  Medications : sedative drugs, 정신과약물, 기타 진통제등
  Lactic acidosis
  High fever
  Hyperglycemia, Hypoglycemia
  Vitamin deficiency

# 의식 (Consciousness)

의식변화에 영향을 주는 인자들 3

- Psychogenic

Derilium : ICU syndrome, Drug withdrawal

# 의식(Consciousness)

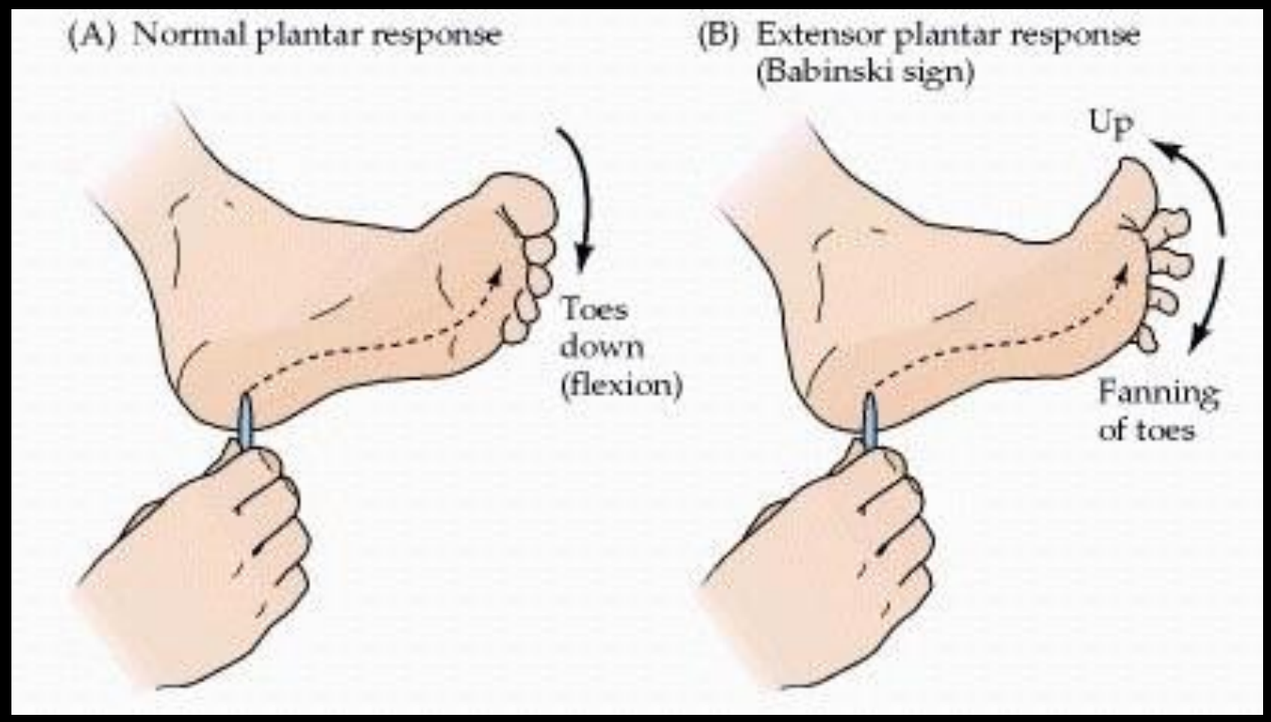
## Hypoxic Brain Damage

주로 수술중 뇌허혈로 인함

의식의 소실

General Seizure P
upil dilation Gene
ral weakness
Extensor plantar response

MRI, 뇌파검사

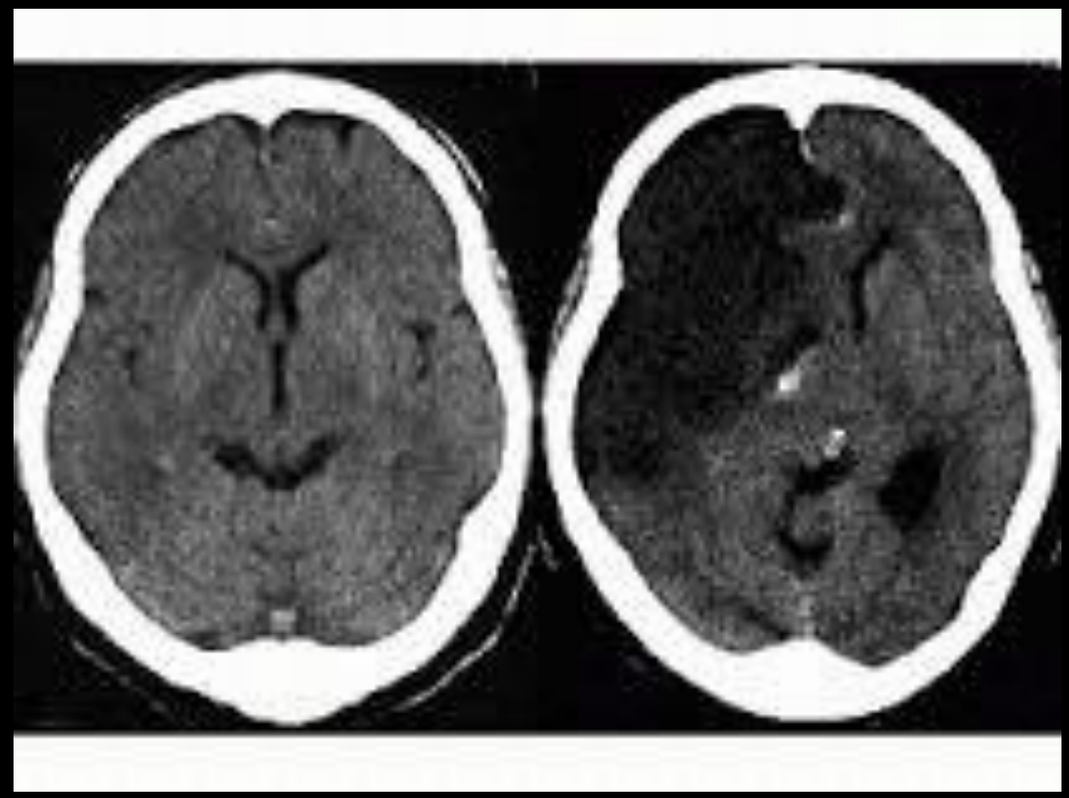


# 의식(Consciousness)

CNS hemorrhage, Stroke

aneuryms rupture
thromboembolism

의식의 소실 Gene
ral Seizure Pupil
dilation General
weakness
Extensor plantar response
+ lateralization



MRI, 뇌파검사, CT
Early intervention

# 의식(Consciousness)

Hypoglycemia, Hyperglycemia

Sudden osmolarity change : brain tissue edema, shrinkage

- Derilium -> Coma like
- General Seizure
- response to glucose injection

# 의식(Consciousness)

## Medication Toxicity

- sedative drugs : Benzodiazepine, opiates
- 기타 항우울제, 페니실린 등

# 의식(Consciousness)

## CNS infection

- 염증반응을 일으켜 toxic encephalopathy를 야기
- 발열, 두통과 같은 전구증상이 관찰됨

# 의식(Consciousness)

Thiamine deficiency

- Confusion, derilium, stupor
- Memory impairment
- anisocoria
- ataxia, nystagmus

# 의식(Consciousness)

Protocol

1. 의식의변화, 운동 및 감각이상을 수시로 check.
2. 이상이 발견되면 즉각 보고 후 신경학적 검사 시행.
3. 영상의학적 검사 : MRI (diffusion), CT
4. Mental change Lab check :
   ABGA, Glucose, ammonia, electrochemistry

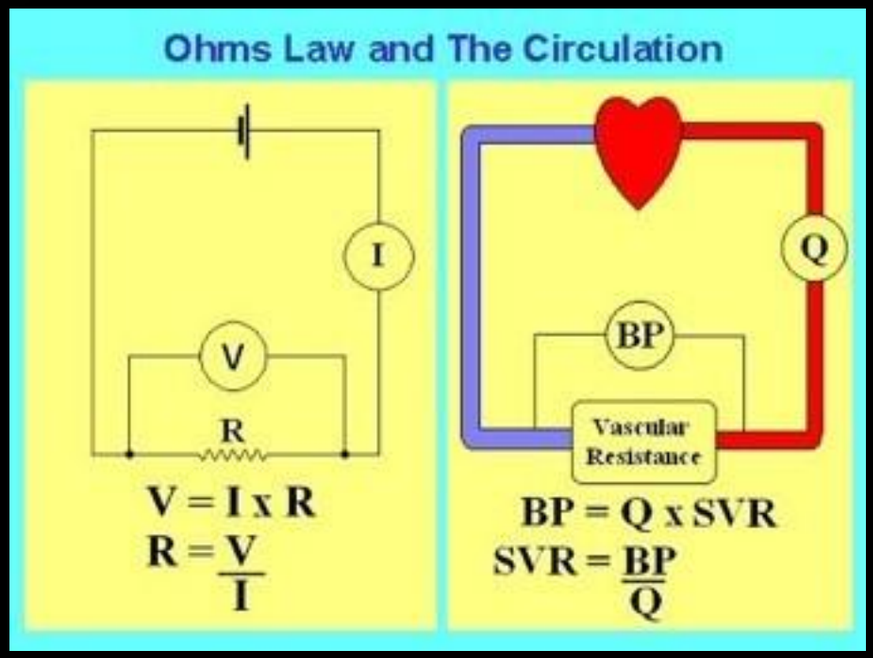
# 혈압(Blood pressure)

혈압의 결정인자

- Ohm의 법칙에 의해 혈류량과 혈관저항이 혈압을 결정한다.

- 정원호스의 물을 더 멀리 보내기 위해서는 물을 더 세게 틀거나 호스의 끝을 눌러 저항을 올리면된다.

- 즉, 적절한 혈압을 유지하기 위해서는 충분한 혈류와 충분한 혈관저항이 필요하다.




# 혈압(Blood pressure)

혈압이 떨어질때 고려사항

1. 혈류량(volume status)은 충분한가?
   심장수축력이 떨어진 것은 아닌가 : Echocardiography !
   Effective Circulatory Volume은 충분한가 :
      CVP, PCWP, continuous cardiac output monitoring
   출혈여부 : Chest tube drainage, Internal bleeding?

2. 혈관저항은 적절한가?
   수술직후에는 혈관저항이 떨어져 있는 경우가 대부분이다.
      - post op SIRS state (shock state)
   과도한 sedation
   vasodilator
   마약성 진통제
   fever
   지속적인 저체온증

# 혈압(Blood pressure)

주의할 점

심장수축력이 떨어진 환자에서 혈관저항을 올리는 vasopressin이나 norepinephrine을 과도하게 사용하면, 혈압은 올라가지만 심박출량이 감소하여 오히려 조직의 malperfusion을 야기할 수 있다.

이로인하여 말단부의 괴사가 일어나는데 손가락, 발가락, 귀 뿐만 아니라 endartery가 들어가는 콩팥의 괴사가 일어난다.

따라서 환자에게서 이러한 합병증이 일어나지 않는 범위에서 적정 혈압을 유지하는것이 중요하다.

# 소변 (Urine Output)

"소변이 줄었어요" 의 의미

## Pre-Renal Azotemia

심장의 수축력 저하
순환혈액량 감소
심박출량감소 신동
맥수축
저혈압

## Intrincic-Renal Azotemia

Acute Tubular Necrosis
수술, 마취, 약물

## Post-Renal Azotemia

도뇨관이 막힌경우

교정하지 못하면 P
ulmonary Edema
Uremia

# 소변 (Urine Output)

AKI

- Acute Kidney Injury (AKI) : 0.5ml/kg/hour for 6hrs.
  if <0.3ml/kg/hour for 6hrs, 사망율 및 투석율 증가.

-Pre-renal azotemia인지 Intrincic-renal azotemia인지 감별하는 것이 중요!

이를 위하여 FeNa를 구하여 지표로 사용하지만 이뇨제를 빈번하게 사용하는 일반적인 임상 환경에서는 정확하지 않을때가 많다.

- 이뇨제에 반응하는 AKI가 반응하지 않는 AKI보다 위험하다.

*Ralib, Azrina Md, et al. "The urine output definition of acute kidney injury is too liberal." Crit Care 17.3) (2013): R112.*

*Han, Seung Seok, et al. "Additional role of urine output criterion in defining acute kidney injury." Nephrology Dialysis Transplantation 27.1 (2012): 161-165.*

# 소변 (Urine Output)

Fractional Excretion of Na+ (FeNa+)

FENa(%) = (100 × Na urine × Cr plasma)/(Na plasma × Cr urine)

예>

(100 × 20mEq × 2.0) /  (130mEq × 70) = 0.43%

(100 × 80mEq × 2.0) /  (130mEq × 10) = 12.3%

(100 × 70mEq × 2.0) /  (130mEq × 50) = 2.15% : ???

# 소변 (Urine Output)

## Low Dose Dopamine과 소변량

- 저용량의 Dopamine이 일시적인 소변량의 증가를 가져올 수는 있지만 이 약을 사용한다고해서 신손상이나 사망율을 줄이지는 못한다.

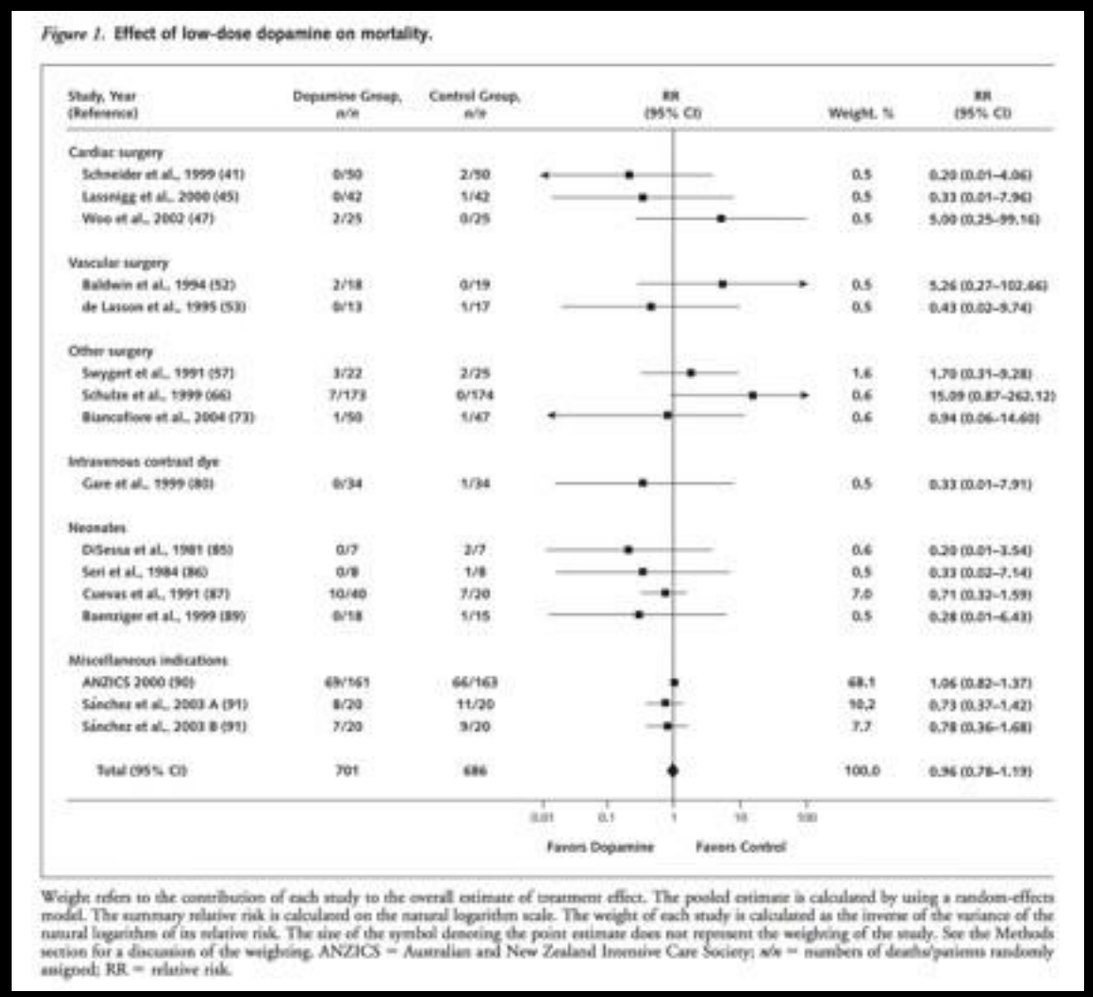


*Figure 1.* Effect of low-dose dopamine on mortality.

| Study, Year (Reference) | Dopamine Group, n/n | Control Group, n/n | RR (95% CI) | Weight, % | RR (95% CI) |
|---|---|---|---|---|---|
| Cardiac surgery | | | | | |
| Schneider et al., 1999 (41) | 0/50 | 2/50 | | 0.5 | 0.20 (0.01–4.06) |
| Lassnigg et al., 2000 (45) | 0/42 | 1/42 | | 0.5 | 0.33 (0.01–7.96) |
| Woo et al., 2002 (47) | 2/25 | 0/25 | | 0.5 | 5.00 (0.25–99.16) |
| Vascular surgery | | | | | |
| Baldwin et al., 1994 (52) | 2/18 | 0/19 | | 0.5 | 5.26 (0.27–102.66) |
| de Lasson et al., 1995 (53) | 0/13 | 1/17 | | 0.5 | 0.43 (0.02–9.74) |
| Other surgery | | | | | |
| Swygert et al., 1991 (57) | 3/22 | 2/25 | | 1.6 | 1.70 (0.31–9.28) |
| Schulze et al., 1999 (66) | 7/173 | 0/174 | | 0.6 | 15.09 (0.87–262.12) |
| Biancofiore et al., 2004 (73) | 1/50 | 1/47 | | 0.6 | 0.94 (0.06–14.60) |
| Intravenous contrast dye | | | | | |
| Gare et al., 1999 (80) | 0/34 | 1/34 | | 0.5 | 0.33 (0.01–7.91) |
| Neonates | | | | | |
| DiSessa et al., 1981 (85) | 0/7 | 2/7 | | 0.6 | 0.20 (0.01–3.54) |
| Seri et al., 1984 (86) | 0/8 | 1/8 | | 0.5 | 0.33 (0.02–7.14) |
| Cuevas et al., 1991 (87) | 10/40 | 7/20 | | 7.0 | 0.71 (0.32–1.59) |
| Baenziger et al., 1999 (89) | 0/18 | 1/15 | | 0.5 | 0.28 (0.01–6.43) |
| Miscellaneous indications | | | | | |
| ANZICS 2000 (90) | 69/161 | 66/163 | | 68.1 | 1.06 (0.82–1.37) |
| Sánchez et al., 2003 A (91) | 8/20 | 11/20 | | 10.2 | 0.73 (0.37–1.42) |
| Sánchez et al., 2003 B (91) | 7/20 | 9/20 | | 7.7 | 0.78 (0.36–1.68) |
| Total (95% CI) | 701 | 686 | | 100.0 | 0.96 (0.78–1.19) |

0.01 0.1 1 10 100

Favors Dopamine Favors Control

Weight refers to the contribution of each study to the overall estimate of treatment effect. The pooled estimate is calculated by using a random-effects model. The summary relative risk is calculated on the natural logarithm scale. The weight of each study is calculated as the inverse of the variance of the natural logarithm of its relative risk. The size of the symbol denoting the point estimate does not represent the weighting of the study. See the Methods section for a discussion of the weighting. ANZICS = Australian and New Zealand Intensive Care Society; n/n = numbers of deaths/patients randomly assigned; RR = relative risk.

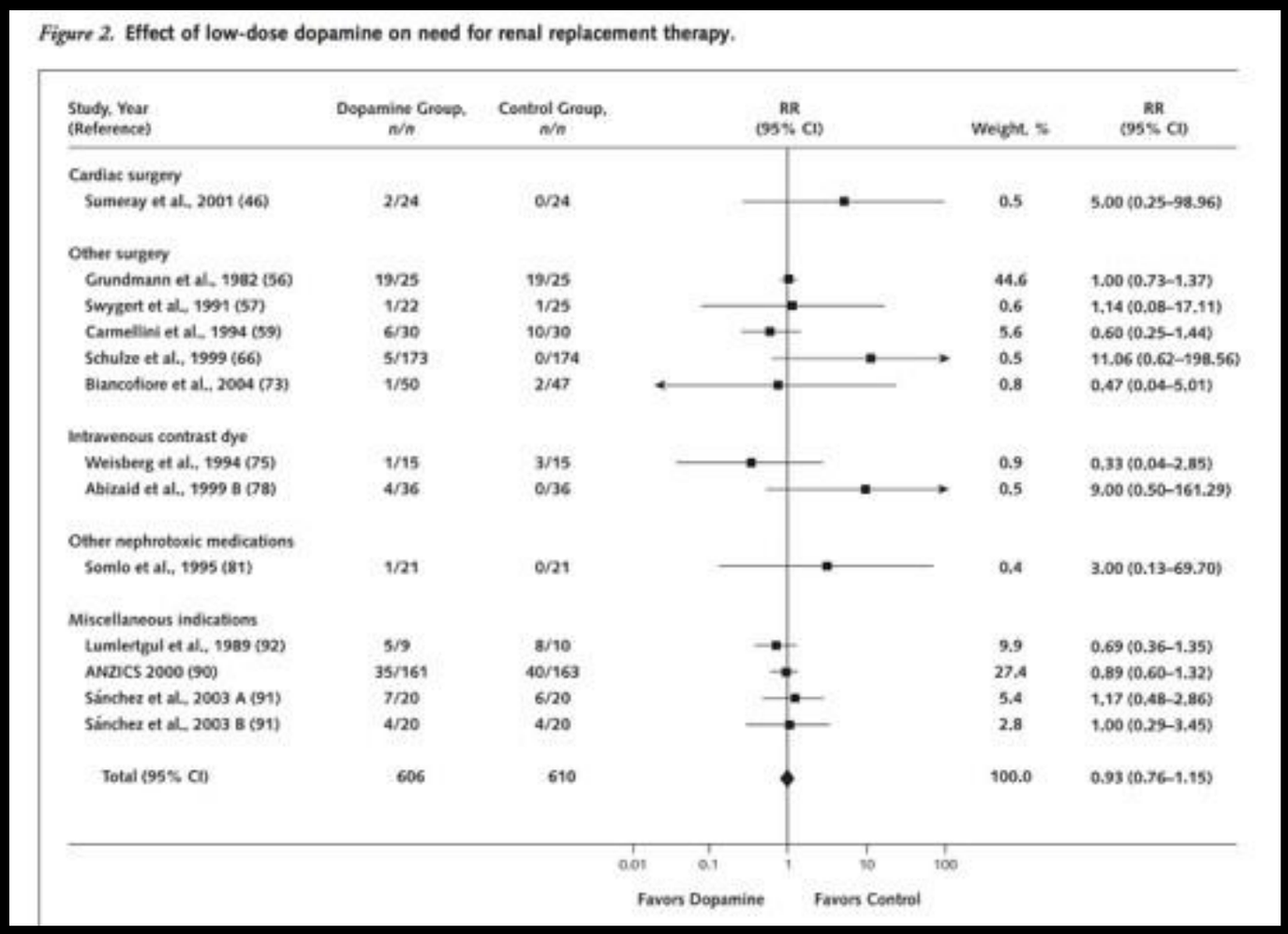


*Figure 2.* Effect of low-dose dopamine on need for renal replacement therapy.

| Study, Year (Reference) | Dopamine Group, n/n | Control Group, n/n | RR (95% CI) | Weight, % | RR (95% CI) |
|---|---|---|---|---|---|
| Cardiac surgery | | | | | |
| Sumeray et al., 2001 (46) | 2/24 | 0/24 | | 0.5 | 5.00 (0.25–98.96) |
| Other surgery | | | | | |
| Grundmann et al., 1982 (56) | 19/25 | 19/25 | | 44.6 | 1.00 (0.73–1.37) |
| Swygert et al., 1991 (57) | 1/22 | 1/25 | | 0.6 | 1.14 (0.08–17.11) |
| Carmellini et al., 1994 (59) | 6/30 | 10/30 | | 5.6 | 0.60 (0.25–1.44) |
| Schulze et al., 1999 (66) | 5/173 | 0/174 | | 0.5 | 11.06 (0.62–198.56) |
| Biancofiore et al., 2004 (73) | 1/50 | 2/47 | | 0.8 | 0.47 (0.04–5.01) |
| Intravenous contrast dye | | | | | |
| Weisberg et al., 1994 (75) | 1/15 | 3/15 | | 0.9 | 0.33 (0.04–2.85) |
| Abizaid et al., 1999 B (78) | 4/36 | 0/36 | | 0.5 | 9.00 (0.50–161.29) |
| Other nephrotoxic medications | | | | | |
| Somlo et al., 1995 (81) | 1/21 | 0/21 | | 0.4 | 3.00 (0.13–69.70) |
| Miscellaneous indications | | | | | |
| Lumlertgul et al., 1989 (92) | 5/9 | 8/10 | | 9.9 | 0.69 (0.36–1.35) |
| ANZICS 2000 (90) | 35/161 | 40/163 | | 27.4 | 0.89 (0.60–1.32) |
| Sánchez et al., 2003 A (91) | 7/20 | 6/20 | | 5.4 | 1.17 (0.48–2.86) |
| Sánchez et al., 2003 B (91) | 4/20 | 4/20 | | 2.8 | 1.00 (0.29–3.45) |
| Total (95% CI) | 606 | 610 | | 100.0 | 0.93 (0.76–1.15) |

0.01 0.1 1 10 100

Favors Dopamine Favors Control

*Friedrich, Jan O., et al. "Meta-analysis: low-dose dopamine increases urine output but does not prevent renal dysfunction or death." Annals of Internal Medicine 142.7 (2005): 510-524.*

# 出血(Beeding)

Post OP Bleeding

- >2cc/kg/hr or >100cc/kg/hr in Adults

- Pre OP anticoagulation and antithrombotic medication
- Coagulopathy state (Hepatic failure, Renal failure)
- Extensive Surgery (Long CPB time, Aorta surgery, Redo surgery)
- **Surgical Bleeding !**

# 피(Beeding)

Post OP Bleeding

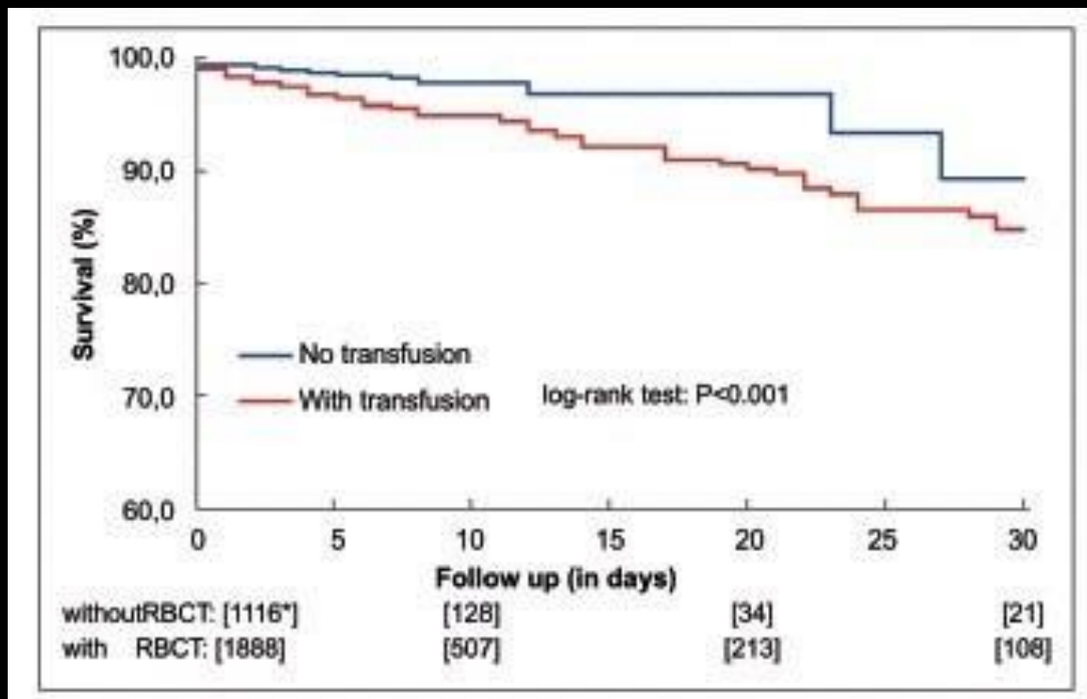
Indications for Re-exploration

1. 1시간동안 500cc이상
2. 300cc/hr로 3시간 이상
3. Tamponade의 sign이나 transfusion에도 불구하고 혈역학적으로 불안정.

# 피(Beeding)

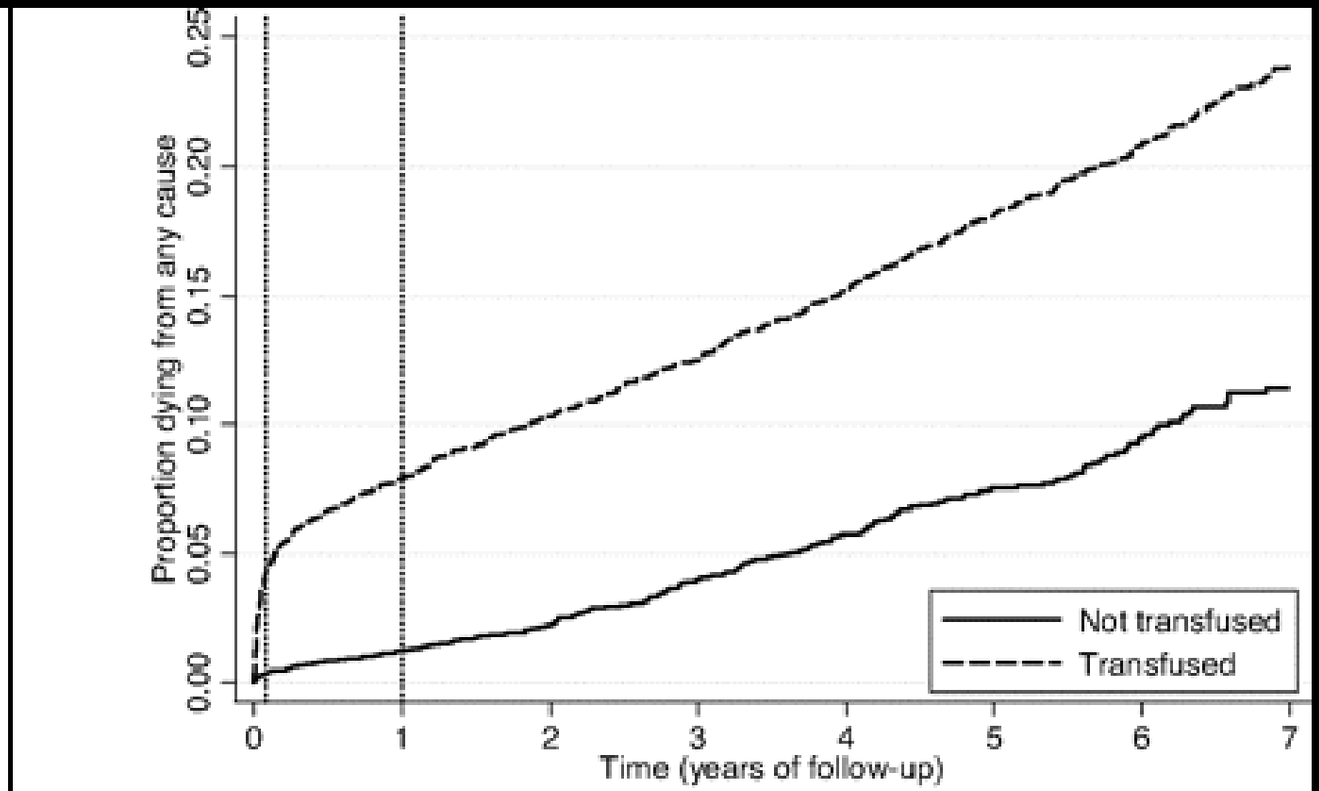
Post O P Bleeding

- 심장 수술 후 Bleeding과 연관된 수혈량이 많아질수록 초기 및 만기 합병증과 사망율이 높아진다.




[*] Number of patients at risk at the time of evaluation; RBCT – red blood cell transfusion.

*Fig. 1 – Kaplan-Meier survival curve in the study of death at 30 days (y-axis starts at 60%)*




*Circulation 2007; 116 (22): 2544-2552*

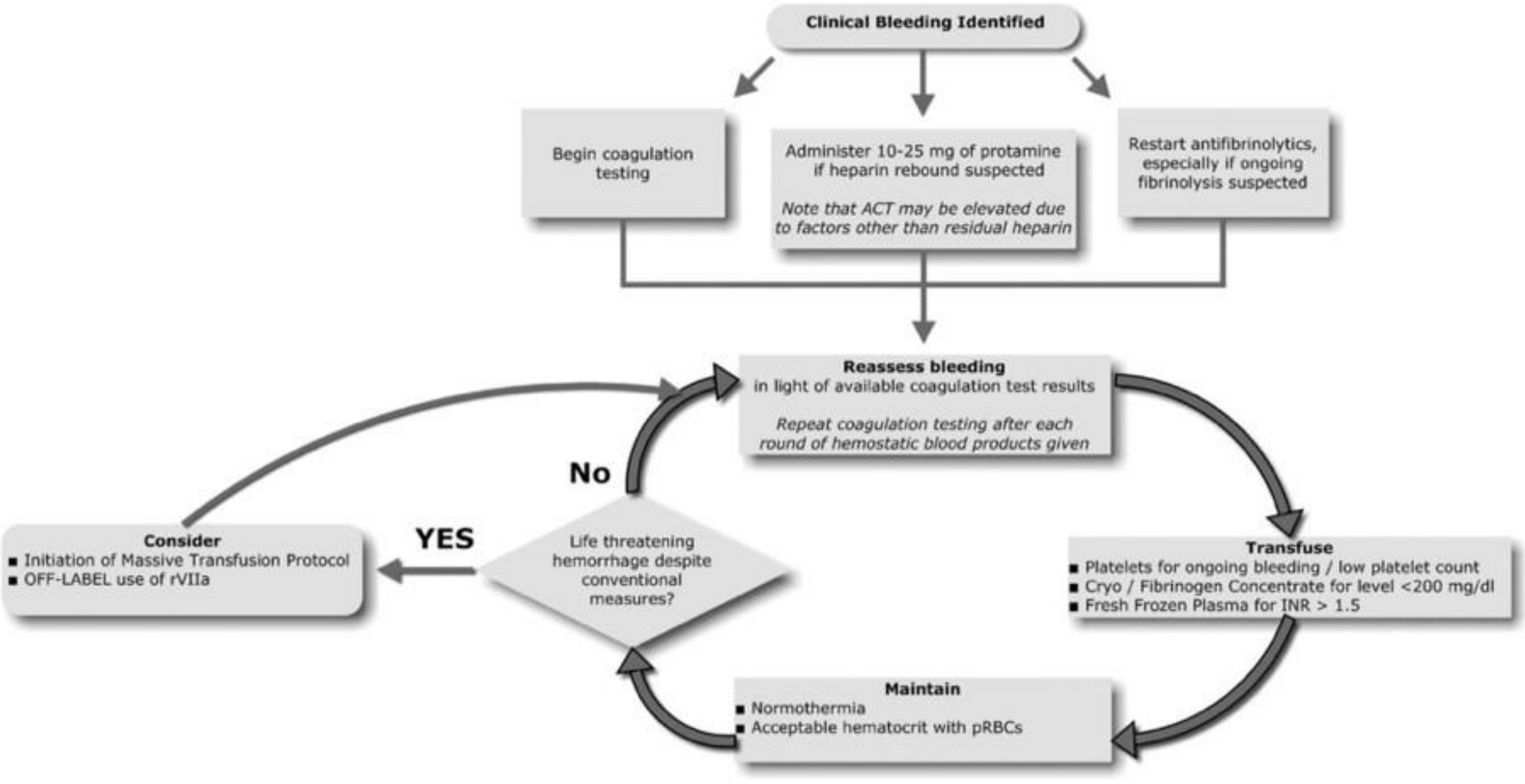
# 피(Beeding)

수혈관 관련된 부작용들

- 수혈과 관련된 각종 전염성 질환들 (AIDS, Hepatitis....)
- 수술후 감염의 위험성을 증가
- 수술후 사망의 위험성을 증가 (0.1% vs. 8.7%)
- Immunomodulation effect
  수혈에 기인한 lung injury, nosocomial infection 증가.
- Hypothermia, lactic acidosis, Hemolysis

# 피(Beeding)

## 대처




*Roman M. et al. JTCS 2011;142(3):662–667.*

# 出血(Beeding)

Check points

1. CBC
2. ACT, aPTT, PT/INR
3. Fibrinogen level
4. D-dimer, FDP
5. Thromboelastography (TEG) : 전체 응고기전에 대해 설명

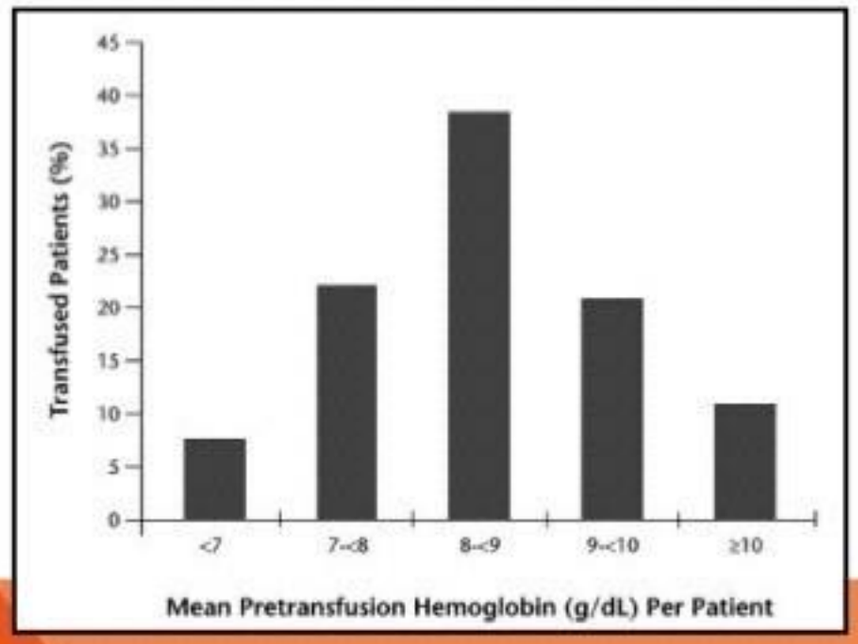
무엇보다 surgical bleeding은 아닌지, 환자의 현재 상태는 어떤지 (혈압, 맥박, 사지창백 등) 관찰하는 것이 중요.

# 出血(Beeding)

## Guidelines for transfusion

### GUIDELINES FOR TRANSFUSION IN CRITICALLY ILL PATIENTS

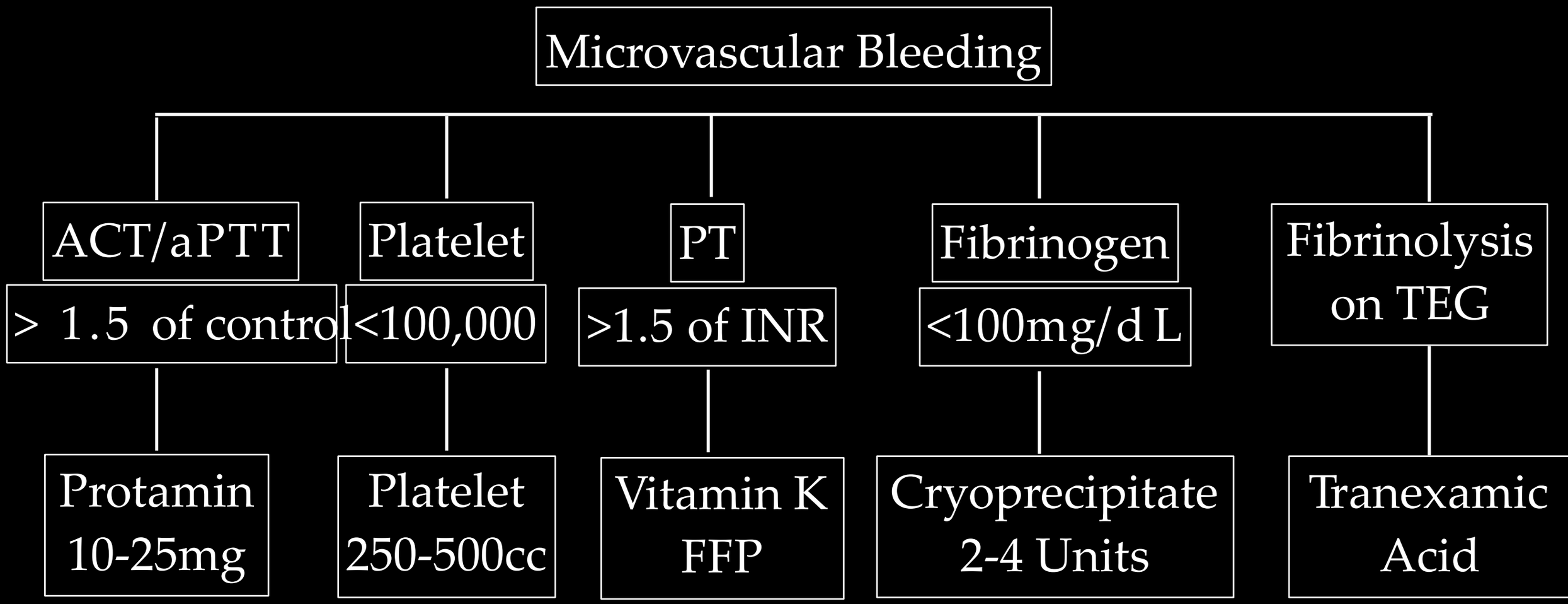
**Mean pre-transfusion hemoglobins:**




Corwin HL, et al: The CRIT Study: Anemia and blood transfusion in the critically ill. Current clinical practice in the United States. *Crit Care Med* 2004; 32:39-52.

# 出血(Beeding)

Guidelines for transfusion



# 피(Beeding)

Guidelines for transfusion

| | 수혈 기준점 Hb level | |
|---|---|---|
| 현재 active bleeding이 있을 때 | 9.0 | |
| 출혈경향이 있으면서 unstable vital sign일 때 | 9.0 | |
| Acidosis가 있고 SVO2가 < 55% | 9.0 | |
| 출혈경향이 있으나 vital sign이 stable할 때 | 7-8 | |
| 출혈경향이 없고 vital sing이 stable 할 때 | 7 | |

*Sidelbotham et al. 2007. Cardiothoracic Critical Care, Philadelphia*

# 리듬(Rhythm)

Post OP rhythm change

# 리듬(Rhythm)

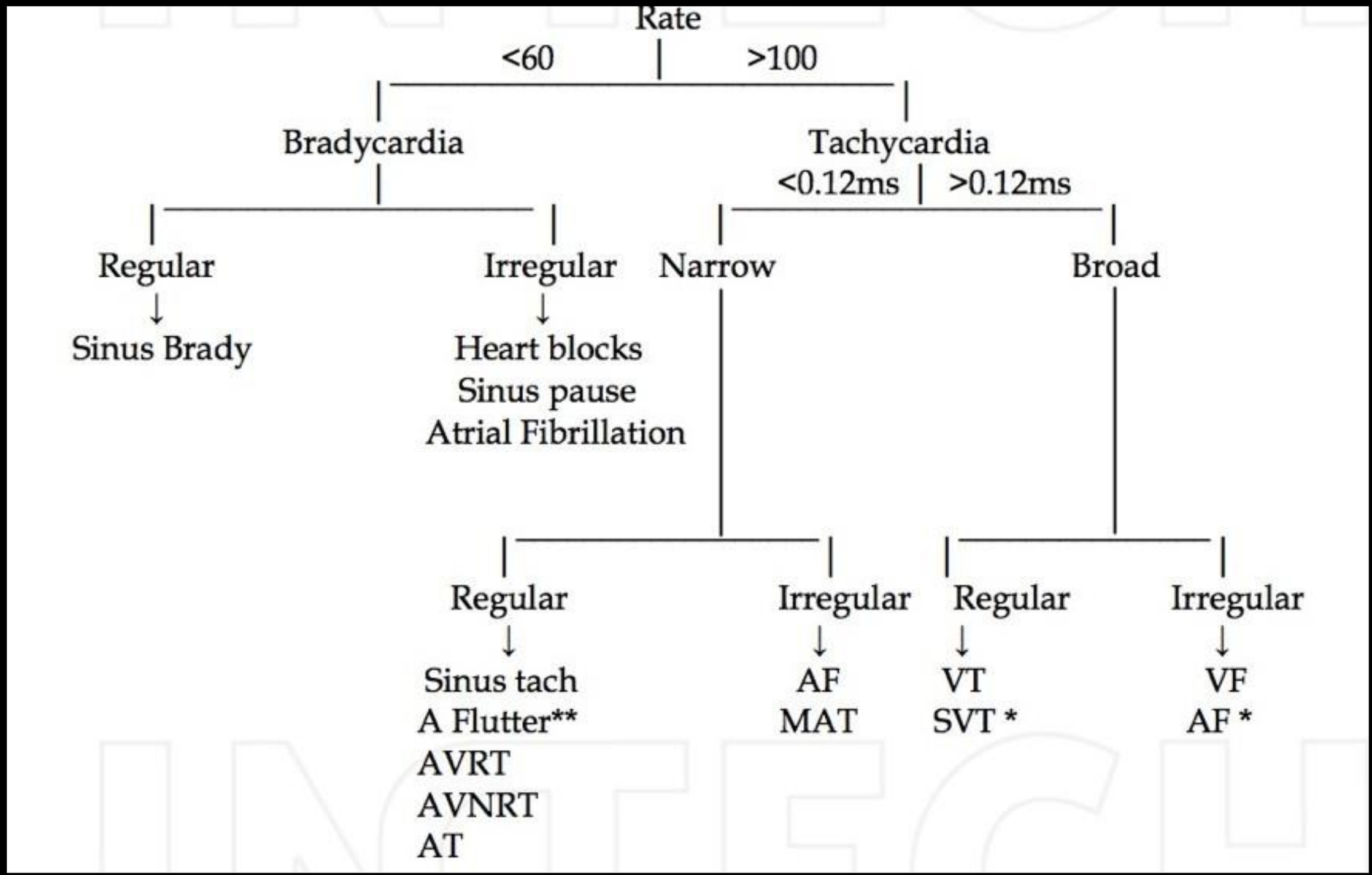
Post OP rhythm change

-유발 및 위험인자.

1. Post OP cardiac dysfunction
2. Scar and Suture site
3. Electrolyte disturbance, ischemic injury, medications
4. Stress response
5. Catecholamine stimulation
6. Pain and Anxiety
7. Inflamatory process
8. Age : decade별로 1.5배씩 A fib 발생율이 증가함.
9. Structural Heart Disease : atrial enlargement

# 리듬(Rhythm)

evaluation using ECG



# 리듬(Rhythm)

## Post OP A fib.

- 심장수술 후 가장 흔한 부정맥은 A fib이며 원인을 교정하면 대부분 좋아진다. 다만, A fib이 있는 경우 cardiac output이 약 30%가량 감소하기 때문에 심부전이 있는 환자에서 주의해야 한다. 또한 A fib with rapid ventricular response의 경우 심실이완기를 줄이고 심장의 산소요구량을 늘여 심한 심박출량의 감소를 가져오기 때문에 매우 위험할 수 있다.

- 또한 A fib의 경우 atrial kicking이 없어져 이완기장애(diastolic dysfunction)가 있는 환자에서 dramatic한 pulmonary congestion을 야기할 수 있다.

- 고위험 환자군에서 post op A fib은 입원기간 내 stroke의 위험성을 증가시킬 수 있다.

- 치료는 antithrombotic + antiarrythmic (rate control or rhythme control)
  DC cardioversion의 적응증은 증상이 있는 A fib 환자.

# 리듬(Rhythm)

## Post O P A fib protocol

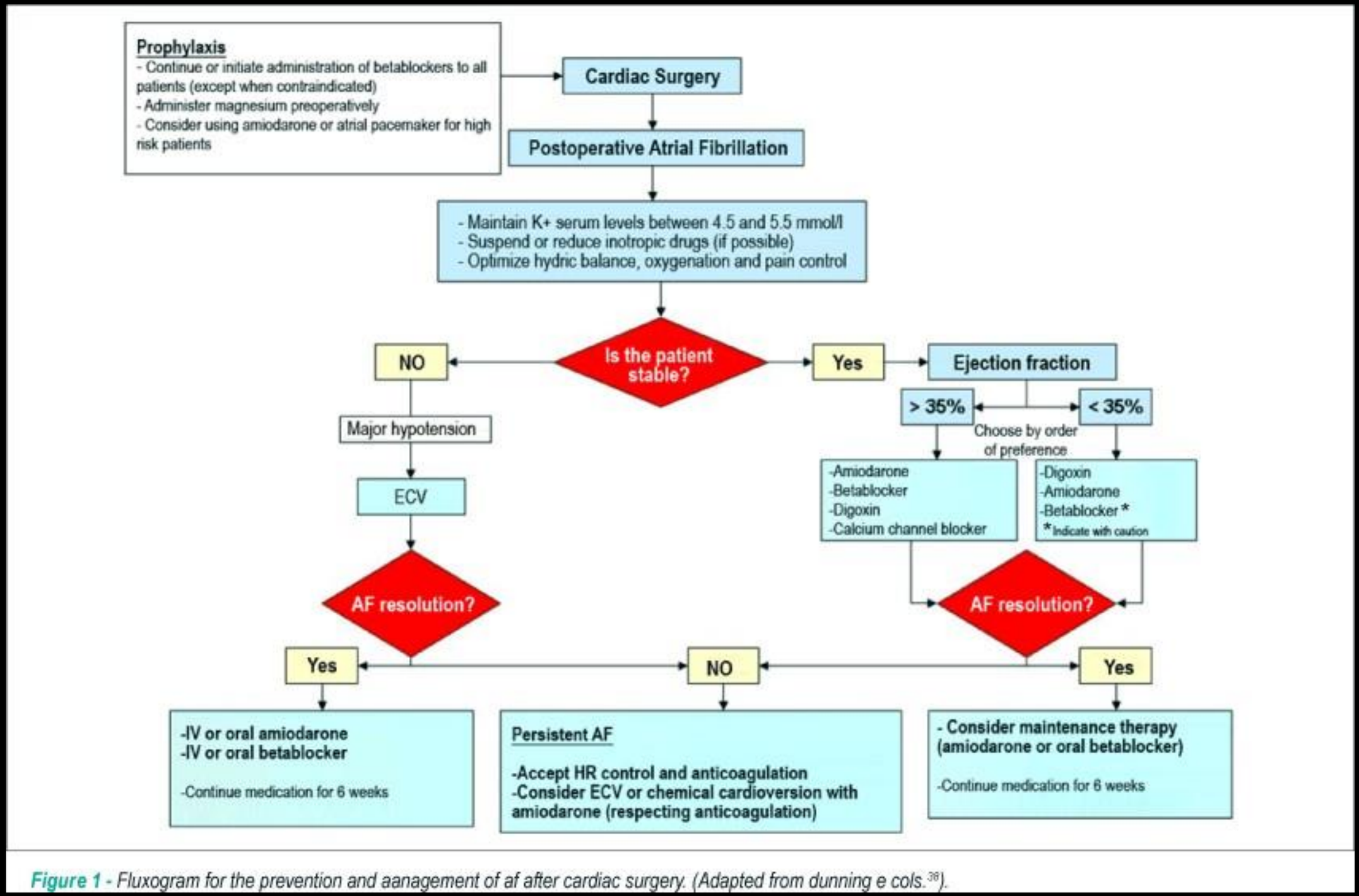
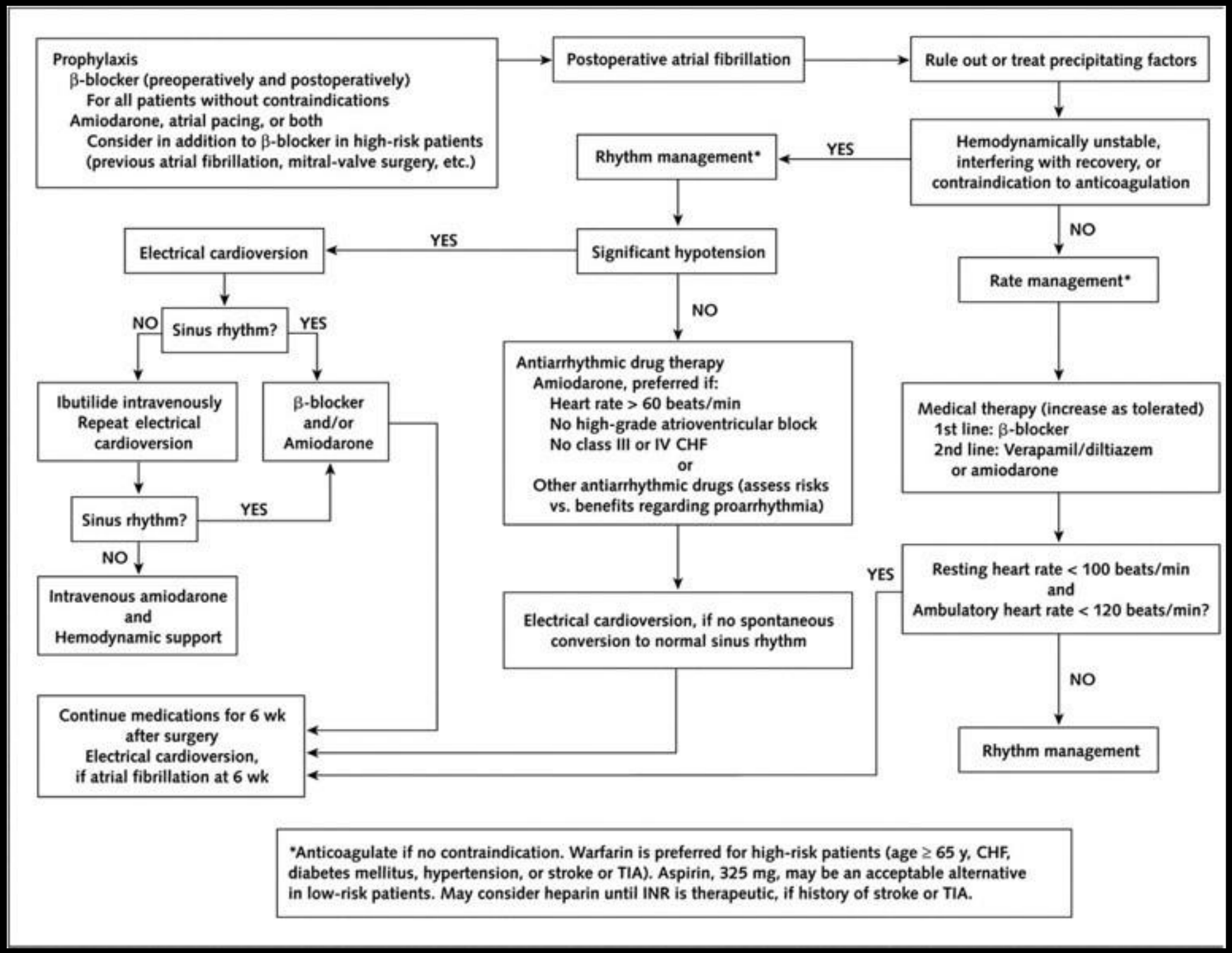



*Figure 1 - Fluxogram for the prevention and aanagement of af after cardiac surgery. (Adapted from dunning e cols.[38]).*

# 리듬(Rhythm)


Prophylaxis
β-blocker (preoperatively and postoperatively)
For all patients without contraindications
Amiodarone, atrial pacing, or both
Consider in addition to β-blocker in high-risk patients (previous atrial fibrillation, mitral-valve surgery, etc.)
Postoperative atrial fibrillation
Rule out or treat precipitating factors
Hemodynamically unstable, interfering with recovery, or contraindication to anticoagulation
YES
Rhythm management*
NO
Rate management*
Significant hypotension
YES
Electrical cardioversion
NO
Sinus rhythm?
YES
Ibutilide intravenously
Repeat electrical cardioversion
β-blocker and/or Amiodarone
Sinus rhythm?
YES
NO
Intravenous amiodarone and Hemodynamic support
NO
Antiarrhythmic drug therapy
Amiodarone, preferred if:
Heart rate > 60 beats/min
No high-grade atrioventricular block
No class III or IV CHF
or
Other antiarrhythmic drugs (assess risks vs. benefits regarding proarrhythmia)
Electrical cardioversion, if no spontaneous conversion to normal sinus rhythm
Medical therapy (increase as tolerated)
1st line: β-blocker
2nd line: Verapamil/diltiazem or amiodarone
YES
Resting heart rate < 100 beats/min and Ambulatory heart rate < 120 beats/min?
NO
Rhythm management
Continue medications for 6 wk after surgery
Electrical cardioversion, if atrial fibrillation at 6 wk
*Anticoagulate if no contraindication. Warfarin is preferred for high-risk patients (age ≥ 65 y, CHF, diabetes mellitus, hypertension, or stroke or TIA). Aspirin, 325 mg, may be an acceptable alternative in low-risk patients. May consider heparin until INR is therapeutic, if history of stroke or TIA.

# 리듬(Rhythm)

Post OP VPC

- non complicated VPC는 술 후 결과에 영향을 미치지 않는다. 따라서 경과관찰만으로 충분하다.

- 시간당 30회 이상으로 발생하는 VPC는 술 후 사망율이 증가한다는 보고가 있으나 단정적이지는 않다.

- Lidocain, class I antiarrhythmic drug, overdirve pacing, ICD등 지금까지 어떠한 치료도 mortality를 감소시킨다는 확실한 근거는 없 다.

# 리듬(Rhythm)

## Post O P VT

- non-sustained VT는 술 후 결과에 특별한 악영향을 미치지 않는다.
유발가능한 원인을 교정하는것이 중요하다.

- Sustained VT의 경우 술 후 원내사망율이 40%에 이르고, 퇴원환자에서도 술 후 2개월 이내 약 50%가 재발하는 것으로 알려져있다.

- 즉각적인 cardioversion이 필요.
  약물, DC cardioversion, ECMO, ICD.

# 리듬(Rhythm)

Post OP Sinus arrest, AVblock

- 판막 수술 이나 MAZE 수술, 특히 대동맥 판막수술이나 감염성 심내막염 수술후에는 AV block이 발생하는지 살펴야 한다.

- MAZE 수술 후에는 A fib뿐만 아니라 sinus arrest, AV block등 다양한 형태의 부정맥이 발생가능하므로 temporal pacemaker를 항상 준비한다.

# 비정상적 통증

수술 후 비정상적 통증

- 수술부위 이외의 부위에 통증이 있는경우 alarming 하고 있어야 한다. 특히, 허혈성 통증인지 늘 주의깊게 살핀다.

- 복부통 : 급성 장간막 혈전증, 장괴사, 상부 혹은 하부위장관 출혈
- 배부통 : 급성 하행대동맥 박리증, 콩팥괴사
- 두통 : subdural hematoma
- 호흡곤란을 동반한 가슴통증 : 폐동맥 색전증, mediastinitis

# Conclusion

## Failure to Prepare is Preparing to Failure

1. 의식
2. 혈압
3. 소변량
4. 피
5. 리듬
6. 비정상적 통증과 호흡곤란

# Acid-base analysis

양산부산대학교병원 흉부외과
김형태

# Basic concepts

- Hydrogen ion concentration and pH
- pH = log (1/[H+]) = - log [H+]
- The normal pH of plasma is indicated as 7.40, which corresponds to a [H+] of 40 nEq/L
- Features of the pH

**Table 31.1 pH and Hydrogen Ion Concentration**

| pH | [H+] (nEq/L) | pH | [H+] (nEq/L) |
|---|---|---|---|
| 6.9 | 1.26 | 7.4 | 40 |
| 7.0 | 100 | 7.5 | 32 |
| 7.1 | 80 | 7.6 | 25 |
| 7.2 | 64 | 7.7 | 20 |
| 7.3 | 50 | 7.8 | 16 |

# Basic concepts

- Features of the pH
- 3 unfortunate features of the pH
- It is a dimensionless number, which has no relevance in chemical or physiological events
- It varies in the opposite direction to change in [H+]
- Changes in pH are not linearly related to changes in [H+] -> as the pH decreases, the changes in [H+] become gradually larger with each change in pH

# Basic concepts

- Hydrogen ion concentration and pH
- Hydrogen ions as a trace element
- [H+] is expressed as nanoequivalents per liter (nEq/L), 1 nEq = 1*10^-6 mEq
- Hydrogen ions are about a million times less dence than the principal ions in extracellular fluid (sodium and choride), whose concentration is expressed in mEq/L
- This gives hydrogen ions the status of a trace element

# Basic concepts

- Classification of acid-base disorders
- The [H+] in extracellular fluid is determined by the balance between the partial pressure of carbon dioxide (PCO2) and the concentration of bicarbonate (HCO3) in the fluid
- [H+] = 24 * (PCO2/HCO3)

**Table 31.2 Primary Acid-Base Disorders and Secondary Responses**

| | $\Delta[H^+] = \Delta PCO_2/\Delta HCO_3$ | |
|---|---|---|
| **Primary Disorder** | **Primary Change** | **Secondary Response†** |
| Respiratory Acidosis | $\uparrow PCO_2$ | $\uparrow HCO_3$ |
| Respiratory Alkalosis | $\downarrow PCO_2$ | $\downarrow HCO_3$ |
| Metabolic Acidosis | $\downarrow HCO_3$ | $\downarrow PCO_2$ |
| Metabolic Alkalosis | $\uparrow HCO_3$ | $\uparrow PCO_2$ |

†Secondary responses are always in the same direction as the primary change.

# Basic concepts

- Classification of acid-base disorders
- Primary acid-base disorders
- A change in either the $PCO_2$ or the $HCO_3$ will cause a change in the [H+] of extracellular fluid

# Basic concepts

- Classification of acid-base disorders
- Secondary responses
- Secondary responses are designed to limit the change in [H+] produced by the primary acid-base disorder
- This is accomplished by changing the other component of the PaCO2/HCO3 ratio in the same direction
- Secondary responses should not be called “compensatory responses” because they do not completely correct the change in [H+] produced by the primary acid-base disorder

# Basic concepts

- Responses to metabolic acid-base disorders
- The response to a metabolic acid-base disorder involves a chage in minute ventilation that is mediated by peripheral chemoreceptors located in the carotid body at the carotid bifurcation in the neck

# Basic concepts

- Responses to metabolic acid-base disorders
- Metabolic acidosis
- The secondary response to metabolic acidosis is an increase in minute ventilation (tidal volume and respiratory rate) and a subsequent decrease in $PaCO_2$
- This response appears in 30-120 minutes, and can take 12 to 24 hours to complete
- $\Delta PaCO_2 = 1.2 * \Delta HCO_3$
- A normal $PaCO_2$ of 40 mmHg and a normal $HCO_3$ of 24 mEq/L
- 40 - Expected $PaCO_2 = 1.2 * (24 – \text{current } HCO_3)$
- Expected $PaCO_2 = 40 – 1.2 * (24 – \text{current } HCO_3)$
- Example: $HCO_3$ = 14 mEq/L
- Expected $PaCO_2 = 40 – 1.2 * (24 – 14) = 40 – 12 * 10 = 28$ mmHg
- if the $PaCO_2$ is >28 mmHg, there is a secondary respiratory acidosis
- If the $PaCO_2$ is <28 mmHg, there is a secondary respiratory alkalosis

# Basic concepts

- Responses to metabolic acid-base disorders
- Metabolic alkalosis
- The secondary response to metabolic alkalosis is a decrease in minute ventilation and a subsequent increase in $PaCO_2$
- This response is not as vigorous as the response to metabolic acidosis (easier to stimulate than inhibit)
- $\Delta PaCO_2 = 0.7 * \Delta HCO_3$
- Expected $PaCO_2 - 40 = 0.7 * (\text{current } HCO_3 - 24)$
- Expected $PaCO_2 = 40 + 0.7 * (\text{current } HCO_3 - 24)$
- Example: a plasma $HCO_3 = 40$ mmEq/L
- Expected $PaCO_2 = 40 + 0.7 * (40 - 24) = 40 + 0.7 * 16 = 40 + 11 = 51$ mmHg
- It demonstrates the relative weakness of the response to metabolic alkalosis

# Basic concepts

- Responses to respiratory acid-base disorders
- The secondary reponse to changes in PaCO2 occurs in the kidneys, where HCO3 absorption in the proximal tubes is adjusted to produce the appropriate change in plasma HCO3
- This renal response is relatively slow, and can take 2 to 3 days to reach completion
- Respiratory acid-base disorders are separated into acute and chronic disorders

# Basic concepts

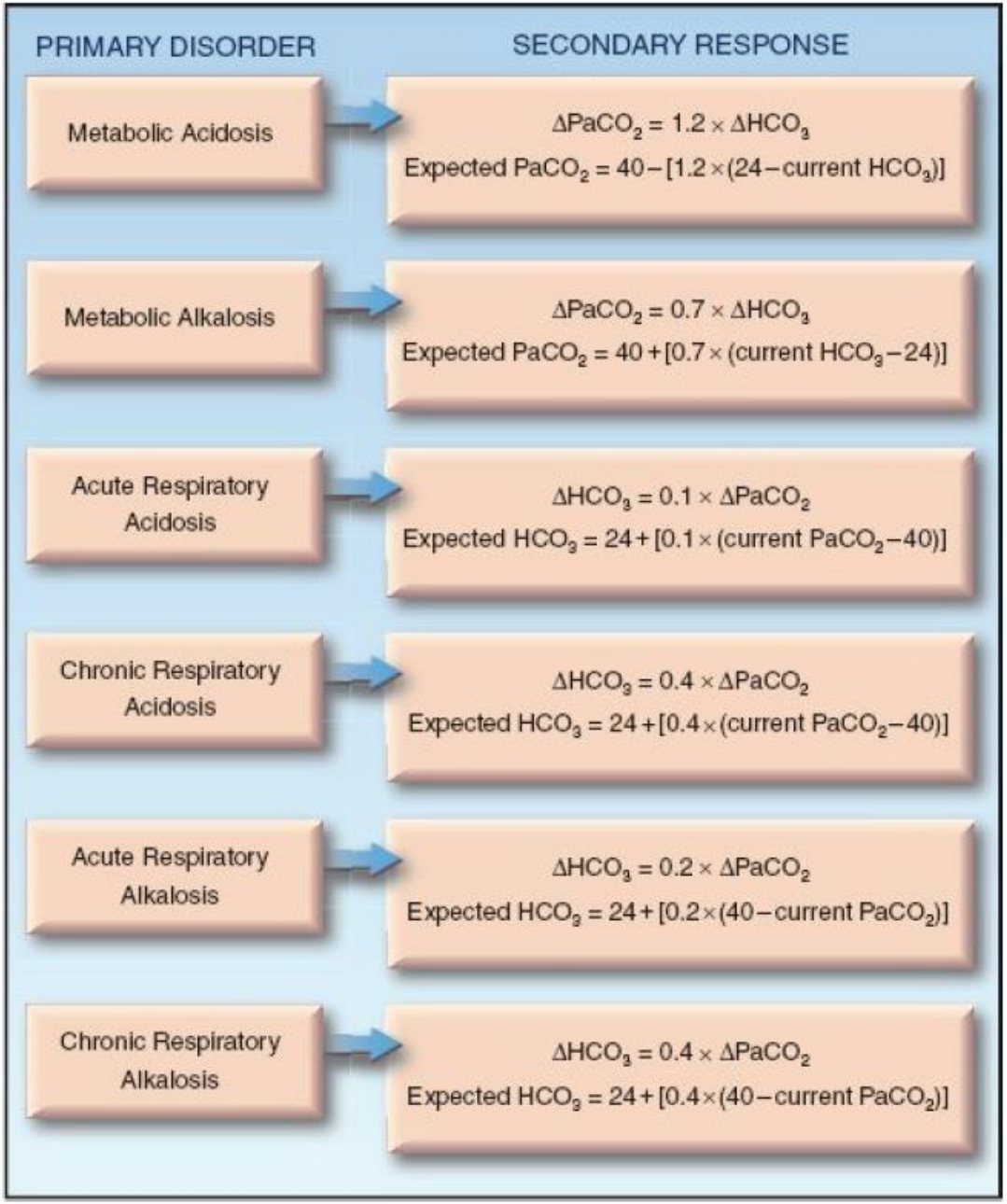
- Responses to respiratory acid-base disorders
- Acute respiratory disorders
- Acute changes in $PaCO_2$ have a small effect on the plasma $HCO_3$
- Acute respiratory acidosis
- $\Delta HCO_3 = 0.1 * \Delta PaCO_2$
- Acute respiratory alkalosis
- $\Delta HCO_3 = 0.2 * \Delta PaCO_2$
- Example: acute increase in $PaCO_2$ to 60 mmHg
- $\Delta HCO_3 = 0.1 * (60-40) = 2$ mEq/L -> expected $HCO_3 = 24 + 2 = 26$ mEq/L

# Basic concepts

- Responses to respiratory acid-base disorders
- Chronic respiratory disorders
- The renal response to an increase in $PaCO_2$ is an increase in $HCO_3$ reabsorption in the proximal renal tubules, which raises the plasma $HCO_3$ concentration
- The response to a decrease in $PaCO_2$ is a decrease in renal $HCO_3$ reabsorption, which lowers the plasma $HCO_3$ concentration
- $\Delta HCO_3 = 0.4 * \Delta PaCO_2$
- Example: an increase in $PaCO_2$ to 60 mmHg that persists for at lease a few days
- $\Delta HCO_3 = 0.4 * (60-40) = 8$, expected $HCO_3 = 24 + 8 = 32$ mEq/L

# Basic concepts

- Predictive equations for evaluating secondary responses to primary acid-base disorders



# Stepwise approach to acid-base analysis

- The reference ranges for arterial pH, PCO2, and HCO3
- pH = 7.36-7.44
- PCO2 = 36-44 mmHg
- HCO3 = 22-26 mEq/L

# Stepwise approach to acid-base analysis

- Stage I: identify the primary acid-base disorder
- The $PaCO_2$ and pH are used to identify the primary acid-base disorder
- Rule 1: If the $PaCO_2$ and/or the pH is outside the normal range, there is an acid-base disorder
- Rule 2: a. If the $PaCO_2$ and pH change in the same direction, there is a primary metabolic acid-base disorder
- b. If the $PaCO_2$ and pH change in opposite directions, there is a primary respiratory acid-base disorder

# Stepwise approach to acid-base anaylsis

- Stege I: identify the primary acid-base disorder
- Example: pH = 7.23, $PaCO_2$ = 23 mmHg
- pH and $PaCO_2$ are both reduced, pH is low -> a primary metabolic acidosis

# Stepwise approach to acid-base analysis

- Rule 3: If only the pH or $PaCO_2$ is abnormal, the condition is a mixed metabolic and respiratory disorder
- a. If the $PaCO_2$ is abnormal, the directional change in $PaCO_2$ identifies the type of respiratory disorder (e.g., high $PaCO_2$ indicates a respiratory acidosis), and the opposing metabolic disorder
- b. If the pH is abnormal, the directional change in pH identifies the type of metabolic disorder (e.g., low pH indicates a metabolic acidosis) and the opposing respiratory disorder

# Stepwise approach to acid-base analysis

- Example: pH = 7.38, PaCO2 = 55 mmHg
- -> mixed metabolic and respiratory disorder
- PaCO2 elevated -> respiratory acidosis, and metabolic alkalosis
- -> therefore, a mixed respiratory acidosis and metabolic alkalosis

# Stepwise approach to acid-base analysis

- Stage II: evaluate the secondary responses
- Rule 4: For a primary metabolic disorder, if the measured PaCO2 is higher than expected, there is a secondary respiratory acidosis, and if the measured PaCO2 is less than expected, there is a secondary respiratory alkalosis

# Stepwise approach to acid-base analysis

- Example: $PaCO_2$ = 23 mmHg, pH = 7.32, $HCO_3$ = 16 mEq/L
- -> pH and $PCO_2$ change, the same direction -> a primary metabolic disorder -> a primary metabolic acidosis
- Expected $PaCO_2$ = 40 – 1.2 * (24 – 16) = 40 – 9.6 = 30.4 mmHg > measured $PaCO_2$ (23 mmHg) -> additional respiratory alkalosis
- -> primary metabolic acidosis with secondary respiratory alkalosis

# Stepwise approach to acid-base analysis

- Rule 5: For a primary respiratory disorder, a normal or near-normal $HCO_3$ indicates that the disorder is acute

# Stepwise approach to acid-base analysis

- Rule 6: a. For a chronic respiratory acidosis, if the HCO3 is lower than expected, there is an incomplete renal response, and if the HCO3 is higher than expected, there is a secondary metabolic alkalosis
- b. For a chronic respiratory alkalosis, if the HCO3 is higher than expected, there is an incomplete renal response, and if the HCO3 is lower than expected, there is a secondary metabolic acidosis

# Stepwise approach to acid-base analysis

- Example: $PaCO_2$ = 23 mmHg, pH = 7.54, $HCO_3$ = 22 mEq/L
- -> $PaCO_2$ and pH change in opposite directions -> a primary respiratory alkalosis
- -> expected $HCO_3$ = 24 – 0.4 * (40 – 23) = 24 – 6.8 = 17.2 mEq/L
- -> 22 > 17.2 mEq/L -> a chronic respiratory alkalosis with an incomplete renal response

# Stepwise approach to acid-base analysis

- Stage III: use the “Gaps” to evaluate a metabolic acidosis
- For patients with a metabolic acidosis, the use of measurements called gaps can help to uncover the underlying cause of the acidosis

# The Gaps

- The anion gap (AG)
- Na + UC (unmeasured cations) = (CL + HCO3) + UA (unmeasured anions)
- UA – UC = Na – (CL + HCO3)
- -> AG = UA – UC = Na – (CL + HCO3)

# The Gaps

- Reference range
- The original reference range for the AG was 12±4 mEq/L (range = 8 to 16 mEq/L)
- Influence of albumin
- Albumin is the principal unmeasured anion, and the principal determinant of the anion gap

**Table 31.3 Determinants of the Anion Gap**

| Unmeasured Anions | Unmeasured Cations |
|---|---|
| Albumin (15 mEq/L) | Calcium (5 mEq/L) |
| Organic Acids (5 mEq/L) | Potassium (4.5 mEq/L) |
| Phosphate (2 mEq/L) | |
| Sulfate (1 mEq/L) | Magnesium (1.5 mEq/L) |
| Total UA: (23 mEq/L) | Total UC: (11 mEq/L) |
| Anion Gap = UA – UC = 12 mEq/L | |

# The Gaps

- influence of albumin
- Since hypoalbuminemia is present in as many as 90% of ICU patients, the following formula for the “corrected AG” (Agc) has been proposed to include the contribution of albumin
- AGc = AG + 2.5 (4.5 – [albumin in g/dL])
- Example: AG = 10 mEq/L, plasma albumin = 2 g/dL -> AGc = 10 + (2.5 * 2.5) = 16 mEq/L

# The Gaps

- Using the anion Gap
- The AG can be used to identify the underlying mechanism of a metabolic acidosis
- An elevated AG occurs when there is an accumulation of fixed or non-volatile acids (e.g., lactic acidosis), while a normal AG occurs then there is a primary loss of bicarbonate (e.g., diarrhea)

**Table 31.4 Classification of Metabolic Acidosis with the Anion Gap (AG)**

| High AG | Normal AG |
|---|---|
| Lactic Acidosis | Diarrhea |
| Ketoacidosis | Isotonic Saline Infusion |
| End-Stage Renal Failure | Early Renal Insufficiency |
| Methanol Ingestion | Renal Tubular Acidosis |
| Ethylene Glycol Ingestion | Acetazolamide |
| Salicylate Toxicity | Ureteroenterostomy |

# The Gaps

- High AG
- Lactic acidosis, diabetic ketoacidosis, and advanced renal failure (where there is loss of H+ secretion in the distal tubules of the kidneys)
- Toxic ingestions of methanol (which produces formic acid), ethylene glycol (which produces oxalic acid), and salicylates (which produce salicylic acid)

# The Gaps

- Normal AG
- Diarrhea, saline infusion, and early renal failure (where there is loss of bicarbonate reabsorption in the proximal tubules)
- The loss of HCO3 is counterbalanced by a gain of chloride ions to maintain electrical charge neutrality; hence the term hyperchloremic metabolic acidosis is used for normal AG metabolic acidosis

# The Gaps

- Reliability
- A recent study shows that the albumin-corrected AG (AGc) provides a more accurate assessment of metabolic acidosis than the AG

# The Gaps

- The Gap-Gap ratio
- AG excess/ $HCO_3$ deficit = (AG – 12) / (24 – $HCO_3$)
- Mixed metabolic acidosis
- In the presence of a high AG metabolic acidosis, a gap-gap ratio < 1 indicates the co-existence of a normal AG (hyperchloremic) metabolic acidosis

# The Gaps

- Diabetic ketoacidosis (DKA)
- DKA presents with a high AG metabolic acidosis -> aggressive infusion of isotonic saline -> create a hyperchloremic (normal AG) metabolic acidosis -> switches from a high AG to a normal AG acidosis
- Therefore, monitoring the serum HCO3 alone will created a false impression that the DKA is not resolving, while the gap-gap ratio provides an accurate measure of the acid-base status of the patient

# The Gaps

- Metabolic acidosis and alkalosis
- When alkali is added in the presence of a high AG acidosis, the decrease in serum bicarbonate is less than the increase in AG, and the gap-gap is greater then unity (>1)
- In the presence of a high AG metabolic acidosis, a gap-gap >1 indicates the co-existence of a metabolic alkalosis

# A final word

- For more than 100 years, the evaluation of acid-base balance has been based on a single reaction sequence, and a single determinant of plasma pH (the $PCO_2/HCO_3$ ratio)
- $CO_2 + H_2O \Leftrightarrow H_2CO_3 \Leftrightarrow H^+ + HCO_3$

# 흉관 및 흉막강 배액 관리

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조 정 수

# 강의 내용

- 폐쇄식 흉관 배액의 목적
- 흉관 삽입 적응증
- 흉막 해부 및 생리
- 흉막강 배액장치의 종류
- 흉막강 배액장치의 유지와 관리
- 흉관 배액의 평가

# 폐쇄식 흉관 배액의 목적

## 흉막강의 음압 회복

## 흉막강의 공기 또는 액체의 제거

폐허탈 (lung collapse) 방지

혈액저류 및 응고 또는 섬유화 방지

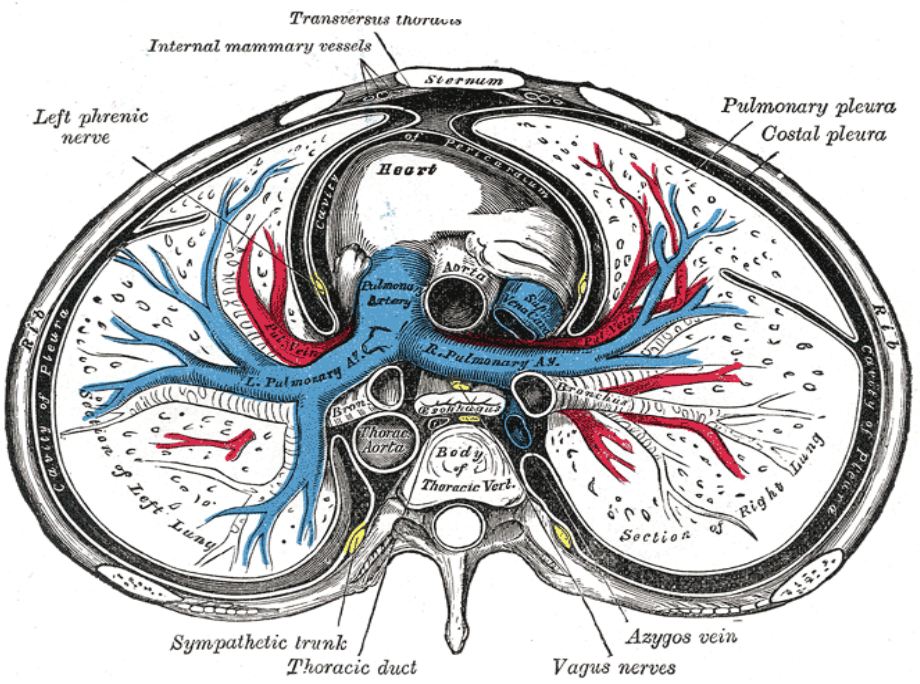
긴장성 기흉, 폐색전, 심장 압전 및 이차감염 등의 합병증 방지

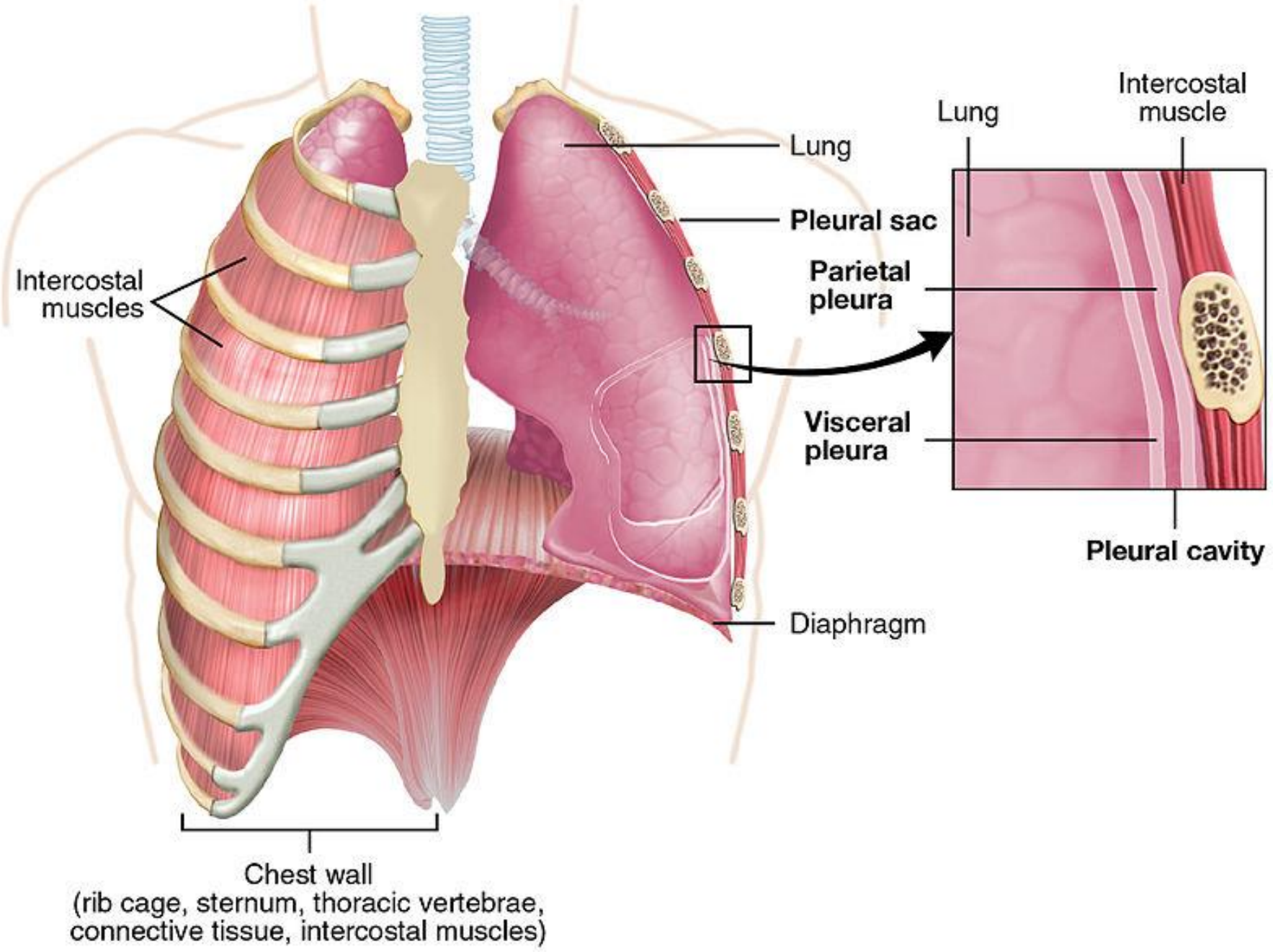
# 흉관삽입의 적응증

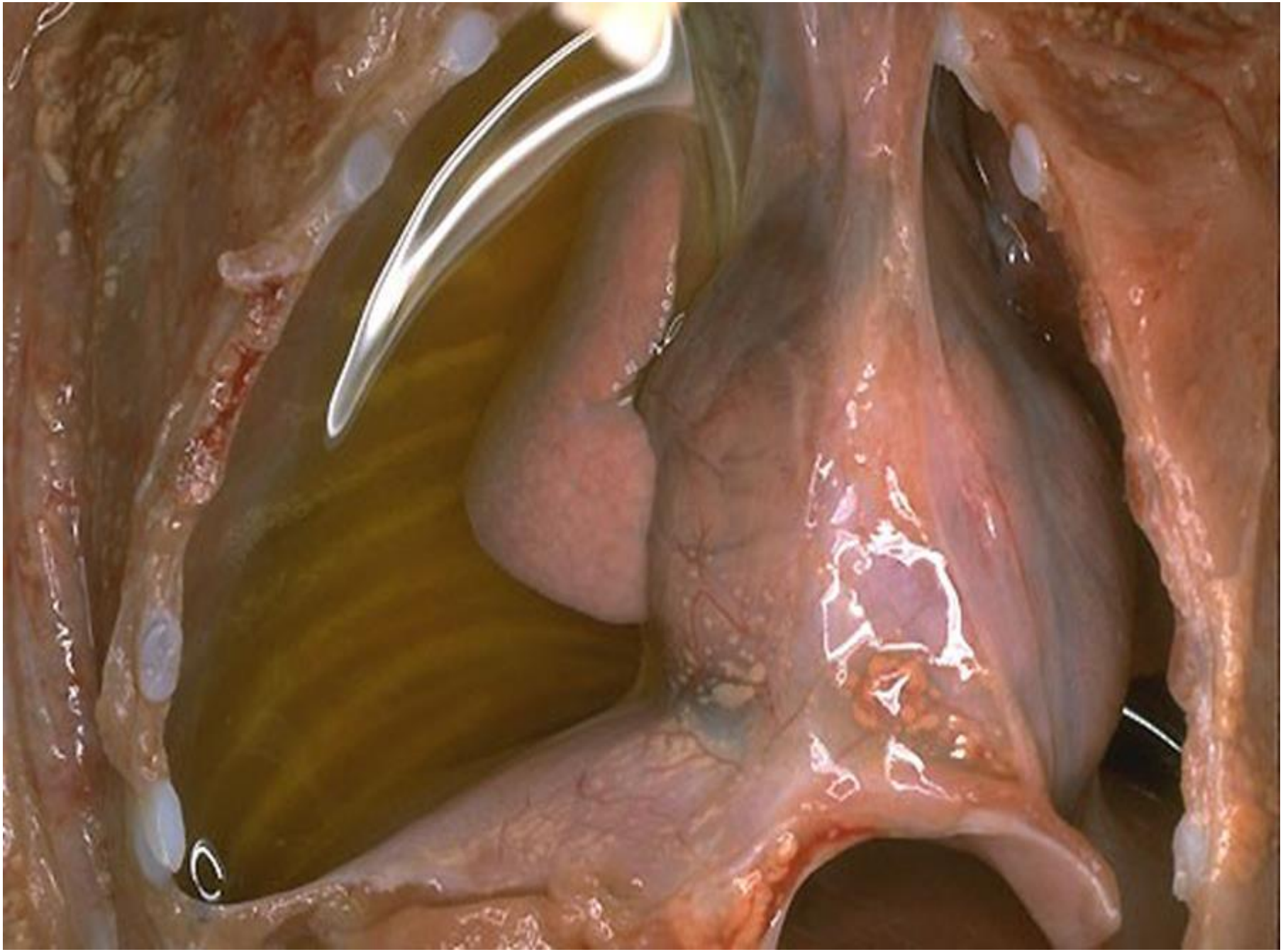
1. Postoperative status(흉부 수술 후)
2. hemothorax(혈흉), pneumothorax(기흉)
3. empyema(농흉)
4. chylothorax(유미흉)
5. emphysema disease
6. others

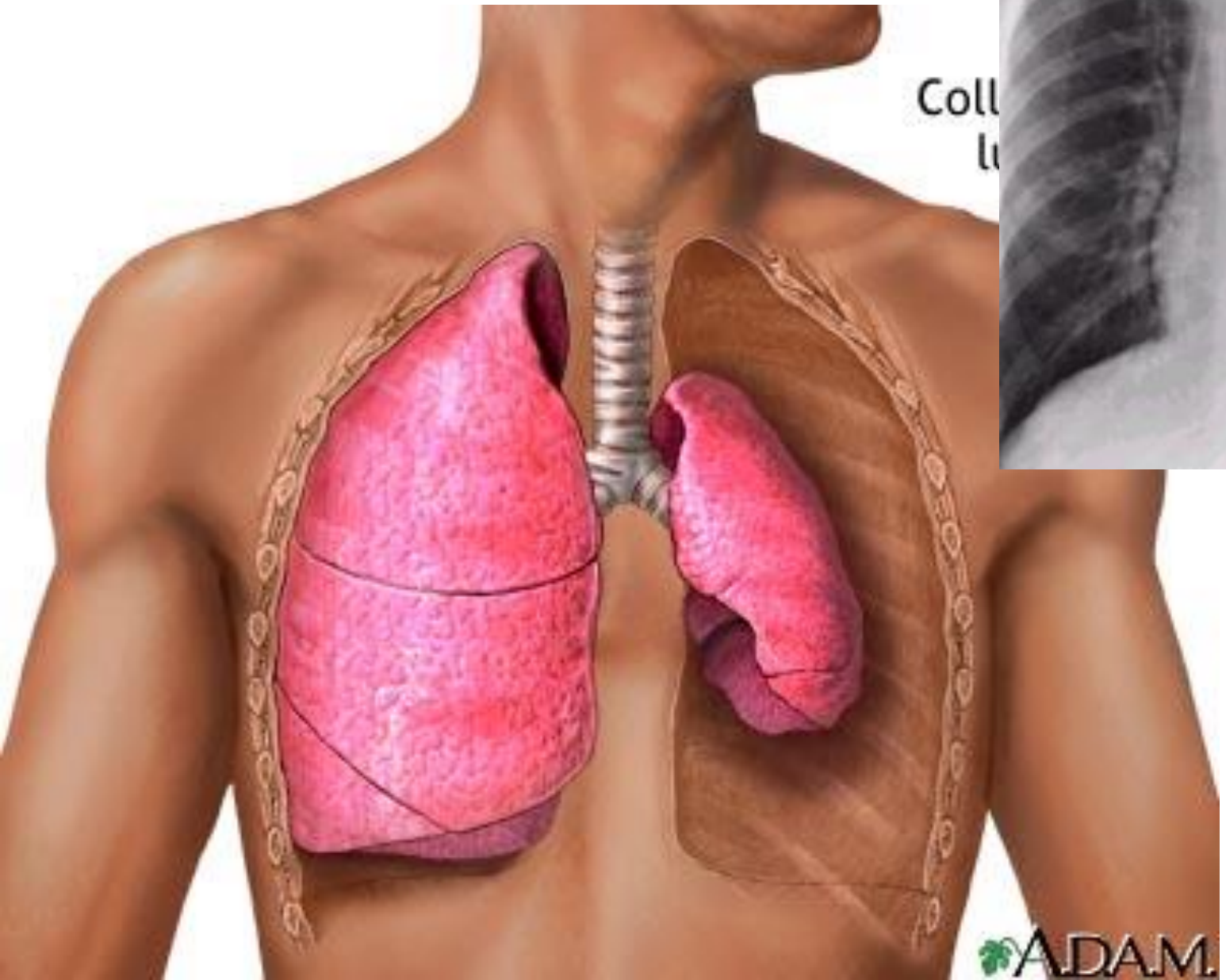
# 흉막의 해부 및 생리

- **흉막의 해부**
  - 소량의 윤활성 장액(10~30 ml)
    이 존재하여 호흡에 따른 흉막
    간의 마찰을 감소




Lung
Pleural sac
Intercostal muscles
Diaphragm
Chest wall
(rib cage, sternum, thoracic vertebrae, connective tissue, intercostal muscles)
Lung
Intercostal muscle
Parietal pleura
Visceral pleura
Pleural cavity

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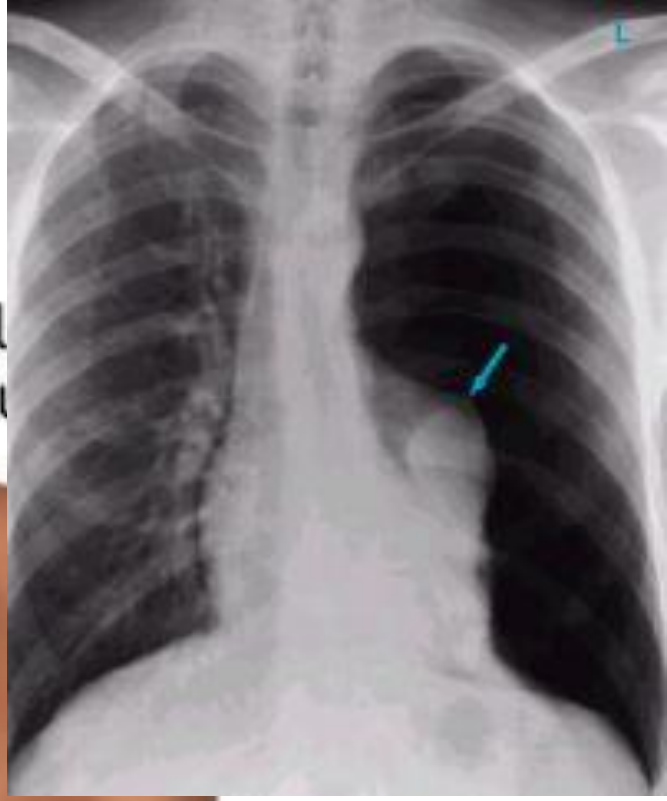


# 흉막의 혈관 분포와 신경

| | **Parietal pleura** | Visceral pleura |
|---|---|---|
| *Blood supply* | **systemic** | pulmonary/ systemic(bronchial) |
| *Venous drainage* | **systemic** | pulmonary |
| *Lymphatics* | **local** | subpleural lymphatic plexus<br>-- intrapulm. lymph. channel |
| *Nerve supply* | **somatic** - intercostal n.<br>phrenic n.<br>**sympathetic /**<br>**parasympathetic** | non of somatic nerve<br>(pain sense가 없다) |

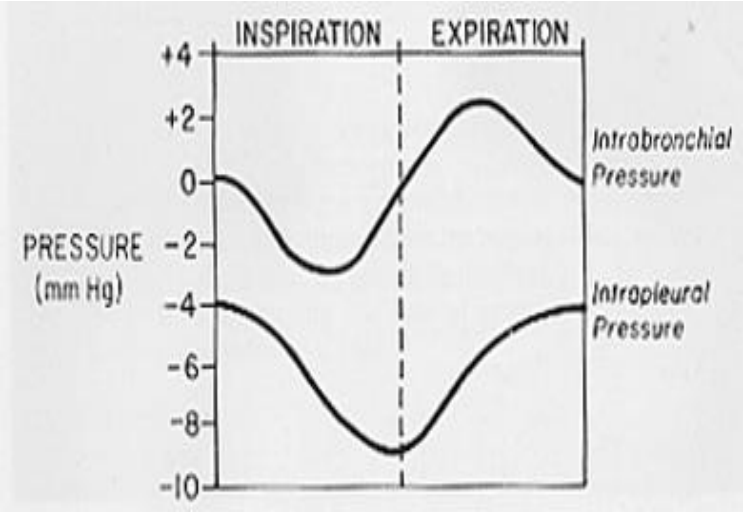
# 흉막의 생리

**흉막강 내압 (intrapleural pressure), 가슴막압 (pleural pressure)**

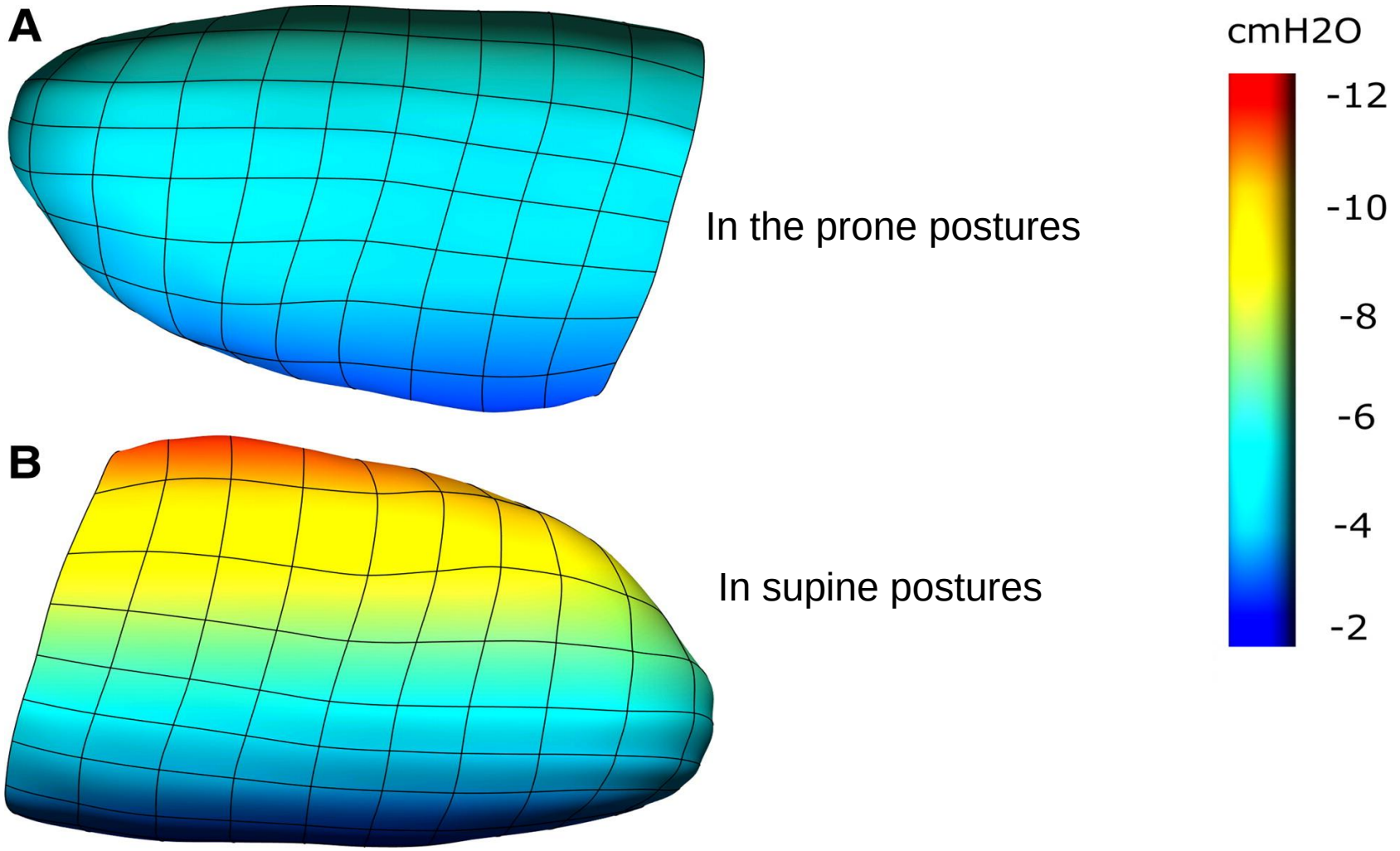
: negative; -4 ~ -8 $cmH_2O$

: deep breathing or cough -20 ~ +4 $cmH_2O$

* Presser tracing of the Intra-bronchial & Intra-pleural pressure
* Valsalva maneuver 때 가장 높은 압력을 가진다.
* 폐첨부가 기저부보다 압력이 더 낮다. (폐 자체의 무게 영향)
* 흉막강 내압의 형성 원리
  ① extensile force of thoracic cage
  ② elastic recoil of lung
  ③ weight(gravity) of lung



Surface (pleural) pressures in a finite-element model of a normal, healthy human lung



# 흉막강 배액 장치

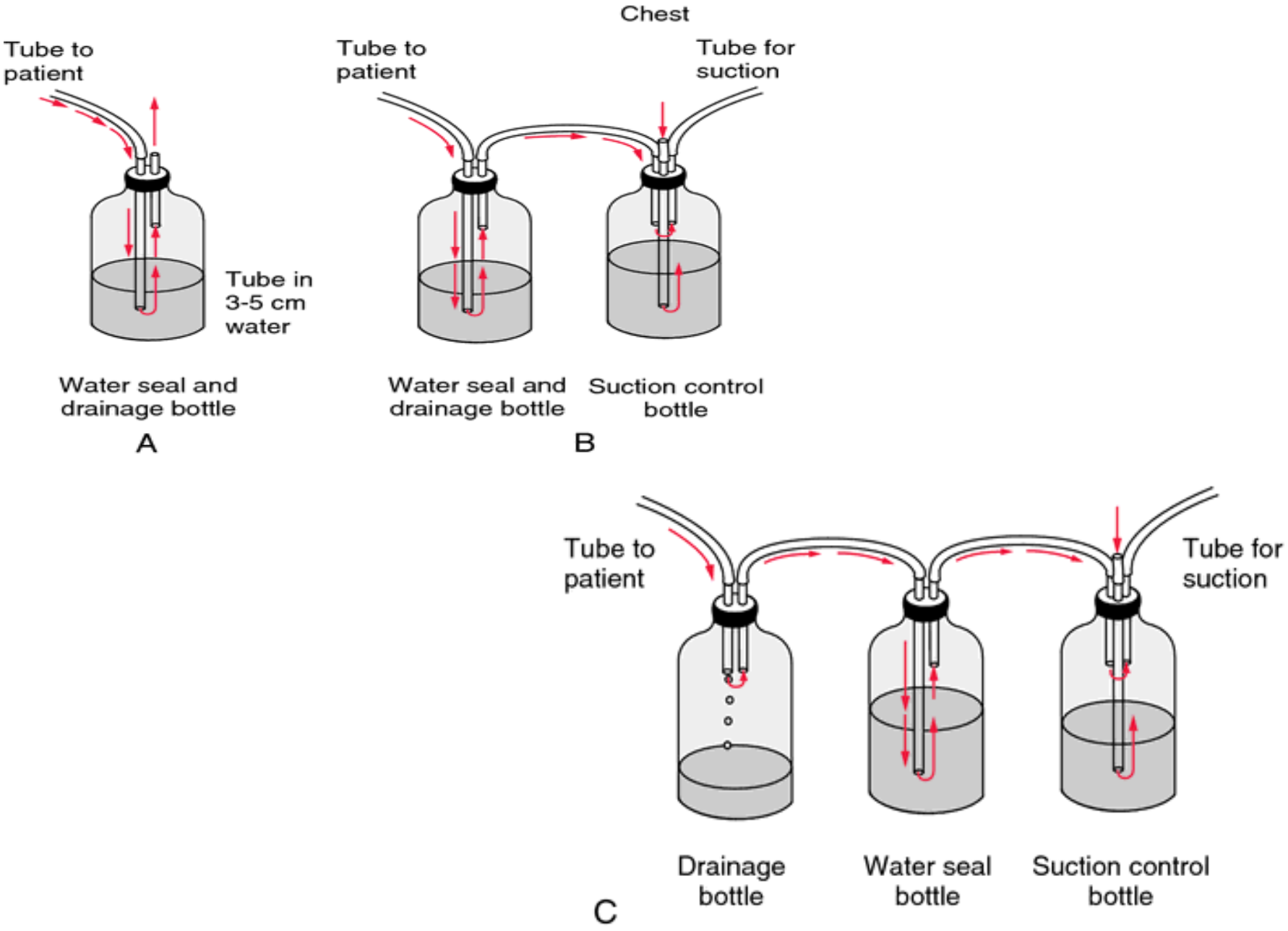
음압인 흉막강에 대한 배액을 위해

수봉식 배액법(under- water seal drainage)이 기본으로 사용

(1) One-bottle system : 수봉식 배액법 ( under-water seal drainage)

(2) Two-bottle system : 수봉식 배액 + 저수조 (collecting bottle)

(3) Tree-bottle system : Two-bottle system + 압력조절장치
(pressure regulation system)


Tube to patient
Tube in 3-5 cm water
Water seal and drainage bottle
A
Chest
Tube to patient
Tube for suction
Water seal and drainage bottle
Suction control bottle
B
Tube to patient
Tube for suction
Drainage bottle
Water seal bottle
Suction control bottle
C


1300
1200
1100
1000
900
800
700
600
500
400
WATER LEVEL
300
200
100
1000
900
800
700
600
500
400
300
200
100
WATER LEVEL

# 흉막강 배액 장치의 관리와 유지

**흉막강 배액(drainage)의 중요성**

부적절한 흉막강 배액은

→ ┌ 공기 또는 수액(혈액)의 저류 ┐

└ 폐조직의 탄력성(팽창성)을 감소 ┘ 를 초래

→ 흉막강 폐쇄억제, 폐조직의 재팽창 방해

→ 흉부 외상 또는 수술 후 합병증과 사망률을 증가시킴

# 흉막강 배액에 영향을 주는 요소

(1) 흉관의 개통 상태

(2) 흉강내 압력

(3) 흉막의 공기 또는 흉수의 흡수 능력

(4) 이차 감염

(5) 술 후 지속되는 공기 누출 및 출혈 여부

(6) 환자의 기저질환 및 기타

# 흉관의 개통성 유지

① clamping 하지 말 것.

② 주기적인 milking (or squeezing)

③ 기능 (working, function) 확인

: 수봉식 배액통의 수면 파동

: 특히 제품화된 two bottle system의 one way valve 기능 확인

④ 기침과 심호흡

# 흉막의 흡수 능력

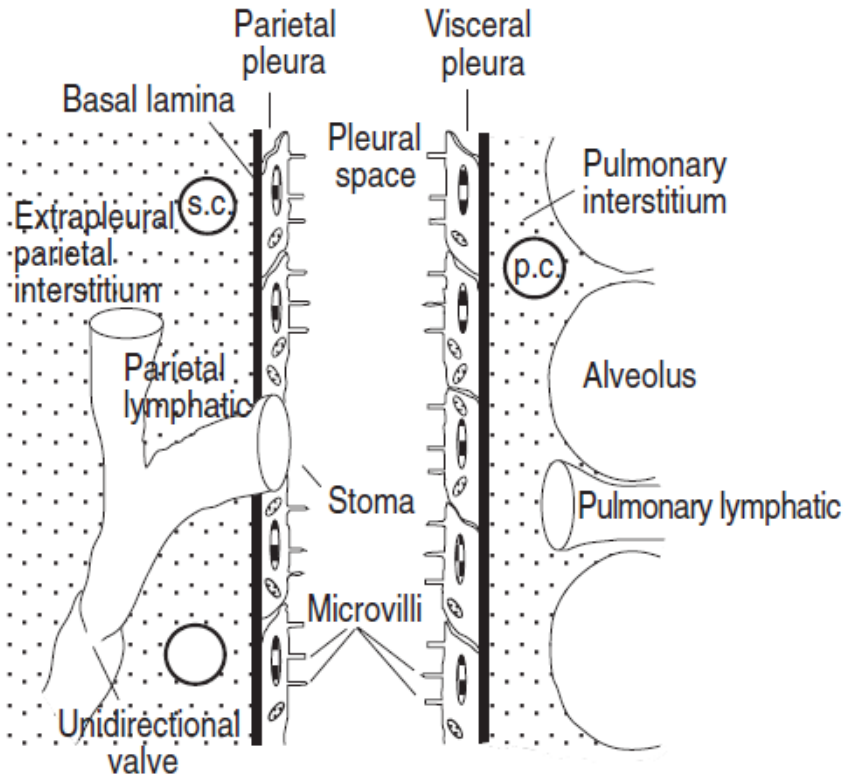
## 흉수 (pleural fluid)

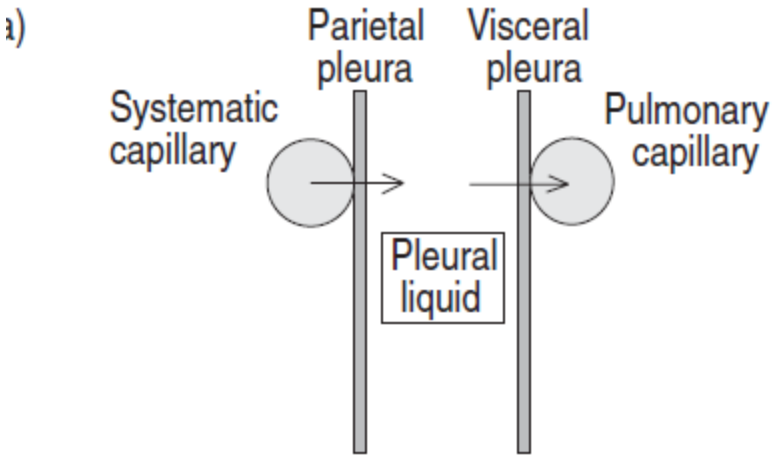
: systemic circulation, pulmonary circulation & pleural space의 hydrostatic pressure와 colloid oncotic pressure에 의해 생성 흡수

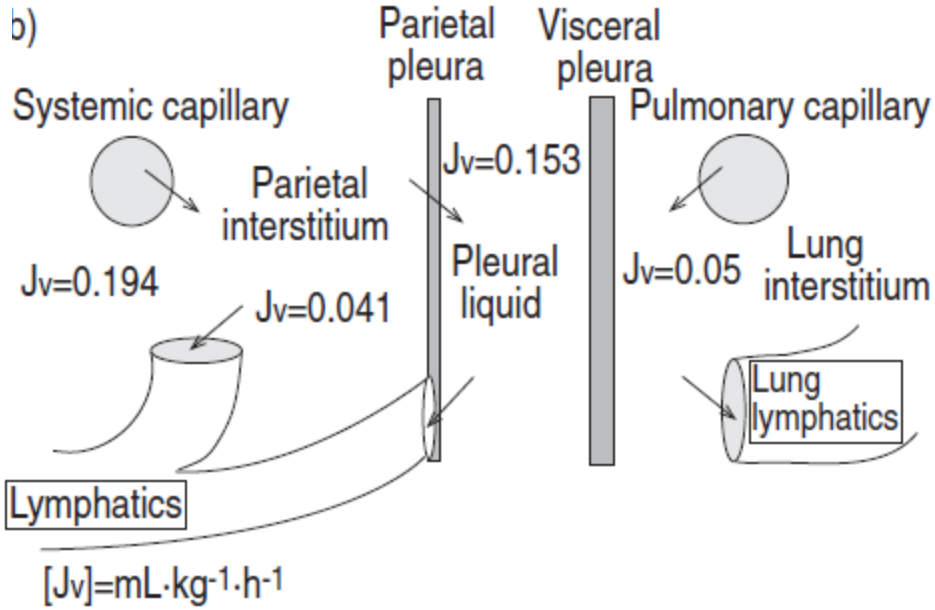
: pleural fluid는 **parietal** & visceral pleura에서 생성되어 대부분 parietal pleura 의 lymphatics 로 흡수

: 성인에서 대략 200ml/day 생성되고  대략 최대 700ml/day 가량 흡수

# 흉수 순환


Parietal pleura
Visceral pleura
Basal lamina
Pleural space
Pulmonary interstitium
Extrapleural parietal interstitium
s.c.
p.c.
Parietal lymphatic
Alveolus
Stoma
Pulmonary lymphatic
Microvilli
Unidirectional valve


a)
Parietal pleura
Visceral pleura
Systematic capillary
Pulmonary capillary
Pleural liquid


b)
Parietal pleura
Visceral pleura
Systemic capillary
Pulmonary capillary
Jv=0.153
Parietal interstitium
Pleural liquid
Jv=0.05
Lung interstitium
Jv=0.194
Jv=0.041
Lung lymphatics
Lymphatics
[Jv]=mL·kg-1·h-1

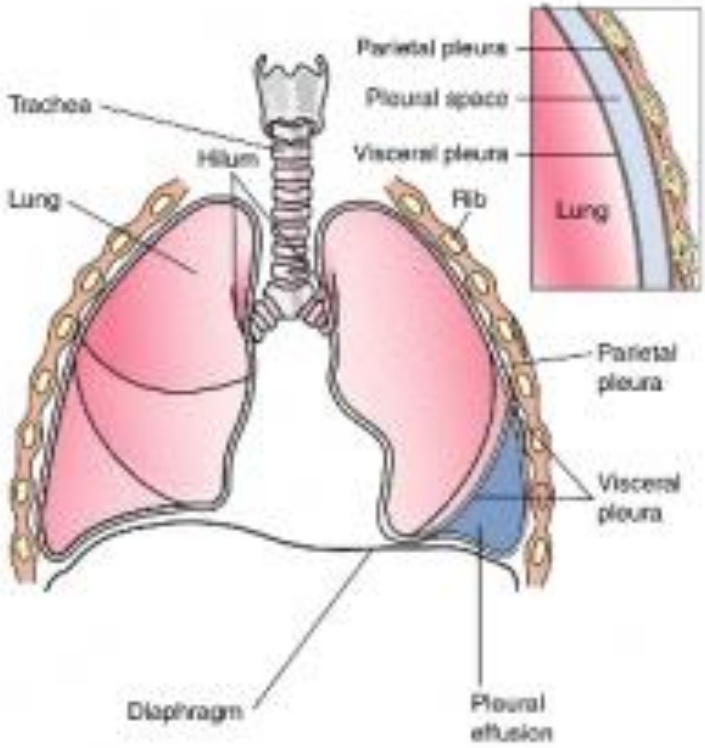
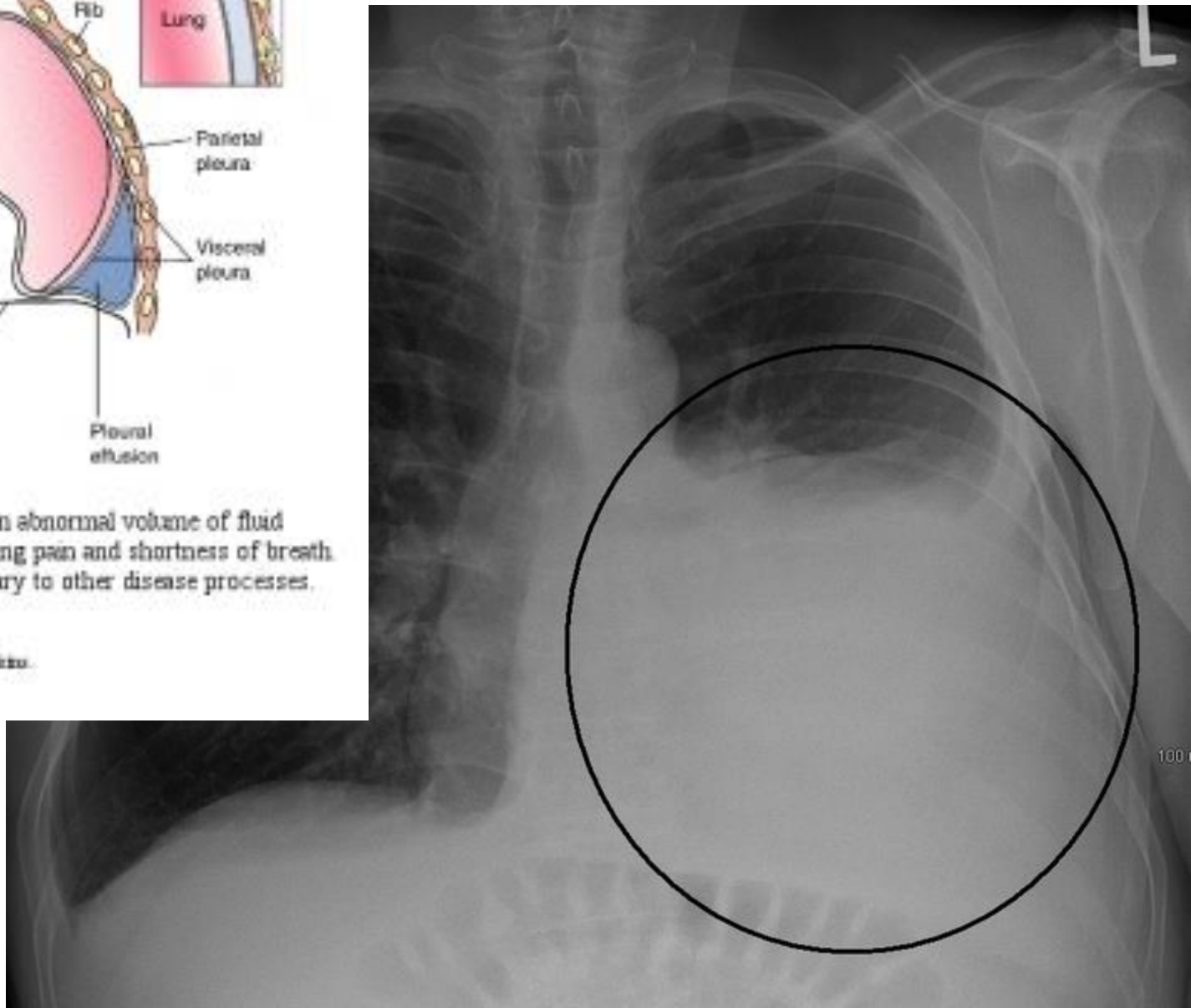



**Figure 23-5** In pleural effusion, an abnormal volume of fluid collects in the pleural space, causing pain and shortness of breath. Pleural effusion is usually secondary to other disease processes.





# 흉관 관리시 확인 사항

❖ 흉관의 끝을 반드시 수면 아래 유지할 것 (수봉식을 유지)

-> 배액병 물의 증발이나 소실 등을 확인

-> 흉막강으로의 공기 흡인 방지

❖ 흉관의 배액병을 환자 가슴높이 아래 (보통 1 M 아래) 유지

-> 물의 역류 방지

❖ 지속적인 (저압력) 흡인 상태의 유지

-> 특히 많은 공기 누출(air-leak)이 있을 때

# 흉관 관리시 확인 사항

- 감염의 예방 : 흉관 삽입부의 소독, 흉관 배액병의 무균적 관리

- 흉관을 가진 대상자의 신체적, 심리적 상태 확인
  - **우발적 흉관 제거 방지**

- 배액의 평가

# 흉관 배액의 평가

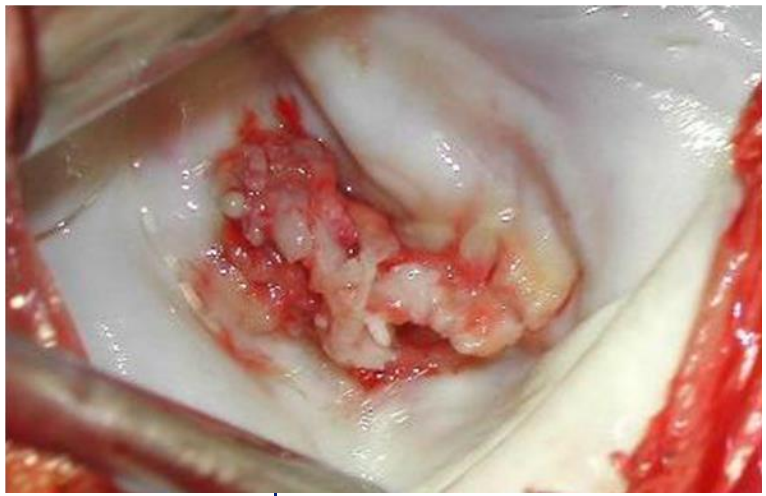
- 흉부사진 (가능하면 up-right position)
- 흉관 배액의 양과 특성 (공기 누출 유무 포함) 관찰 및 기록
  - ➢ 흉관 제거 여부 및 시기 결정

KYUNGPOOK NATIONAL UNIVERSITY HOSPITAL

# 예방적 항생제의 사용원칙

경북대학교병원
김 근 직

경북대학교병원
KYUNGPOOK NATIONAL UNIVERSITY HOSPITAL



# 감염성 심내막염
# Infective endocarditis

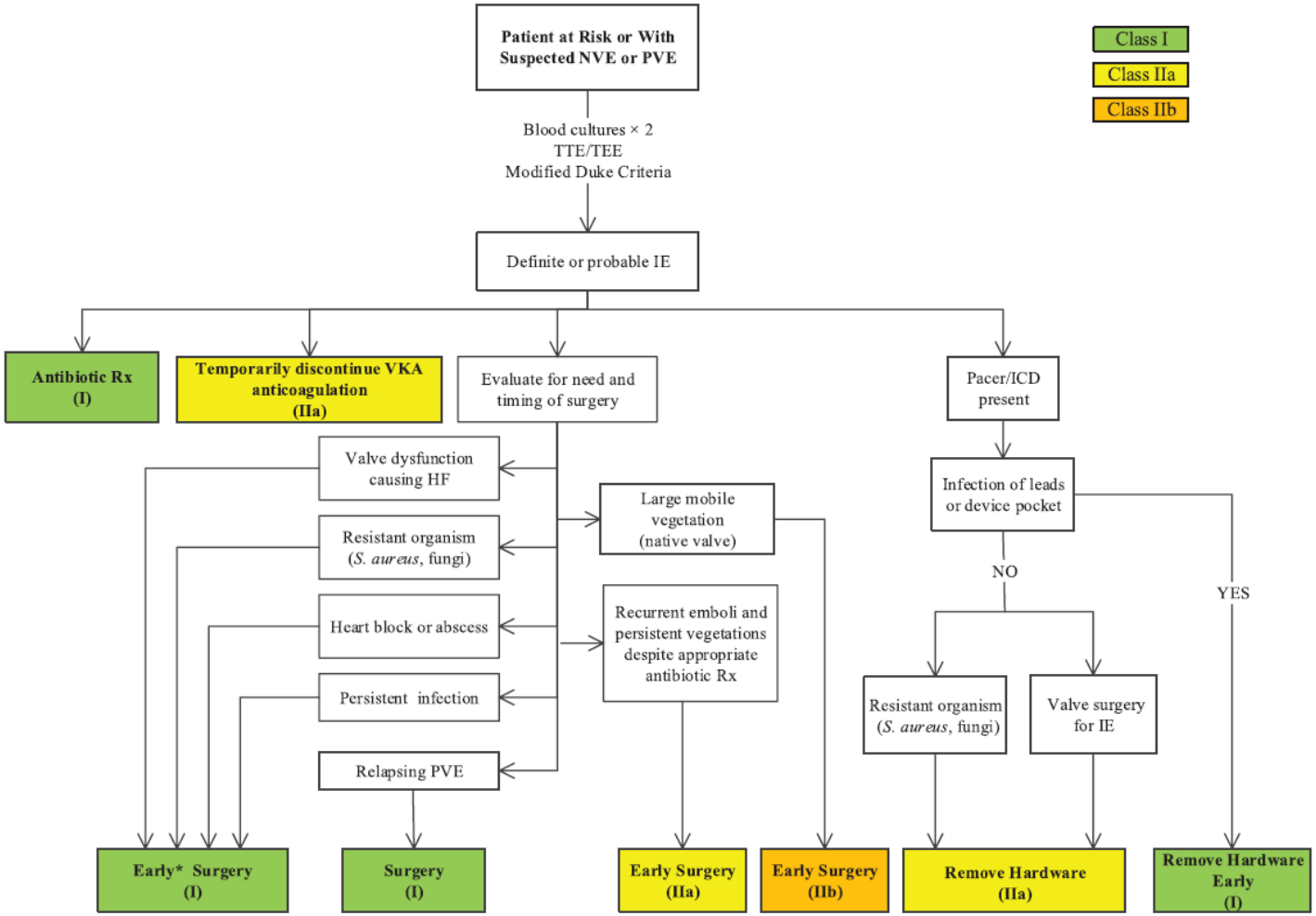



**Figure 9.** Diagnosis and Treatment of IE. *Early surgery defined as during initial hospitalization before completion of a full therapeutic course of antibiotics.HF indicates heart failure; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis; Rx, therapy; *S. aureus*, *Staphylococcus aureus*; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; and VKA, vitamin K antagonist.

# 감염성 심내막염
# 예방

# Prophylaxis of infective endocarditis

**The most recent recommendations differ dramatically from previous guidelines and provide new insights into the prophylaxis of IE**

*only for patients with the highest risk of IE undergoing the highest risk dental procedures.*

*Good oral hygiene &regular dental review*
*: very important role in reducing the risk of IE.*

*the levels of evidence of current recommendations are low.*

# 예방적 항생제사용이 필요한 심장상태는?

# 2007 AHA Guideline
# : Prevention of Infective endocarditis

| |
|---|
| Prosthetic cardiac valve or prosthetic material used for cardiac valve repair |
| Previous IE |
| Congenital heart disease (CHD)* |
| Unrepaired cyanotic CHD, including palliative shunts and conduits |
| Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure† |
| Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization) |
| Cardiac transplantation recipients who develop cardiac valvulopathy |

# 2009 ESC Guideline

| Recommendations: prophylaxis | Class[a] | Level[b] |
|---|---|---|
| **Antibiotic prophylaxis should only be considered for patients at highest risk of IE**<br>1. Patients with a prosthetic valve or a prosthetic material used for cardiac valve repair<br>2. Patients with previous IE<br>3. Patients with congenital heart disease<br>a. cyanotic congenital heart disease, without surgical repair, or with residual defects, palliative shunts or conduits<br>b. congenital heart disease with complete repair with prosthetic material whether placed by surgery or by percutaneous technique, up to 6 months after the procedure<br>c. when a residual defect persists at the site of implantation of a prosthetic material or device by cardiac surgery or percutaneous technique | IIa | C |
| **Antibiotic prophylaxis is no longer recommended in other forms of valvular or congenital heart disease** | III | C |

# 예방적 항생제는 어떤 시술을 할 때 필요한가?

# 2007 AHA Guideline
# : Prevention of Infective endocarditis

**Table 6. Summary of Major Changes in Updated Document**

We concluded that bacteremia resulting from daily activities is much more likely to cause IE than bacteremia associated with a dental procedure.

We concluded that only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis even if prophylaxis is 100% effective.

Antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of IE.

Limit recommendations for IE prophylaxis only to those conditions listed in Table 3.

Antibiotic prophylaxis is no longer recommended for any other form of CHD, except for the conditions listed in Table 3.

Antibiotic prophylaxis is reasonable for all dental procedures that involve manipulation of gingival tissues or periapical region of teeth or perforation of oral mucosa only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).

Antibiotic prophylaxis is reasonable for procedures on respiratory tract or infected skin, skin structures, or musculoskeletal tissue only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).

Antibiotic prophylaxis solely to prevent IE is not recommended for GU or GI tract procedures.

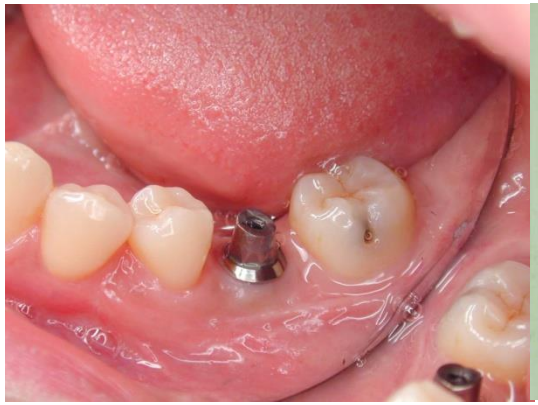
Although these guidelines recommend changes in indications for IE prophylaxis with regard to selected dental procedures (see text), the writing group reaffirms that those medical procedures listed as not requiring IE prophylaxis in the 1997 statement remain unchanged and extends this view to vaginal delivery, hysterectomy, and tattooing. Additionally, the committee advises against body piercing for patients with conditions listed in Table 3 because of the possibility of bacteremia, while recognizing that there are minimal published data regarding the risk of bacteremia or endocarditis associated with body piercing.

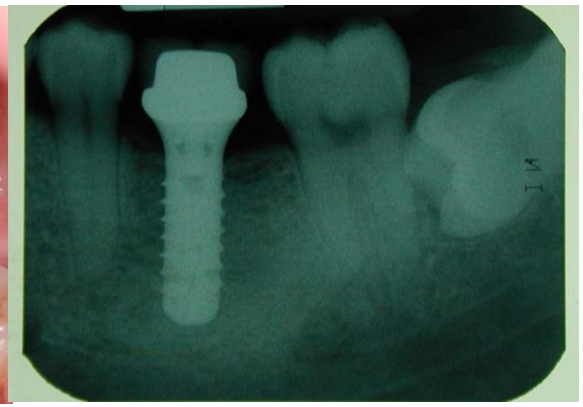
## PROPHYLAXIS IS REASONABLE*

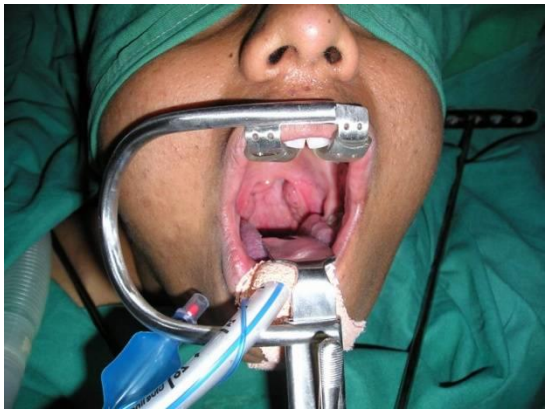
Dental: All dental procedures involving manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa

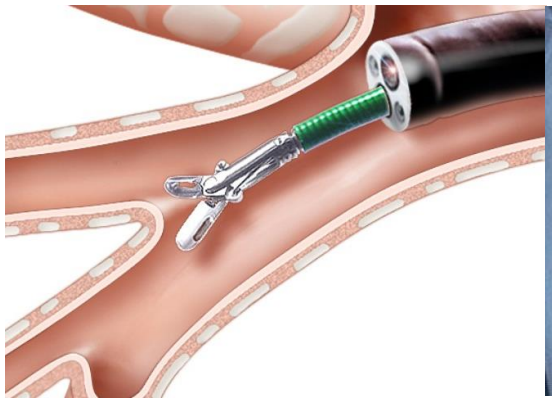
Respiratory: Procedures involving incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy

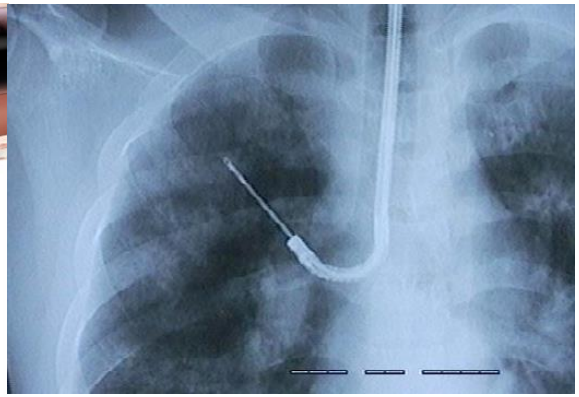
Other: Infected skin, skin structures, or musculoskeletal tissue











## PROPHYLAXIS IS NOT RECOMMENDED

Dental: Routine anesthetic injections through noninfected tissue, dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, bleeding from trauma to the lips or oral mucosa

Respiratory: Procedures not involving incision or biopsy of the respiratory mucosa, including bronchoscopy (unless the procedure involves incision of the respiratory tract mucosa)

Genitourinary: Antibiotic prophylaxis solely to prevent infective endocarditis is not recommended

Gastrointestinal: Antibiotic prophylaxis solely to prevent infective endocarditis is not recommended


**Table 6. Summary of Major Changes in Updated Document**

| |
|---|
| We concluded that bac … likely to cause IE than … |
| We concluded that only an extremely small number of cases of IE might be prevented by antibiotic prophylaxi… |
| Antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of IE. |
| Limit recommendations for IE prophylaxis only to those conditions listed in Table 3. |
| Antibiotic prophylaxis is no longer recom… except for the conditions listed in Table … |
| Antibiotic prophylaxis is reasonable for all dental procedures that involve manipulation of gingival tissues or periapical region of teeth or perforation of oral mucosa only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3). |
| Antibiotic prophylaxis is reasonable for procedures on respiratory tract or infected skin, skin structures, or musculoskeletal tissue only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3). |
| Antibiotic prophylaxis solely to prevent IE is not re… tract procedures. |
| Although these guidelines recommend changes in indications for IE prophylaxis with regard to selected dental procedures (see text), the writing group reaffirms that those medical procedures listed as not requiring IE prophylaxis in the 1997 statement remain unchanged and extends this view to vaginal delivery, hysterectomy, and tattooing. Additionally, the committee advises against body piercing for patients with conditions listed in Table 3 because of the possibility of bacteremia, while recognizing that there are minimal published data regarding the risk of bacteremia or endocarditis associated with body piercing. |

**bacteremia resulting from daily activities is much more**

**only an extremely small number of cases of IE**

**Limit recommendations**

**no longer recommended** for **any other form of CHD**, except for the conditions listed in Table 3.

**GU or GI tract procedures: not recommended**

**advises against body piercing**

# 2009 ESC Guideline

| Recommendations: prophylaxis | Class[a] | Level[b] |
|---|---|---|
| **A - Dental procedures:**<br>**Antibiotic prophylaxis should only be considered for** dental procedures requiring manipulation<br>periapical region of the teeth or perforation of the oral mucosa | IIa | C |
| **Antibiotic prophylaxis is not recommended for** local anaesthetic injections in non-infected tissu<br>sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliance<br>Prophylaxis is also not recommended following the shedding of deciduous teeth or trauma to the lips | III | C |
| **B - Respiratory tract procedures*:**<br>**Antibiotic prophylaxis is not recommended for respiratory tract procedures, including** br<br>laryngoscopy, transnasal or endotracheal intubation | III | C |
| **C - Gastrointestinal or urogenital procedures*:**<br>**Antibiotic prophylaxis is not recommended for** gastroscopy, colonoscopy, cystoscopy or transo<br>echocardiography | III | C |
| **D - Skin and soft tissue*:**<br>**Antibiotic prophylaxis is not recommended for any procedure** | III | C |

## Antibiotic Prophylactic Regimens for Dental Procedures

| Situation | Agent | Regimen—Single Dose 30-60 minutes before procedure | |
|---|---|---|---|
| | | Adults | Children |
| Oral | Amoxicillin | 2 g | 50 mg/kg |
| Unable to take oral medication | Ampicillin **OR** | 2 g IM or IV* | 50 mg/kg IM or IV |
| | Cefazolin or ceftriaxone | 1 g IM or IV | 50 mg/kg IM or IV |
| Allergic to penicillins or ampicillin—Oral regimen | Cephalexin**† | 2 g | 50 mg/kg |
| | **OR** | | |
| | Clindamycin | 600 mg | 20 mg/kg |
| | **OR** | | |
| | Azithromycin or clarithromycin | 500 mg | 15 mg/kg |
| Allergic to penicillins or ampicillin and unable to take oral medication | Cefazolin or ceftriaxone† | 1 g IM or IV | 50 mg/kg IM or IV |
| | **OR** Clindamycin | 600 mg IM or IV | 20 mg/kg IM or IV |

*IM—intramuscular; IV—intravenous

**Or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.

†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema or urticaria with penicillins or ampicillin.

# Incidence of Infective Endocarditis Caused by Viridans Group Streptococci Before and After Publication of the 2007 American Heart Association's Endocarditis Prevention Guidelines

Daniel C. DeSimone, MD; Imad M. Tleyjeh, MD, MSc; Daniel D. Correa de Sa, MD; Nandan S. Anavekar, MBBCh; Brian D. Lahr, MS; Muhammad R. Sohail, MD; James M. Steckelberg, MD; Walter R. Wilson, MD; Larry M. Baddour, MD; for the Mayo Cardiovascular Infections Study Group

***Background***—The American Heart Association published updated guidelines for infective endocarditis (IE) prevention in 2007 that markedly restricted the use of antibiotic prophylaxis in certain at-risk patients undergoing dental and other invasive procedures. The incidence of IE caused by viridans group streptococci (VGS) in the United States after publication of the 2007 American Heart Association guidelines has not been reported.

***Methods and Results***—We performed a population-based review of all definite or possible cases of VGS-IE using the Rochester Epidemiology Project of Olmsted County, Minnesota. Patient demographics and microbiological data were collected for all VGS-IE cases diagnosed from January 1, 1999, through December 31, 2010. We also examined the Nationwide Inpatient Sample hospital discharge database to determine the number of VGS-IE cases included between 1999 and 2009. We identified 22 cases with VGS-IE in Olmsted County over the 12-year study period. Rates of incidence (per 100 000 person-years) during time intervals of 1999–2002, 2003–2006, and 2007–2010 were 3.19 (95% confidence interval, 1.20–5.17), 2.48 (95% confidence interval, 0.85–4.10), and 0.77 (95% confidence interval, 0.00–1.64), respectively ($P=0.061$ from Poisson regression). The number of hospital discharges with a VGS-IE

**there has been no perceivable increase in the incidence of VGS-IE in Olmsted County, Minnesota, since the publication of the 2007 American Heart Association endocarditis prevention guidelines. (*Circulation. 2012;126:60-64.)***

ACC.14
TCT@ACC-i2 | innovation in intervention

A1933
JACC April 1, 2014
Volume 63, Issue 12

## Valvular Heart Disease

# TRENDS IN INFECTIVE ENDOCARDITIS (IE) INCIDENCE AND MICROBIOLOGY BEFORE AND AFTER 2007 IDSA/ACC/AHA IE PROPHYLAXIS GUIDELINES CHANGE

Moderated Poster Contributions
Hall C
Monday, March 31, 2014, 10:15 a.m.-10:30 a.m.

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Session Title: Valvular Heart Disease V
Abstract Category: 28. Valvular Heart Disease: Clinical
Presentation Number: 1281M-368C

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Authors: *Sadip Pant, Abhishek Deshmukh, Kathan Mehta, Nileshkumar Patel, Neeraj Shah, Apurva Badheka, Smith Giri, Naga Venkata Pothineni, Ankit Chothani, Kaustubh Dabhadkar, Jawahar Mehta, University of Arkansas for Medical Sciences, Little Rock, AR, USA*

**Background:** The goal of this study was to evaluate the trend in incidence and the microbiology associated with before and after the change in IE prophylaxis guideline in 2007 by IDSA/ACC/AHA.

**Methods:** Healthcare Cost and Utilization Project - National Inpatient Sample (NIS) database was used to perform a retrospective observational cohort study to investigate the incidence of IE in the United States (US) from 2000 through 2011. Poisson regression model (PROC GENMOD, SAS 9.3) was used to compare the trend of incidence as well as outcome between periods 2000-2007 and 2008-2011.

**Results:** There were 453,111 estimated discharges with a diagnosis of IE from 2000-2011. Overall, there was a significant increase in the

**Conclusion:** Our study shows that the incidence of IE has increased consistently over the last decade in the US without any significant difference before and after the prophylactic guideline change in 2007. However, the actual rise in the number of cases is mainly related to Staphylococcal etiology of IE

etiology of IE

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TCTJACC-63 | Innovation in Intervention

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JACC April 1, 2014
Volume 63, Issue 12

## Congenital Heart Disease

# INFECTIVE ENDOCARDITIS PROPHYLAXIS - CURRENT PRACTICE AMONGST PEDIATRIC CARDIOLOGISTS: ARE WE FOLLOWING 2007 GUIDELINES?

Poster Contributions
Hall C
Monday, March 31, 2014, 9:45 a.m.-10:30 a.m.

Session Title: Advanced Imaging and Practice Patterns in Pediatric and Congenital Heart Disease
Abstract Category: 10. Congenital Heart Disease: Pediatric
Presentation Number: 1266-270

Authors: *Nishant C. Shah, Neil Patel, Ronak Naik, Penn State Hershey Children's Hospital, Hershey, PA, USA, University of Tennessee Health Science Center, Le Bonheur Children's Hospital, Memphis, TN, USA*

**Background:** The indications for antibiotics prophylaxis for prevention of infective endocarditis (IE) have been revised in 2007. A web-based, anonymous survey was conducted in 2013 to evaluate the current practice for IE prophylaxis amongst the pediatric cardiologists.

Table 1: Clinical scenario and IE prophylaxis

| Clinical scenario | IE prophylaxis recommended (%) | IE prophylaxis not recommended (%) |
|---|---|---|
| Rheumatic heart disease (more than mild degree of valvular lesion) | 53 | 47 |
| Fontan palliation without fenestration | 55 | 45 |
| Ross procedure | 45 | 55 |
| Intravenous pacemaker lead in right ventricle and small VSD | 44 | 56 |
| > mild degree of valvular lesion in single ventricle | 62 | 38 |
| Residual Aortic valve lesion post repair | 38 | 62 |
| Pulmonary valve replacement surgery in TOF | 62 | 38 |
| Cardiac transplant recipient without valvulopathy | 34 | 66 |
| Residual Mitral valve lesion post repair | 34 | 66 |

Results:
Total 302 responses were received. The lesions, for which significant level of non-agreement for IE prophylaxis exist, are shown in table1.

Most cardiologists indicated no prophylaxis in cases of clinically silent PDA (97%), small muscular ventricular septal defect (VSD) (95%) and
bicuspid aortic valve without valvulopathy (94%).

Despite current guidelines, IE prophylaxis is not recommended in “Post Glenn/hemiFontan procedure” and “VSD repair with residual shunt” by 35% and 32% respectively.

**57% do not follow 2007 IE guidelines** exclusively for various reasons including **conservative approach (20%), patient/family’ s unwillingness (13%)** and **lack of clarity in 2007 guidelines (12%).**
Only 33% discuss the
importance of dental hygiene with patients who are at risk of IE regularly.

Table 1 Classes of recommendations

| Classes of Recommendations | Definition |
|---|---|
| Class I | Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective. |
| Class II | Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure. |
| *Class IIa* | Weight of evidence/opinion is in favour of usefulness/efficacy. |
| *Class IIb* | Usefulness/efficacy is less well established by evidence/opinion. |
| Class III | Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful. |

Table 2 Levels of evidence

| | |
|---|---|
| Level of Evidence A | Data derived from multiple randomized clinical trials or meta-analyses. |
| Level of Evidence B | Data derived from a single randomized clinical trial or large non-randomized studies. |
| Level of Evidence C | Consensus of opinion of the experts and/or small studies, retrospective studies, registries. |

# Perioperative management of antiplatelet and anticoagulation therapy

경북대학교병원
김 근 직

- Bleeding risk :
  - Low
    - cataract extraction,
    - most cutaneous surgery,
    - laparoscopic cholecystectomy or
    - hernia repair,
    - CAG)
  - Moderate
    - major intraabdominal surgery,
    - major intrathoracic surgery,
    - major orthopedic surgery,
    - pacemaker insertion)
  - High
    - neurosurgical procedure
    - prostatectomy or bladder surgery, heart valve replacement
    - CABG,
    - major vascular surgery
    - renal biopsy
    - bowel polypectomy
    - major cancer surgery

- Cardiac event risk
  - low( AF, CHF, IHD stent)
  - high( IHD stent)

- Thromboembolic risk
  - Low :
    - AF - $CHADS_2$ score of 0 to 2(no stroke, TIA) /
    - VTE - single VTE occurred > 12 mo ago(no risk factor) /
    - mechanical heart valve - bileaflet AV prosthesis AF(no risk factor)
  - High :
    - AF - $CHADS_2$ score of 5 or 6,
    - recent(within 3 mo) stroke or TIA,
    - RHD / VTE - recent(within 3 mo) VTE,
    - severe thrombophilia /
    - mechanical heart valve - any MV prosthesis,
    - older(caged-ball or tilting disc) AV prosthesis,
    - recent(within 6 mo) stroke or TIA

# Antiplatelet (aspirin/clopidogrel)

- Bleeding risk

  Low : cataract extraction, most cutaneous surgery
  laparoscopic cholecystectomy or hernia repair, CAG

  Moderate : major intraabdominal surgery
  major intrathoracic surgery
  major orthopedic surgery
  Pacemaker insertion

- Cardiac event risk

  Low : AF, CHF

  High : IHD stent

- Recommend to keep aspirin
- Suggest keeping plavix

# Antiplatelet (aspirin/clopidogrel)

- Bleeding risk : high
- Cardiac event risk : low

➢ Stop both before 7~10 days

# Antiplatelet (aspirin/clopidogrel)

- Bleeding risk : moderate
- Cardiac event risk : low

- ➢ Recommend to keep aspirin
- ➢ stop both before 7 days

# Antiplatelet (aspirin/clopidogrel)

- Bleeding risk : moderate
- Cardiac event risk : high

- ➢ Recommend to keep aspirin
- ➢ stop both before 5 days

# Antiplatelet (aspirin/clopidogrel)

- Bleeding risk : high
- Cardiac event risk : high

➢ Stop both before 4~5days

# Anticoagulation (warfarin)

- Bleeding risk : low
- Thromboembolic risk : low, high

➢ Recommand to keep warfarin

# Anticoagulation (warfarin)

- Bleeding risk : moderate, high
- Thromboembolic risk : low

➢ Stop warfarin before 5 days

➢ No bridging therapy

# Anticoagulation (warfarin)

- Bleeding risk ; moderate, high
- Thromboembolic risk : high

- ➢ Stop warfarin before 4~5days
- ➢ Bridging therapy
- ➢ Start 24h after surgery

# Acute Postoperative Pain Management(술 후 통증 관리)

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마취통증의학과
민두재

# 통증이란?

* 실질적인 또는 잠재적인 조직손상과 연관된 감각적, 정서적인 불유쾌한 경험.

* 수술 후 통증
  - 조직의 손상, 내장기관의 팽창, 질병 등 여러가지 원인으로 인해 발생하는 복합적인 생리적 반응.

# 통증의 전달 경로

* Nocieption(침해수용)
  - 열, 전류, 약물 등 물리적, 화학적 자극 또는 기계적 자극의 감지 및 전달
  - nocieptor(침해수용체)
    : C형 및 A-delta 신경섬유의 말단부

* 침해수용체를 통해 감지된 자극은 척수를 통해 중추 신경으로 전달된다.

# Spinothalamic Tract(척수시상로)

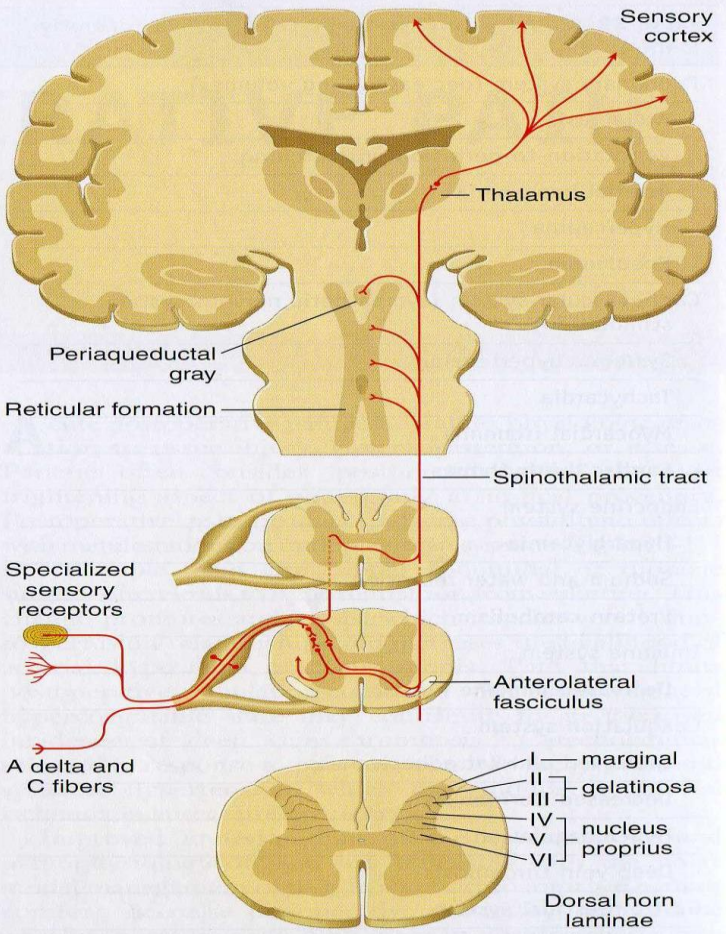


**Figure 39-1** Afferent sensory pathways for recognition and transmission of painful stimuli. (From Lubenow TR, Ivankovich AD, Barkin RL. Management of acute postoperative pain. *In* Barash PG, Cullen BF, Stoelting RK [eds]: Clinical Anesthesia. Philadelphia: Lippincott Williams & Wilkins, 2006, pp 1405-1440, with permission.)

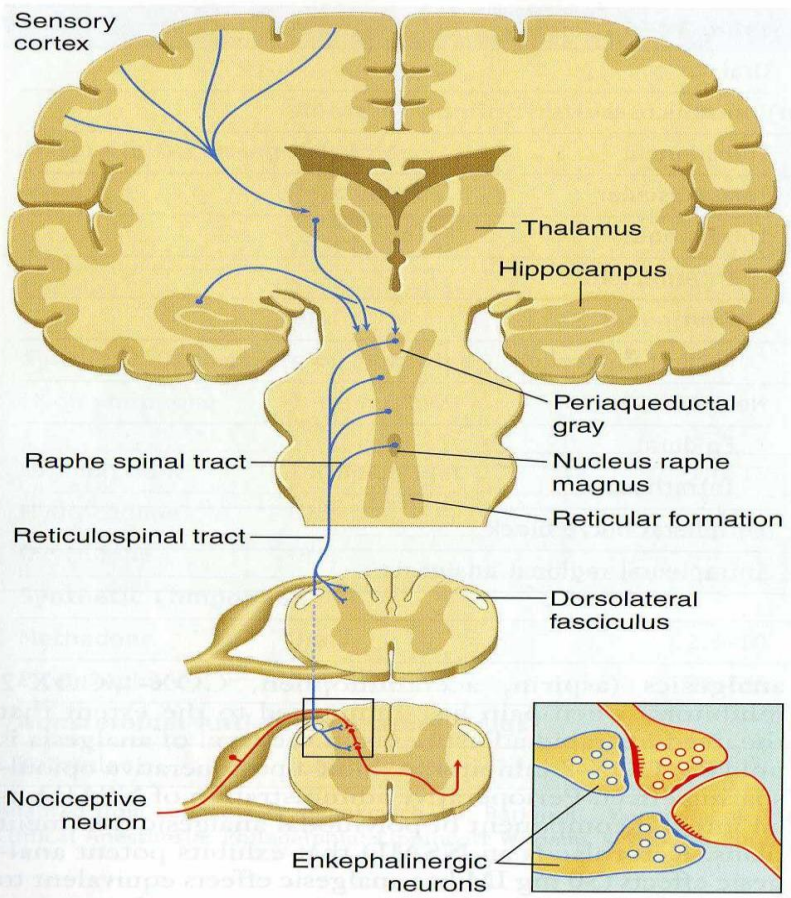


**Figure 39-2** Descending efferent inhibitory (modulating) pathways involved in nociceptive regulation. (From Lubenow TR, Ivankovich AD, Barkin RL. Management of acute postoperative pain. *In* Barash PG, Cullen BF, Stoelting RK [eds]: Clinical Anesthesia. Philadelphia: Lippincott Williams & Wilkins, 2006, pp 1405-1440, with permission.)

# 침해수용체에 영향을 미치는 물질

* Neurotransmitter(신경 전달 물질)

1. Excitatory(활성화 물질)
   - Glutamate, Aspartate, Cholecystokinin, Vasoactive Intestinal Polypeptide, Gastrin-releasing peptide, Angiotensin, Substance P

2. Inhibitory(억제 물질)
   - Enkephalins, Endorphins, Substance P, Somatostatin

# 통증의 종류(1)

## 1. 체성 통증(somatic pain)

### 1) 표재성 통증(superficial pain)

- 피부나 점막 부위의 기계적, 화학적, 물리적 자극에 의해 발생
- 통증의 양상은 날카롭고, 찌르는 듯하고, 욱신거리는 등 다양
- 국소부위에 한정되어 나타남.

### 2) 심재성 통증(deep pain)

- 관절, 인대, 근육 또는 근막 및 흉막을 자극함으로써 발생
- 무디고 쑤시는 듯한 통증
- 국소적으로 나타나는 경우는 드물다.
- 특히 통증이 심할 경우 다른 부위로 전파되는 경향이 있어 연관통을 일으키는 경우가 많다.

# 통증의 종류(2)

## 2. 내장통(Visceral Pain)

- 내장에 분포된 통각섬유에 의해 몸 속 깊이 느껴지는 둔한 통증
- 통증의 국소부위가 명확하지 않고 오심 및 구토 등 여러가지 자율신경성 증상을 동반한다.

## 3. 연관통(Referred Pain)

- 내장에 분포된 통각섬유가 흥분했음에도 불구하고 통증은 내장과 멀리 떨어진 체성조직에 나타나는 경우
- 대체로 그 통증을 발생케하는 조직과 발생학적으로 같은 체절에 나타남.
- 예) 협심증이 있는 경우 우측어깨와 좌완내부에 투사
  요관이 늘어날 경우 음낭에 통증이 나타남

# 통증의 종류(3)

## 4. 심인성 통증(Psychogenic Pain)

- 신체적으로 만족할  만한 원인을 발견할 수 없으며 해부학적인 견지로도 설명이 불가능한 통증을 호소하고 그 원인이 심리적인 원인으로 간주될 때
- 환경에서의 자극과 관련되어 증상이 악화되거나 감소하게 됨
- 급작스럽게 나타나서 수일에서 수주간 또는 수년간 지속되기도 하고 신체 여러 부위에서 통증을 느끼는 경우가 많다.

## 5. 중추성 통증(Cental Pain)

- 종양, 뇌출혈, 척수공동증(syringomyelia), AIDS 등 중추 신경 조직의 손상으로 척수, 뇌간, 시상, 피질등을 자극하여 타는 듯한 격한 통증이 나타나게 된다.

# 수술 후 통증의 부작용

1. 호흡기계 – 무기폐, 저산소증, 폐렴 등
2. 심혈관계 – 고혈압, 빈맥, 심근경색증 등
3. 내분비계 – 고혈당, 수분저류, 단백 소실 등.
4. 면역계 – 면역력 감소
5. 지혈 관련 – 혈소판 소모, 과응고증,
   심부정맥 혈전증 등
6. 내장기관 – 장폐색증 등
7. 비뇨기계 – 뇨 저류 등.

# 급성 통증 치료에 영향을 주는 요인

1. 연령
   – 나이가 많을 수록 요구량 감소
2. 체중
   - 체중과 아편유사제의 요구량은 관계가 없음
3. 문화
   - 공격적인 성격이거나 불안한 환자일수록 통증 점수고 더 높고 통증 치료에 필요한 약물의 요구량이 더 많다.
4. 수술 부위와 범위
   - 개흉술, 상복부 수술, 신적출술이 허니아 봉합, 유방절제술 및 고관절 치환술 등에 비해 통증 정도도 심하고 진통제 요구량도 많다.
5. 약물 중독이나 아편유사제의 병력
   - 약물 중독 환자들에게는 아편유사제의 투여를 제한하는 경향

# 통증 치료에 사용하는 약물 종류

## 1. 아편 유사제

- 뇌와 척수에 존재하는 아편유사제 수용체에 결합하여 효과를 나타냄

## 2. 비스테로이드성 소염 진통제(NSAIDs)

- Prostaglandine
  : 통증수용체의 역치를 낮추어 신경말단을 기계적, 화학적 자극에 민감하게 하는 물질
- NSAIDs는 prostaglandine 합성을 방해하여 진통작용을 나타냄

## 3. 보조 진통제

- 진통제의 약리효과를 상승시키고 부작용을 최소화 하기 위해 병용하는 약제
- 항우울제, 항불안제, 항경련제, 신경근 이완제, 항히스타민제 등

# 술 후 제통 약물 예시

**Table 39–7** Oral and Parenteral Analgesics for Treatment of Acute Postoperative Pain

| | Route of Administration | Dose (mg) | Half-Life (hr) | Analgesic Action (hr) | | |
|---|---|---|---|---|---|---|
| | | | | *Onset* | *Peak* | *Duration* |
| **Naturally Occurring Alkaloids** | | | | | | |
| Morphine | Intravenous | 2.5-15 | 2-3.5 | | 0.125 | |
| | Intramuscular | 10-15 | 3 | 0.3 | 0.5-1.5 | 3-4 |
| | Oral | 30-60 | | 0.5-1 | 1-2 | 4 |
| Codeine | Intramuscular | 15-60 | | 0.25-0.5 | 1-5 | 4-6 |
| | Oral | 15-60 | | 0.25-1 | 0.5-2 | 3-4 |
| **Synthetic Derivatives of Morphine** | | | | | | |
| Hydromorphone | Intramuscular | 1-4 | 2-3 | 0.3-0.5 | 1 | 2-3 |
| | Oral | 1-4 | 2-3 | 0.5-1 | 1 | 3-4 |
| Oxymorphone | Intramuscular | 1.0-1.5 | 3.3-4.5 | 0.5 | 1 | 2-4 |
| Hydrocodone | Oral | 5-7.5 | 2-3 | | | 3-8 |
| Oxycodone | Oral | 5 | | 0.5 | 1-2 | 3-6 |
| **Synthetic Compounds** | | | | | | |
| Methadone | Oral | 2.5-10 | 3-4 | 0.5-1 | 1.5-2 | 4-8 |
| Propoxyphene | Oral | 32-65 | 12-16 | 0.25-1 | 1-2 | 3-6 |
| **Nonsteroidal Anti-inflammatory Drugs** | | | | | | |
| Ketorolac | Intramuscular | 30 | 5 | | 0.75-1 | 3-6 |

Adapted from Lubenow TR, Ivankovich AD, Barkin RL. Management of acute postoperative pain. *In* Barash PG, Cullen BF, Stoelting RK (eds): Clinical Anesthesia. Philadelphia: Lippincott Williams & Wilkins, 2006, pp 1405-1440.

# 아편 유사제의 분류

1. 작용제(Agonist)
   - 아편유사제 수용체에 결합하고 수용체를 자극하여 최대 반응을 유발시킬수 있는 약제
2. 길항제(Antagonist)
   - 아편유사제 수용체에 결합하지만 수용체를 자극하지 못하고 아편양 작용제의 효과를 반전시키는 약제
3. 부분길항제(Partial Agonist)
   - 아편유사제 수용체를 자극하지만 천장효과가 있고 작용제에 비해 최대 반응을 유발시키지 모사는 약제
4. 작용길항제(Agonist-Antagonist)
   - 어떤 아편유사제 수용체에는 작용제로 작용하고 다른 아편양 수용체에는 길항제로 작동하는 약제

# 아편유사제 수용체의 종류 및 효과

**Table 10–2** Classification of Opioid Receptors

| Features | $Mu_1$ | $Mu_2$ | Kappa | Delta |
|---|---|---|---|---|
| Effects | Analgesia (supraspinal, spinal)<br>Euphoria<br>Low abuse potential<br>Miosis<br>Bradycardia<br>Hypothermia<br>Urinary retention | Analgesia (spinal)<br>Depression of ventilation<br>Physical dependence<br>Constipation (marked) | Analgesia (supraspinal, spinal)<br>Dysphoria, sedation<br>Low abuse potential<br>Miosis<br>Diuresis | Analgesia (supraspinal, spinal)<br>Depression of ventilation<br>Physical dependence<br>Constipation (marked)<br>Urinary retention |
| Agonists | Endorphins<br>Morphine<br>Synthetic opioids | Endorphins<br>Morphine<br>Synthetic opioids | Dynorphins | Enkephalins |
| Antagonists | Naloxone<br>Naltrexone<br>Nalmefene | Naloxone<br>Naltrexone<br>Nalmefene | Naloxone<br>Naltrexone<br>Nalmefene | Naloxone<br>Naltrexone<br>Nalmefene |

Adapted from Atcheson R, Lambert DG. Update on opioid receptors. Br J Anesth 1994;73:132-134.

# 아편유사제의 부작용

1. 가려움증(Pruritus)
2. 오심(nausea) 및 구토(vomiting)
3. 뇨저류(urinary retention)
4. 호흡저하(depression of ventilation)
5. 진정(sedation)
6. 중추신경계 항진
   (Central nervous system excitation)
7. 잠복 바이러스 감염의 활성
   (Activation of latent viral infections)
8. 성기능 장애(Sexual dysfunction)
9. 수분 저류(Water retention)

# NSAIDs의 종류 및 효과

1. Aspirin(Acetylsalicylic acid)
   - 두통이나 골관절염 등으로 인한 경미한 통증에 유용
   - 해열작용
2. Indomethacin
   - 항염증 효과 우수 : 관절염, 강직성척추염의 일차약
3. Ketorolac(Tarasyn)
   - 중증도 이하의 통증에 효과적
   - 아편유사제의 진통효과를 상승시킴
4. Diclofenac(Valentac)
   - 진통작용, 해열작용, 소염작용
   - 류마티스 관절염 같은 만성 염증성 질환의 통증치료
5. Ibuprofen
   - 항염증 효과, 해열작용 : 가장 널리 사용되는 약제
6. Acetaminophen(Tylenol)
   - 경하거나 중증도의 통증치료 : 위장관 자극이 거의 없다.

# NSAIDs의 부작용

1. **위산분비 촉진 & 위점액과 중탄산나트륨의 분비 감소**
   - 위궤양 유발, 십이지장 궤양, 위장관 염증, 위장관 출혈, 위장관 천공 등이 드물게 보고되고 있다.
2. **신장 손상**
   - 신질환이 있거가 혈류량이 감소된 환자에서 장기간 복용할 경우 발생 가능
3. **출혈 경향**
   - Prostaglandin 합성 차단, 혈소판 응집 억제로 인하여 수술 후 사용시 출혈가능성을 높일 수 있다
   - Acetaminophen은 혈소판 응집에 영향이 없다.
4. **Indomethacin의 경우**
   - 골수 억제 증상 : 장기간 복용시
   - 과민성 반응 : 발진, 소양증, 두드러기, 천식 발작
5. **Ibuprofen**
   - 속쓰림, 복부 팽만감, 구역 등

# 수술 후 통증을 치료하는 방법

1. 전신적 아편유사제의 투여
   1) 근주법
      - 주입시의 통증
      - 간헐적으로 투여하기 때문에 일정하게 혈중 농도를 유지할 수 없는 단점
      - 주입부위에 따라 흡수 정도가 다름
   2) 정맥투여
      - 간헐적 투여 : 편리함, 진통 효과가 빠름.
        : 갑작스런 혈중 농도의 증가에 의해 부작용이 나타날 수 있다.
      - 지속적 투여 : 혈중 농도는 일정하게 유지됨
        : 시간에 따라 통증 양상이 변하여 적절한 용량 예측이 어려움.
2. 자가 통증 조절법(Patient controlled analgesia)
3. 국소마취법
   - 호흡기, 심혈관계, 신경내분비계를 호전시키며 회복기간을 단축시킴
   - 국소마취제를 사용 : 부위 침윤법, 말초신경 차단법, 흉막간 차단법,
     신경초 차단법, 척추마취와 경막외마취
4. 척수강내 투여
   - 아편유사제나 국소마취제를 척수강내에 일회 주사하거나 지속적으로 주입
   - 단일제제 사용할 경우 용량과다에 의한 부작용이 나타날 수 있다.
   - 아편유사제와 국소마취제를 병용하는 것이 부작용이 적다.

# 자가 통증 조절법(PCA)

*** 장점**

1) 환자마다 다른 요구량을 맞출수 있음
2) 환자가 통증을 느낄 때 바로 추가 투여 가능
3) 환자가 통증 느끼는 정도에 따라 약물 투여량을 빠르게 적정할 수 있음.
4) 환자의 활동을 제약하지 않음
5) 의료진의 시간을 절약할 수 있음

**1. 정맥로를 이용한 자가 통증 조절법(IV-PCA)**

- 지속 주입과 간헐적 주입의 병용
- 환자 상태, 수술 종류, 부작용의 최소화 등을 고려하여 다양하게 적용
- 아편유사제, 비스테로이드성 소염제, 항구토제 등을 복합적으로 사용.

**2. 경막외 자가통증조절법(Epidural PCA)**

- IV PCA에 비해 아편 유사제 요구량이 적고 통증 효과는 더 좋음
- 아편유사제, 국소마취제를 병용함

# PCA에 사용되고 있는 약물 예시

**표 18-2.** 정맥로를 이용한 자가통증조절법의 약물투여

| 아편유사제 | 농도 | 부하량 | 일시투여량 | 폐쇄간격(min) | 지속주입량(/hr) |
|---|---|---|---|---|---|
| Morphine | 1 mg/mℓ | 3-10 mg | 0.5-1.5 mg | 6-8 | 0.5-1.5 mg |
| Meperidine | 10 mg/mℓ | 25-50 mg | 5-15 mg | 6-8 | |
| Hydromorphone | 0.2 mg/mℓ | 0.5-1 mg | 0.1-0.3 mg | 6-8 | 0.1-0.3 mg |
| Oxymorphone | 0.1 mg/mℓ | 0.3-1 mg | 0.1-0.2 mg | 6-8 | 0.1-0.2 mg |
| Fentanyl | 20 μg/mℓ | 30-100 μg | 10-20 μg | 5-6 | 10-20 μg |

**표 18-4.** 경막외 자가통증조절법을 위한 약물 투여

| 아편유사제 | 지방용해도 | 농도(μg/mℓ) | 부하량 | 일시투여량(μg) | 폐쇄간격(분) | 지속주입량(μg/h) |
|---|---|---|---|---|---|---|
| Morphine | 1 | 50 | 2-4 mg | 100-200 | 10-15 | 300-600 |
| Hydromorphone | 1 | 10 | 0.5-1.5 mg | 20-30 | 6-8 | 80-120 |
| Fentanyl | 800 | 5 | 75-100 μg | 10-15 | 6 | 30-75 |
| Sufentanil | | 2 | 30-50 μg | 4-6 | 6 | 5-10 |

# 부적절한 진통과 부작용에 대한 관리

**1. 부적절한 진통**

- 수술이나 손상후 발생할 수 있는 합병증 등 다른 원인 관찰
- 평균 시간 당 2회 이하의 일시투여량을 투여받았다면 요구 버튼을 더 자주 사용하도록 격려
- 3회 이상 투여 받았을 경우에는 일시투여량의 용량을 증가시킴

**2. 부작용**

1) 오심 및 구토 – 항구토제 투여, 일시투여량 또는 주입속도 감소
   – 효과가 없으면 약물이나 제통 방법을 바꿈
2) 가려움증 – morphine에서 많음 : 다른 약제로 바꿈
   – 항히스타민 제제 : 진정 효과의 부작용 주의
3) 진정 효과 및 호흡 억제 – 일시투여량 감소,
   심할 경우 naloxone 투여를 고려
4) 뇨저류 – 카테터를 삽입하여 배출시키거나 도뇨관 삽입
5) 의식혼란 – 부적절한 PCA 버튼 사용 가능, PCA를 중지시킴

# 수혈 가이드라인

신홍주

연세대학교 세브란스 심장혈관병원 심장혈관외과

June 20 / 2015

# Contents

1. General aspects
2. Cardiac surgery
3. STS guideline
4. Recent trends

RECOMMENDATION

# Recommendations for the transfusion management of patients in the peri-operative period. III. The post-operative period.

Giancarlo Maria Liumbruno[1], Francesco Bennardello[2], Angela Lattanzio[3], Pierluigi Piccoli[4], Gina Rossetti[5] for the Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) Working Party

*[1]Units of Immunohaematology, Transfusion Medicine and Clinical Pathology, "San Giovanni Calibita" Fatebenefratelli Hospital, Rome; [2]Service of Immunohaematology and Transfusion Medicine, "Civile-Maria Paternò Arezzo" Hospital, Ragusa; [3]Service of Immunohaematology and Transfusion Medicine, Hospital of Carbonara, Bari; [4]Service of Immunohaematology and Transfusion Medicine, Hospital of Verona, Verona; [5]Service of Immunohaematology and Transfusion Medicine, Hospital of Trento, Trento; Italy*

Blood Transfus 2011;9:320-35

**Table I** - Possible causes of surgery-related anaemia in the post-operative period.

| |
|---|
| **Acute or chronic blood loss** |
| - Intra-operative or post-operative bleeding |
| - Repeated blood sampling |
| - Gastrointestinal bleeding |
| **Reduced erythropoiesis** |
| - Reduced production of erythropoietin |
| - Resistance to the action of erythropoietin |
| - Reduced ability to use iron |
| **Shortened red blood cell survival** |

**Table II** - Strategies that can be used to reduce the need for blood transfusions.

| |
|---|
| - Constant monitoring of the critically ill patient |
| - Prophylaxis against gastrointestinal bleeding |
| - Limitation of iatrogenic blood losses |
| - Optimisation of oxygen release to tissues |
| - Containment of oxygen consumption by tissues |
| - Optimisation of erythropoiesis |

**Table III -** Clinical parameters to evaluate for transfusion purposes.

| | |
|---|---|
| Age | Cardiac function |
| Signs and symptoms of anaemia | Lung function |
| Speed of blood loss | Ischaemic heart disease |
| Amount of blood loss | Drug treatments |

**Table IV -** Clinical and instrumental parameters indicative of hypoxia in the anaemic, normovolaemic patient in the post-operative period.

**Cardiopulmonary symptoms**

- Tachycardia
- Hypotension
- Acute hypotension of unknown origin
- Dyspnoea

**Electrocardiographic signs typical of ischaemia**

- Newly occurring ST segment elevation or depression
- Onset of arrhythmias
- Newly occurring localised altered contractility of the myocardium

**Global indices of insufficient $O_2$ release, evaluated by invasive methods**

- Increase in overall $O_2$ extraction greater than 50%
- Reduction of $O_2$ uptake by more than 10% of the initial value
- Reduction of mixed venous $O_2$ saturation to below 50%
- Reduction of peripheral mixed venous $pO_2$ to below 32 mmHg
- Reduction of central venous $O_2$ saturation to below 60%
- Lactate acidosis (lactates >2 mmol/L + acidosis)

**Table V -** Decision criteria for the transfusion of patients with acute post-operative anaemia: reduction of volaemia

| Class of haemorrhage | Reduction of volaemia (%) | Blood loss (mL)* | Indication for transfusion of RCC | GoR |
|---|---|---|---|---|
| Class I | <15% | <750 | Not necessary, unless pre-existing anaemia | 1C+ |
| Class II | 15-30% | 750-1,500 | Not necessary, unless pre-existing anaemia and/or cardiopulmonary disease | 1C+ |
| Class III | 30-40% | 1,500-2,000 | Probably necessary | 1C+ |
| Class IV | >40% | >2,000 | Necessary | 1C+ |

Legend:
RCC: red cell concentrate; GoR: Grade of recommendation; *: in an adult weighing 70 kg with an intravascular blood volume of 5,000 mL.

**Table VI -** Decision criteria for the transfusion of patients with acute post-operative anaemia

| Hb value | Presence of risk factors/mechanisms of compensation | TT with RCC | GoR |
|---|---|---|---|
| ≤60 g/L | TT is almost always necessary* | YES* | 1C+ |
| 60-80 g/L | Absence of risk factors/adequate mechanisms of compensation | NO | 1C+ |
| | Presence of risk factors (e.g. coronary artery disease, heart failure, cerebrovascular disease/ limited mechanisms of compensation) | YES | 1C+ |
| | Presence of symptoms indicative of hypoxia (physiological transfusion triggers: tachycardia, hypotension, electrocardiographic signs of ischaemia, lactic acidosis, etc.) | YES | 1C+ |
| 80-100 g/L | Presence of symptoms indicative of hypoxia (physiological transfusion triggers: tachycardia, hypotension, electrocardiographic signs of ischaemia, lactic acidosis, etc.) | YES | 2C |
| >100 g/L | TT is very rarely needed** | NO** | 1A |

**Notes:**
- The Hb value is not an adequate indicator of a person's capacity to release $O_2$ to the tissues.
- In the presence of hypovolaemia the Htc does not reßect blood loss.
- The presence of individual risk factors can mean that the transfusion triggers need to be different from those indicated.

Legend:
RCC: red cell concentrate; GoR: grade of recommendation; TT: transfusion therapy;
*: Hb values below 60 g/L may be tolerated if evaluation of the patient shows that there are no risk factors and that compensatory mechanisms are adequate;
**: the individual patient must be evaluated in order to determine whether transfusion therapy is indicated to raise the Hb above 100 g/L.

# Contents

*Table 9.5 • Management of Postoperative Mediastinal Bleeding*

1. Explore early for significant ongoing bleeding or tamponade
2. Ensure that chest tubes are patent
3. Warm patient to normothermia
4. Control hypertension, agitation, and shivering
5. Check results of coagulation studies (INR, PTT, platelet count or TEG)
6. Protamine 25 mg IV for two doses if elevated PTT
7. Consider use of 10 cm PEEP with caution
8. Packed cells if hematocrit <26%
9. Platelets, 1–2 "six packs"
10. Fresh frozen plasma, 2–4 units
11. Cryoprecipitate, 6 units
12. Desmopressin (DDAVP) 0.3 µg/kg IV over 20 minutes (if suspect platelet dysfunction from uremia or aspirin)
13. Recombinant factor VIIa 60 µg/kg if severe coagulopathy
14. **Transesophageal echocardiography** if concerned about tamponade
15. **Urgent exploration** for significant ongoing bleeding or tamponade
16. **Emergency exploration** for exsanguinating hemorrhage or near cardiac arrest from tamponade

Bojar R. Manual of Perioperative Care in Adult Cardiac Surgery, Fifth Edition. West Sussex,UK: Wiley-Blackwell, 2011:364-70.

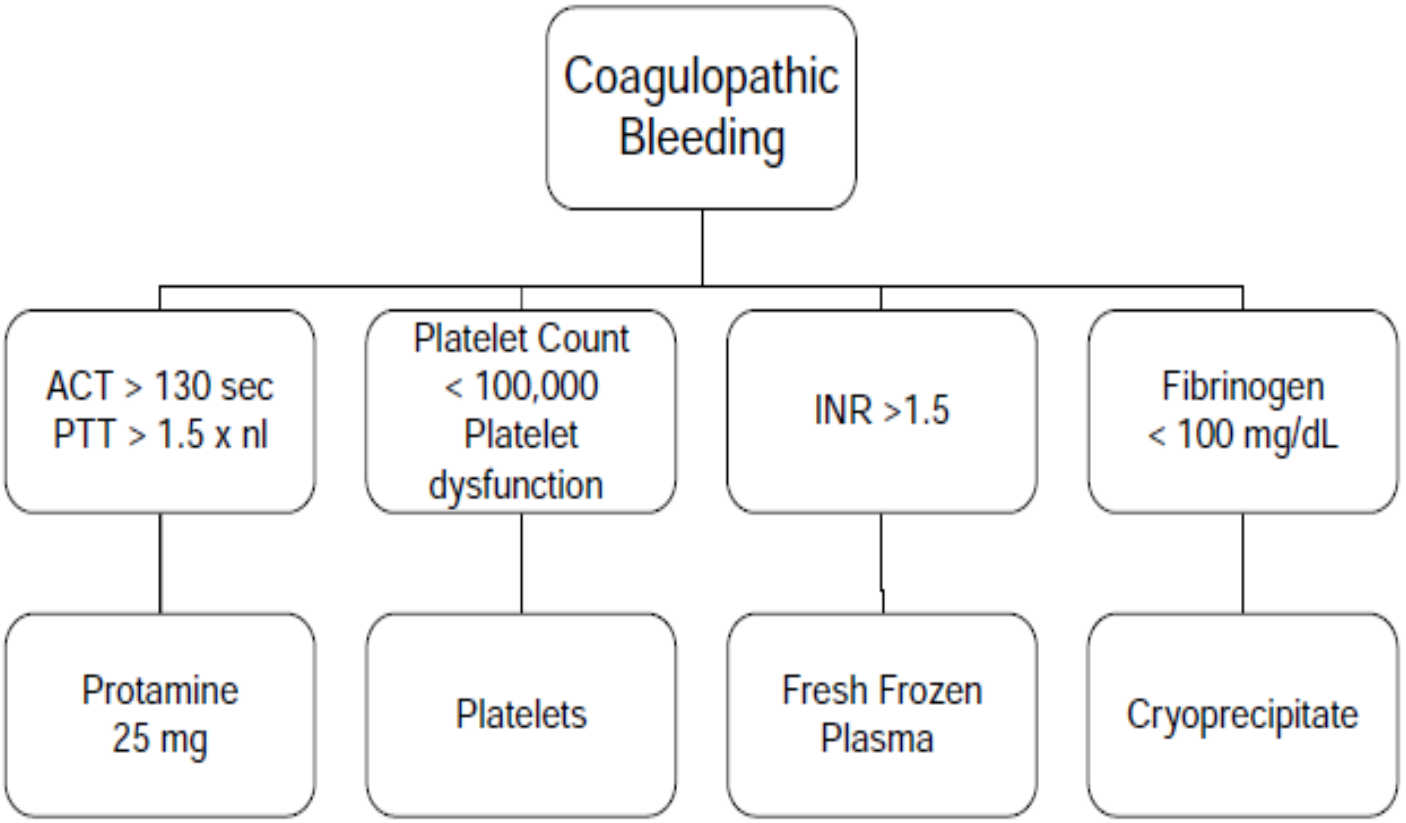


**Figure 9.4** • Point-of-care testing of routine coagulation studies to treat postoperative bleeding.

- The patient who has received aspirin, clopidogrel, or IIb/IIIa inhibitors, or is uremic, is likely to have platelet dysfunction and will benefit primarily from platelet transfusions, even if the platelet count is normal

Plt. Life span
-> 7days

- Platelets, FFP, and cryoprecipitate may be necessary in patients who have had a long duration of CPB (>3 hours) or who have received multiple blood products during surgery

- Thromboelastogram

  to identify the exact nature of the hemostatic defect, allowing for more prompt initiation of appropriate therapy

- An elevated PT - FFP and/or cryoprecipitate
- An elevated PTT or ACT

  - Additional protamine should be given first

  - with an understanding that an elevated PTT may not be related to heparin

  - protamine could exacerbate a coagulopathy

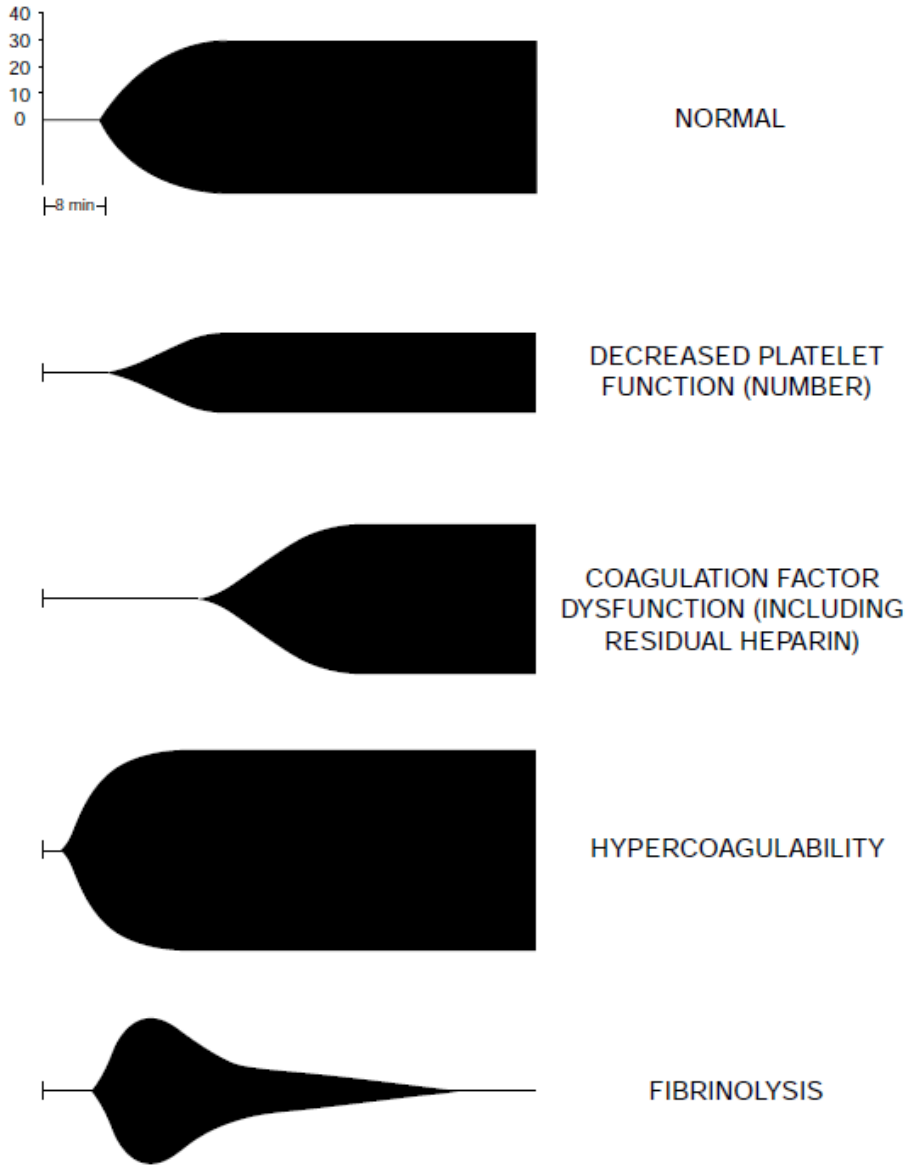


**Figure 9.1** • Representative thromboelastogram tracings.

- Fibrinogen levels <100 mg/dL – cryoprecipitate
- A platelet < 100,000/mL - platelet transfusions
- Because CPB induces platelet dysfunction, suspicion of a qualitative defect in the actively bleeding patient should be treated with platelets even if the platelet count is adequate
- Note: if the patient has minimal bleeding

  Abnormal results do not need to be treated

- Platelet transfusions are not indicated in the nonbleeding patient until the platelet count approaches 20,000–30,000/mL
- Ongoing mediastinal bleeding should be transfused to maintain a hematocrit at a reasonable level (>25%) as a safety margin

- Notably, platelet function is impaired in the profoundly anemic patient
- Red cells increase platelet-to-platelet interaction and facilitate the interaction of platelets with the subendothelium to improve hemostasis

- Protamine may be given in a dose of 25–50 mg (5 mg/min) if the PTT is elevated
- Reinfusion of cell-saver blood may reintroduce a small amount of heparin that contributes to bleeding
- This may occur because the half-life of protamine is only about 5 minutes

- Excess protamine

  platelet dysfunction

  enhances fibrinolysis

  decreases clot strength

-> will elevate the ACT and cause bleeding

# Packed red blood cells (RBCs)

- Approximately 200mL
- 1 unit will raise the Hct of a 70 kg man by 3%
- At least 70% of transfused cells survive 24hrs
- Fresh whole blood (less than 6 hours old) has a hematocrit of about 35% and contains clotting factors and platelets

# Platelets

- If the platelet count is less than 10,000/mL
- 6-unit bag
- Each unit should increase the platelet count by about 7000–10,000/mL in a 75 kg adult
- One unit of platelets contains 70% of the platelets in a unit of fresh blood, but platelets lose some of their functional capacity during storage

- Those stored at 4℃ are useful for only 24 hours (50–70% of total platelet activity is present at 6hrs)
- Note: Platelet function is impaired in patients with hypofibrinogenemia and when the Hct < 30%
- Thus, use of cryoprecipitate and red cell transfusion to raise the hematocrit towards 30% can be considered to improve platelet function

- The decision to transfuse platelet concentrates must not be based exclusively on the platelet count, but must also take into account the patient's clinical condition

  (in particular a body temperature above 38.5 °C, plasma coagulation disorders, recent haemorrhages and neurological deficits)

Blood Transfus 2011;9:320-35

# Fresh frozen plasma (FFP)

- Due to the hemodilutional effects of CPB and the progressive loss of clotting factors during ongoing bleeding,

  one should not hesitate to administer FFP

- To improve hemostasis even if the INR is minimally abnormal

- One unit of FFP - about 250mL of volume
- Usually 2–4 units for the average adult
- 4 units will increase clotting factors by 10%
- FFP may be given to patients with AT III deficiency, presence of bleeding not related to the surgery, microvascular bleeding in patients undergoing massive transfusion, acute DIC in the presence of ongoing bleeding, together

- The recommended initial dose of FFP is 10-15 mL/kg of body weight
- The patient's clinical condition and laboratory parameters should be monitored as these may justify the administration of higher doses (up to 30 mL/kg) of FFP

# Post-operative blood salvage

- Washed / Unwashed
- Reduces requirement of transfusion
- The efficacy of the procedure is greater in orthopaedic surgery (Washed) than in heart surgery (Unwashed)

# Contents

REPORT FROM THE STS WORKFORCE ON EVIDENCE BASED SURGERY

# Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery: The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists Clinical Practice Guideline*

The Society of Thoracic Surgeons Blood Conservation Guideline Task Force: Victor A. Ferraris, MD, PhD (Chair), Suellen P. Ferraris, PhD, Sibu P. Saha, MD, Eugene A. Hessel II, MD, Constance K. Haan, MD, MS, B. David Royston, MD, Charles R. Bridges, MD, ScD, Robert S. D. Higgins, MD, George Despotis, MD, and Jeremiah R. Brown, PhD

The Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion: Bruce D. Spiess, MD, FAHA (Chair), Linda Shore-Lesserson, MD, Mark Stafford-Smith, MD, C. David Mazer, MD, Elliott Bennett-Guerrero, MD, Steven E. Hill, MD, and Simon Body, MB, ChB

University of Kentucky Chandler Medical Center, Lexington, Kentucky (VAF, SPF, SPS, EAH), University of Florida, Jacksonville, Florida (CKH), University of Pennsylvania Health System, Philadelphia, Pennsylvania (CRB), Harefield Hospital, London, United Kingdom (BDR), Rush Presbyterian St. Lukes' Medical Center, Chicago, Illinois (RSDH), Washington University Medical Center, St. Louis, Missouri (GD), Center for the Evaluative Clinical Sciences, Dartmouth Medical School, Lebanon, New Hampshire (JRB), Virginia Commonwealth University, Richmond, Virginia (BDS), Montefiore Medical Center, Bronx, New York (LS-L), Duke University Medical Center, Durham, North Carolina (MS-S, EB-G, SEH), Keenan Research Center in the Li Ka Shing Knowledge Institute of St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada (CDM), and Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (SB)

Ann Thorac Surg 2007;83:S27–86

# Six variables as important indicators

1) Advanced age

2) Low preoperative red blood cell Volume

3) Preoperative antiplatelet or antithrombotic drugs

4) Reoperative or complex procedures

5) Emergency operations

6) Noncardiac patient comorbidities

- They must be viewed as guidelines and recommendations

  Not absolutes

*Table 2. Risks of Blood Transfusion*

| Type | Occurrence in Red Blood Cell Units Transfused |
|---|---|
| *Infectious* | |
| Human immunodeficiency virus [669, 670] | 1 in 1.4–2.4 $\times$ $10^6$ |
| Hepatitis B [669] | 1 in 58,000–149,000 |
| Hepatitis C [670] | 1 in 872,000–1.7 $\times$ $10^6$ |
| Bacterial infection [671] | 1 in 2,000 |
| *Immunologic reactions* | |
| Febrile nonhemolytic transfusion reactions [672–675] | 1 in 100 |
| Anaphylactic transfusion reactions [676] | 1 in 20,000–50,000 |
| ABO mismatch [677] | |
| Hemolysis | 1 in 60,000 |
| Death | 1 in 600,000 |
| Leukocyte-related target organ injury [3–5, 678] | 1 in 20 to 1 in 50 |
| Transfusion-related acute lung injury [679] | 1 in 2000 |
| Post-transfusion purpura [680] | Rare |
| *Transfusion services error* | |
| Donor screening error [669] (malaria, *T cruzi*, babesioses, Creutzfeld-Jakob disease) | 1 in 4 $\times$ $10^6$ |
| Transfusion services error [681] | 1 in 14,000 |

*Table 6. Summary of Recommendations for Perioperative Prophylactic Measures for Blood Conservation*

| Recommendation | Level of Evidence | Class |
|---|---|---|
| Preoperative screening of the intrinsic coagulation system is not recommended unless there is a clinical history of bleeding diathesis. | B | III |
| Screening preoperative bleeding time is not unreasonable for high-risk patients, especially those who receive preoperative antiplatelet drugs. | B | IIb |
| Preoperative hematocrit and platelet count are indicated for risk prediction, and abnormalities in these variables are amenable to intervention. | A | I |
| Devices aimed at obtaining direct hemostasis at catheterization access sites are not unreasonable for blood conservation if operation is planned within 24 hours. | C | IIb |
| Alternatives to laboratory blood sampling (eg, oximetry instead of arterial blood gasses) are reasonable means of blood conservation before operation. | C | IIa |
| A comprehensive, integrated, multimodality blood conservation program in the intensive care unit is a reasonable means to limit blood transfusion. | B | IIa |

- Enhanced oxygen-carrying capacity [7], improved hemostasis
- associated with blood component therapy [8, 9],
- and volume support of cardiac output are three accepted
- benefits of blood transfusion
- 10/30” rule of
- blood transfusion. These authors suggested that the
- minimal ideal level of oxygen-carrying capacity is maintained
- by a hematocrit of around 30% and hemoglobin of
- 10 g/dL.

- Certain of the variables stand out as high-risk predictors
- including advanced age, preoperative anemia or small
- body size (ie, low red blood cell volume), the duration or
- urgency of operative intervention, the presence of antiplatelet
- or antithrombotic drugs taken shortly before
- operation, and the presence of multiple noncardiac comorbidities
- (eg, renal failure, diabetes mellitus, acquired
- or congenital coagulopathy, and so forth
- Hypothermia related to cardiopulmonary
- bypass influences platelet function and coagulation

- Caution must be used with sudden
- withdrawal of antiplatelet therapy in the presence of
- drug-eluting stents. That can lead to stent thrombosis,
- and the surgical team should consider various alternatives
- to maintain stent patency.

# *Transfusion Triggers*

- **With hemoglobin levels below 6 g/dL, red blood**
- **cell transfusion is reasonable**
- **It is not unreasonable to transfuse red cells in certain**
- **patients with critical noncardiac end-organ ischemia (eg,**
- **central nervous system and gut) whose hemoglobin levels**
- **are as high as 10 g/dL**

- **2011 Update to The Society of Thoracic Surgeons**
- **and the Society of Cardiovascular Anesthesiologists**
- **Blood Conservation Clinical Practice Guidelines***

# 2011 Update to The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guidelines*

The Society of Thoracic Surgeons Blood Conservation Guideline Task Force:
Victor A. Ferraris, MD, PhD (Chair), Jeremiah R. Brown, PhD, George J. Despotis, MD, John W. Hammon, MD, T. Brett Reece, MD, Sibu P. Saha, MD, MBA, Howard K. Song, MD, PhD, and Ellen R. Clough, PhD

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Linda J. Shore-Lesserson, MD, Lawrence T. Goodnough, MD, C. David Mazer, MD, Aryeh Shander, MD, Mark Stafford-Smith, MD, and Jonathan Waters, MD

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**Ann Thorac Surg 2011;91:944–82**

- Given that the risk of transmission of known viral diseases with blood transfusion is currently rare, fears of viral disease
- transmission should not limit administration of INDICATED blood products. (This recommendation only applies to
- countries/blood banks where careful blood screening exists.) (Level of evidence C)
- IIa
- Transfusion is unlikely to improve oxygen transport when the hemoglobin concentration is greater than 10 g/dL and is
- not recommended. (Level of evidence C)
- III
- With hemoglobin levels below 6 g/dL, red blood cell transfusion is reasonable since this can be life-saving. Transfusion
- is reasonable in most postoperative patients whose hemoglobin is less than 7 g/dL but no high level evidence
- supports this recommendation. (Level of evidence C)
- IIa
- It is reasonable to transfuse nonred-cell hemostatic blood products based on clinical evidence of bleeding and preferably
- guided by point-of-care tests that assess hemostatic function in a timely and accurate manner. (Level of evidence C)
- IIa
- During cardiopulmonary bypass (CPB) with moderate hypothermia, transfusion of red cells for hemoglobin 6 g/dL is
- reasonable except in patients at risk for decreased cerebral oxygen delivery (ie, history of cerebrovascular attack,
- diabetes, cerebrovascular disease, carotid stenosis) where higher hemoglobin levels may be justified. (Level of
- evidence C)
- IIa
- In the setting of hemoglobin values exceeding 6 g/dL while on CPB, it is reasonable to transfuse red cells based on the
- patient's clinical situation, and this should be considered as the most important component of the decision making
- process. Indications for transfusion of red blood cells in this setting are multifactorial and should be guided by
- patient-related factors (ie, age, severity of illness, cardiac function, or risk for critical end-organ ischemia), the clinical
- setting (massive or active blood loss), and laboratory or clinical parameters (eg, hematocrit, SVO2, electrocardiogram,
- or echocardiographic evidence of myocardial ischemia etc.). (Level of evidence C)

- ***c) Blood Derivatives Used for Blood Conservation***
- **PLASMA TRANSFUSION**
- ***Class IIa.***
- **1. Plasma transfusion is reasonable in patients with**
- **serious bleeding in context of multiple or single**
- **coagulation factor deficiencies when safer fractionated**
- **products are not available. (Level of evidence B)**
- **2. For urgent warfarin reversal, administration of prothrombin**
- **complex concentrate (PCC) is preferred,**
- **but plasma transfusion is reasonable when adequate**
- **levels of Factor VII are not present in PCC.**
- **(Level of evidence B)**

- Consensus guidelines for blood component therapy in
- ECMO patients advocates transfusion to assure adequate
- oxygen carrying capacity, normal AT III activity (80% to
- 120% of control) and fibrinogen levels (250 to 300 mg/dL),
- while maintaining a platelet count greater than 80,000 to
- 100,000/L with platelet transfusion

- **Bleeding is a common complication in ECMO patients.**
- **Likely causes of bleeding include overanticoagulation**
- **and decreased platelet number and function. Significant**
- **bleeding occurs from minimal interventions such as**
- **tracheal suction or nasogastric tube placement, or from**
- **minor surgical interventions**

- **Use of modified ultrafiltration (MUF) is indicated**
- **for blood conservation and reducing postoperative**
- **blood loss in adult cardiac operations using CPB.**

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# Liberal or Restrictive Transfusion after Cardiac Surgery

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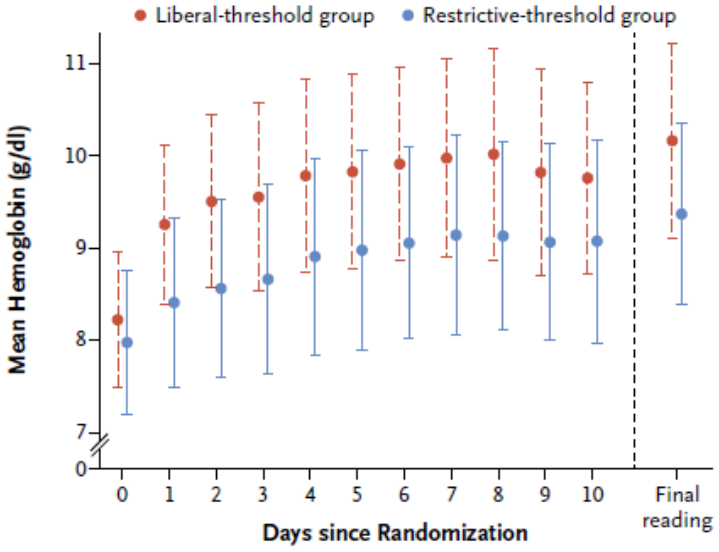
## ABSTRACT

**Table 2. Transfusions.***

| Type of Transfusion | Restrictive Transfusion Threshold (N = 1000) | Liberal Transfusion Threshold (N = 1003) | Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *number (percent)* | | | |
| ≥1 Units of red cells transfused before randomization — no. of patients (%)† | 250 (25.0) | 264 (26.3) | | |
| Units of red cells transfused after randomization‡ | | | | |
| Total units transfused — no. | 1494 | 2494 | | |
| Median — no. | 1.0 | 2.0 | | |
| Interquartile range | 0–2.0 | 1.0–3.0 | | |
| Distribution — no. of patients (%) | | | 0.58 (0.54–0.62)§ | <0.001 |
| 0 units | 466 (46.6) | 78 (7.8) | | |
| 1 unit | 193 (19.3) | 341 (34.0) | | |
| 2 units | 152 (15.2) | 262 (26.1) | | |
| 3 units | 66 (6.6) | 141 (14.1) | | |
| 4 units | 50 (5.0) | 62 (6.2) | | |
| ≥5 units | 73 (7.3) | 119 (11.9) | | |
| Transfused red cells during entire index admission — no. of patients (%)¶ | 637 (63.7) | 952 (94.9) | | |
| Other transfusions — no. of patients (%)¶ | | | | |
| Fresh-frozen plasma | 297 (29.7) | 284 (28.3) | 1.08 (0.88–1.33) | 0.45 |
| Platelets | 376 (37.6) | 362 (36.1) | 1.08 (0.89–1.31) | 0.42 |
| Cryoprecipitate | 99 (9.9) | 102 (10.2) | 0.99 (0.72–1.35) | 0.95 |
| Activated factor used — no. of patients (%)¶ | 7 (0.7) | 5 (0.5) | 1.41 (0.45–4.45) | 0.56 |
| Human blood coagulation factor IX used — no. of patients (%)¶ | 52 (5.2) | 48 (4.8) | 1.21 (0.73–2.03) | 0.46 |
| Severe nonadherence — no. of patients (%)‖ | 97 (9.7) | 62 (6.2) | | |
| Any nonadherence — no. of patients (%)** | 300 (30.0) | 453 (45.2) | | |




**No. at Risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Liberal-threshold group | 994 | 967 | 894 | 773 | 732 | 501 | 405 | 338 | 245 | 204 | 170 | 998 |
| Restrictive-threshold group | 998 | 971 | 894 | 758 | 713 | 502 | 401 | 303 | 226 | 175 | 147 | 1003 |

**Figure 1. Mean Daily Nadir in Hemoglobin Level.**

I bars indicate standard deviations, which were calculated independently at each time point.

**Table 3. Outcomes.**

| Outcome | Restrictive Transfusion Threshold (N=1000) | Liberal Transfusion Threshold (N=1003) | Estimated Treatment Effect | |
|---|---|---|---|---|
| | | | Odds Ratio or Hazard Ratio (95% CI) | P Value |
| **Serious infection or ischemic event: primary outcome** | | | | |
| Overall | 331/944 (35.1) | 317/962 (33.0) | 1.11 (0.91–1.34)* | 0.30 |
| Infectious event† | 238/936 (25.4) | 240/954 (25.2) | 1.02 (0.83–1.26)* | 0.83 |
| Sepsis | 210/982 (21.4) | 214/983 (21.8) | | |
| Wound infection | 55/921 (6.0) | 46/936 (4.9) | | |
| Ischemic event | 156/991 (15.7) | 139/99 (114.0) | 1.16 (0.90–1.49)* | 0.26 |
| Permanent stroke | 15/989 (1.5) | 17/985 (1.7) | | |
| Myocardial infarction | 3/987 (0.3) | 4/981 (0.4) | | |
| Gut infarction | 6/987 (0.6) | 1/982 (0.1) | | |
| Acute kidney injury | 140/989 (14.2) | 122/989 (12.3) | | |
| Stage 1 | 49/989 (5.0) | 40/989 (4.0) | | |
| Stage 2 | 39/989 (3.9) | 35/989 (3.5) | | |
| Stage 3 | 50/989 (5.1) | 46/989 (4.7) | | |
| **Secondary outcomes** | | | | |
| No. of hours in ICU or high-dependency unit‡ | | | | |
| Median | 49.5 | 45.9 | 0.97 (0.89–1.06)§ | 0.53 |
| Interquartile range | 21.9–99.7 | 20.1–94.8 | | |
| No. of days in hospital¶ | | | | |
| Median | 7.0 | 7.0 | 1.00 (0.92–1.10)§ | 0.94 |
| Interquartile range | 5.0–10.0 | 5.0–10.0 | | |
| All-cause mortality at 90 days | 42/1000 (4.2) | 26/1003 (2.6) | 1.64 (1.00–2.67)§ | 0.045 |
| Clinically significant pulmonary complications | 127/979 (13.0) | 116/982 (11.8) | 1.11 (0.85–1.45)* | 0.45 |
| All-cause mortality at 30 days | 26/1000 (2.6) | 19/1003 (1.9) | | |

| Subgroup | No. of Patients | Restrictive | Liberal | Odds Ratio (95% CI) | P Value for Interaction |
|---|---|---|---|---|---|
| | | *no. of events/total no. (%)* | | | |
| Surgery type | | | | | 0.64 |
| CABG | 400 | 77/192 (40.1) | 85/208 (40.9) | 0.92 (0.61–1.40) | |
| Non-CABG | 1487 | 251/743 (33.8) | 229/744 (30.8) | 1.17 (0.94–1.46) | |
| Age | | | | | 0.45 |
| <75 yr | 604 | 108/296 (36.5) | 94/308 (30.5) | 1.30 (0.92–1.84) | |
| ≥75 yr | 1302 | 223/648 (34.4) | 223/654 (34.1) | 1.03 (0.81–1.30) | |
| Diabetes | | | | | 0.76 |
| Yes | 567 | 114/275 (41.5) | 118/292 (40.4) | 1.04 (0.74–1.47) | |
| No | 1337 | 217/669 (32.4) | 199/668 (29.8) | 1.14 (0.90–1.45) | |
| COPD or asthma | | | | | 0.16 |
| Yes | 239 | 49/106 (46.2) | 48/133 (36.1) | 1.59 (0.93–2.71) | |
| No | 1667 | 282/838 (33.7) | 269/829 (32.4) | 1.06 (0.86–1.30) | |
| Renal impairment | | | | | 0.67 |
| Estimated GFR ≤60 | 371 | 85/181 (47.0) | 85/190 (44.7) | 1.05 (0.69–1.59) | |
| Estimated GFR >60 | 1535 | 246/763 (32.2) | 232/772 (30.1) | 1.13 (0.90–1.41) | |
| Sex | | | | | 0.27 |
| Male | 583 | 114/270 (42.2) | 129/313 (41.2) | 1.01 (0.72–1.42) | |
| Female | 1323 | 217/674 (32.2) | 188/649 (29.0) | 1.19 (0.94–1.51) | |
| LV function | | | | | 0.33 |
| Good | 1145 | 218/569 (38.3) | 204/576 (35.4) | 1.14 (0.89–1.46) | |
| Moderate or poor | 761 | 113/375 (30.1) | 113/386 (29.3) | 1.04 (0.76–1.42) | |

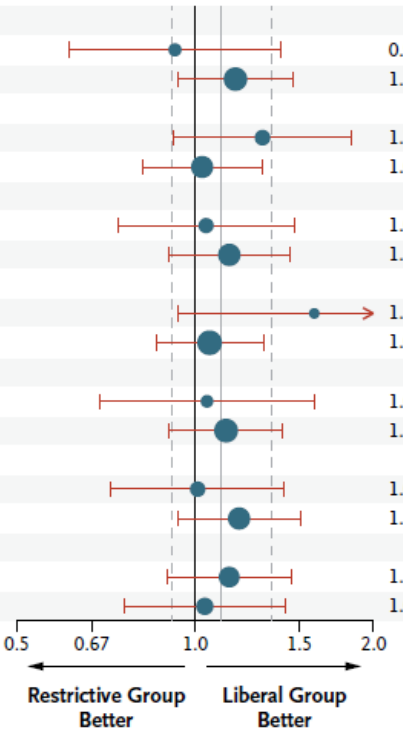



**Figure 2. Subgroup Analyses.**

The gray vertical lines represent the overall treatment estimate (solid line) and the 95% confidence interval (dashed lines) for the primary outcome as calculated for the entire analysis cohort. The sizes of the circles designating the point estimates reflect the sizes of the subgroups. The restrictive transfusion threshold for hemoglobin was less than 7.5 g per deciliter, and the liberal transfusion threshold was less than 9 g per deciliter. CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, GFR glomerular filtration rate, and LV left ventricular.


## CONCLUSIONS

A restrictive transfusion threshold after cardiac surgery was not superior to a liberal threshold with respect to morbidity or health care costs. (Funded by the National Institute for Health Research Health Technology Assessment program; Current Controlled Trials number, ISRCTN70923932.)

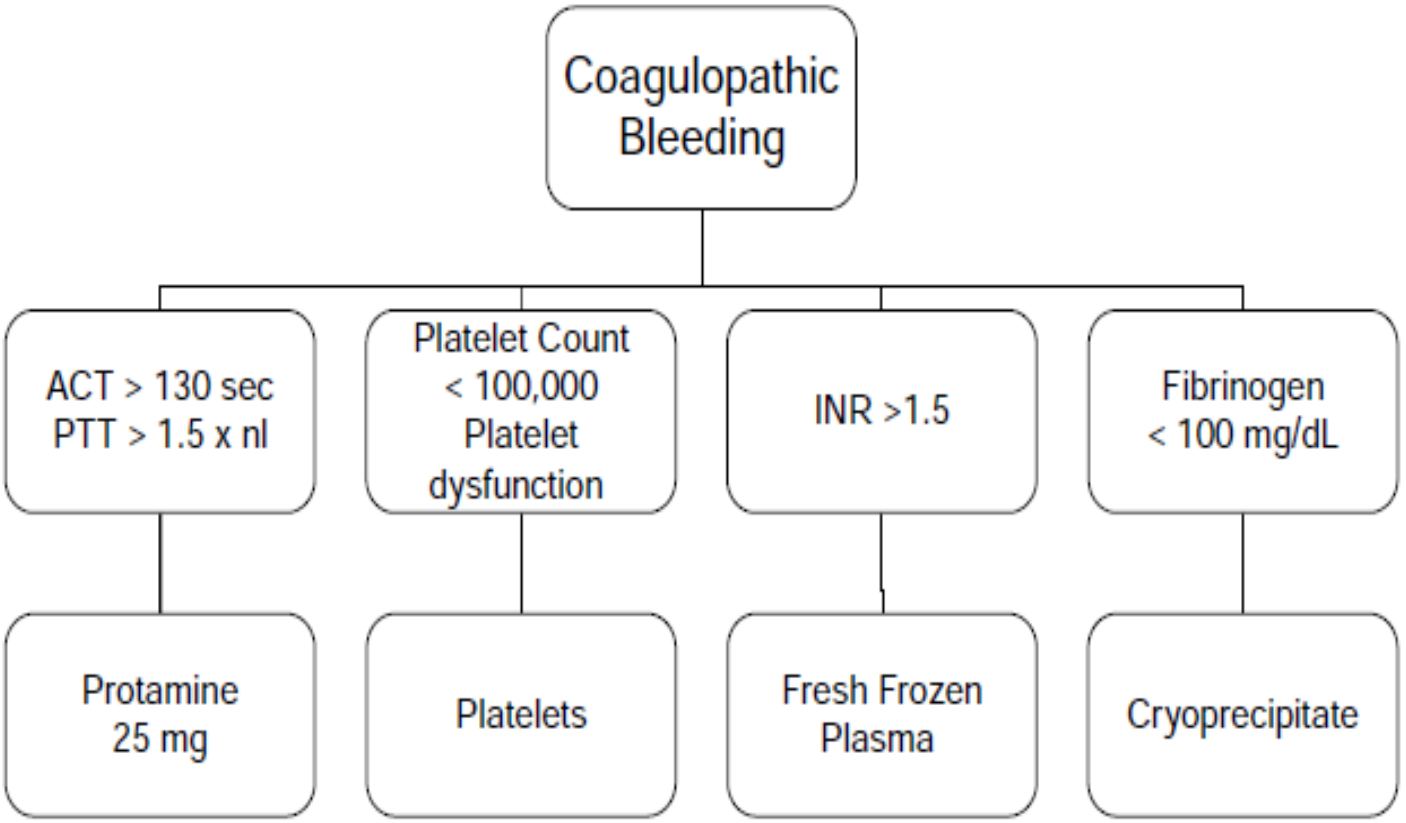



**Figure 9.4** • Point-of-care testing of routine coagulation studies to treat postoperative bleeding.

# References


- Bojar R. *Manual of Perioperative Care in Adult Cardiac Surgery, Fifth Edition*. West Sussex,UK: Wiley-Blackwell, 2011:364-70.

# CPB in Minimally Invasive Cardiac Surgery

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## 서론

최근 대동맥판막과 승모판막 그리고 삼첨판막에 대한 최소 침습수술은 술 후 출혈량이 적고, 호흡기 합병증과 심방세동의 발생이 드물며, 수술 후 통증이 적고 회복이 빨라 정중흉골절개술을 이용한 고식적인 심장수술의 접근방법을 점차 대치하고 있다. 이러한 최소침습 심장판막수술의 여러 장점들로 인해 동료 의사 및 환자들의 요구가 증가하고 있으며, 이러한 술기를 더욱 용이하게 하는 새로운 캐뉼라, 심폐기 회로 및 발전된 심폐기 가동 기술에 대한 연구 및 보고가 끊이지 않고 있다. 이번 강의에서는 부산대학교 양산병원에서 450예 이상의 최소침습 심장수술을 시행하면서 국내 실정에 맞추어 단순화한 수술, 마취 및 심폐기 가동 원칙의 변화를 살펴보고 본원에서 시행되고 있는 최소침습 심장수술에서의 환자선택, 마취방법, 동-정맥 삽관의 방법, 캐뉼라의 선택, 심근보호법 및 심폐기 가동 원칙에 대해서 문헌고찰과 함께 살펴 보았다.

# 본론

## 1. 환자의 선택

최근의 여러 연구에서는 최소침습 심장수술은 심장판막 질환 및 일부 선천성 심질환의 수술 시 정중흉골절개를 이용한 수술법과 동등한 수술 결과를 보여주고 있다. 따라서 최소침습 심장수술의 적응증은 심장수술의 복잡성 보다는, 심장 및 대혈관의 해부학적 구조에 따라 결정된다. 최소침습 수술을 위해서 필수적인 말초삽관을 위해 수술 전 환자 혈관의 해부학적 구조 및 이상소견을 확인해야 하며, 이를 위해 가장 적절한 검사는 CT angiography 이다. 이를 통해 수술이 요하는 심장 병변의 3차원적인 영상을 통해 수술의 계획을 수립하고 동반된 심-폐 질환을 확인하는데 유용하다. 수술 전 CT angiography를 시행함으로써 얻는 정보는 아래와 같다.

가) 우측 흉강의 흉막유착을 예측, 동반 절제 가능한 종양 확인

나) 동맥내 동맥경화성 변변 확인; 대동맥, 장골동맥, 대퇴동맥

다) 정맥이상 확인: 하대정맥, 상대정맥

라) 동반심장질환; 관상동맥 질환, 폐색전증

## 2. 마취과와의 협조

제한적인 시야에서 진행되는 최소침습 심장수술의 특성상 마취과 의사와의 협조는 매우

중요하다. 따라서 수술 과정 전반에 완벽한 정보공유가 요하며, 최소침습 심장수술을 시행함에 있어서 마취과 의사의 협조가 요하는 부분은 아래와 같다.

가) 경피적 상대정맥 삽관: 우측 내경정맥

나) TEE 수행:

① 대퇴 동정맥 삽관시 철선 및 캐뉼라 위차 확인

② 전향적 심정지액 투여시 대동맥 역류 확인

③ 심장 수술 결과 확인: 판막 성형술, 좌심실 기능 확인, 심장내 잔존공기

④ Endoclamp (Intracluder), ProPlege, EndoVent (Edwards Lifesciences; Irvine, CA)

다) 폐 환기 조절; double lumen tube vs. single lumen tube

라) 조기 발관 노력 (Fast tract protocol), 술 후 통증관리

## 3. 동맥관 삽관

### A. 동맥관 삽관의 위치 결정

최소침습 심장수술시 동맥관 삽관의 위치는 절개방법 및 대동맥내 병변의 유무에 따라서 결정된다. 상부 혹은 하부 부분 흉골절개술을 시행하는 경우 상행대동맥에 삽관하는 경우가 가장 흔하며, 우측 혹은 좌측 개흉술을 통해 수술을 진행하는 경우 대퇴동맥이 가장 흔한 삽관 위치가 된다. 최근 몇몇 보고에서는 대퇴동맥을 이용한 최소침습 수술 시 수술 후 신경학적 합병증의 빈도가 더 흔하다는 보고가 있으나, 다른 문헌에서는 수술 전 CT를 이용하

여 동맥내부의 죽상경화성 병변을 면밀하게 검사하며, Endoballon을 이용하지 않은 경우에는 신경학적인 합병증의 빈도가 증가하지 않는다고 보고하였다. 저자는 최소침습 심장수술을 계획하는 모든 환자에서 CT angiography를 수술 전 기본검사로 시행하고 있다. 수술 전 CT angiography 검사에서 대퇴동맥을 이용한 삽관이 불가능할 것으로 판단되는 경우에는 우 쇄골하동맥이나 액와동맥을 이용하여 삽관이 가능하다.

### B. 캐뉼라의 선택

대동맥내 풍선차단을 시도하는 경우라면 환자의 우측 대퇴동맥을 통해 EndoReturn (Edwards Lifesciences; Irvine, CA) 캐뉼라를 삽입 후 IntraClude Intra-Aortic Occlusion Device (Edwards Lifesciences; Irvine, CA) 를 이용하여 전신 관류, 대동맥 차단 및 심근보호에 이용이 가능하다. 하지만 2015년 5월 현재 국내에서 허가 승인을 획득한 대동맥내 풍선차단용 카테터 및 캐뉼라는 전무한 실정이며, 국내에서 사용가능 한 대퇴동맥용 캐뉼라는 2015년 5월 현재 아래의 3종류 이다.

가) Fem-Flex II (Edwards Lifesciences, Irvine, CA)

나) Bio-Medicus (Medtronic, Minneapolis, MN)

다) DLP (Medtronic, Minneapolis, MN)

가장 흔하게 쓰이는 것은 나) 이며, 다) 캐뉼라의 경우 17Fr에서 혈류에 따른 압력값이 낮다는 장점을 가지고 있다. 개별 캐뉼라의 장단점에 대해서는 강의 슬라이드를 통해 설명한다.

### C. 대퇴 동정맥을 이용한 삽관 술기

경피적 대퇴 동정맥 삽관도 가능하나, 대퇴동맥의 경우 수술 후 노출하여 삽관부위를 교정해야 하며 삽관과 관련된 합병증이 증가할 수 있으므로, 보다 안전한 삽관을 위해 부분 개방성 방법을 이용하고 있다. 우측 서혜부에 피부주름을 따라 2-3 cm 정도의 사선절개를 가하여 우측 대퇴동정맥을 노출한다. 대퇴동정맥의 박리시에는 피하조직까지 사선절개 후 지방층부터는 종절개 하여 주변의 임파관의 손상을 최소화 하고, 대퇴동정맥 근처의 박리를 위해서는 전기 소작기의 사용을 최소화 하여 인접하여 주행하는 신경의 손상이 발생하지 않도록 주의 하여야 한다. 대퇴동정맥은 삽관을 위해 혈관의 전면부만 노출시키고, 노출된 혈관에 5-0 prolene으로 1회 쌈지봉합을 시행한다. 심폐기 가동을 위해 300U/Kg 용량의 헤파린을 정주한 후 안내철선을 따라 경식도 초음파의 가이드 하에 Seldinger technique으로 대퇴동정맥의 삽관을 시행한다. 경식도 초음파를 이용하여 우심방내의 정맥 캐뉼라의 위치를 확인하고 동맥관을 통한 혈류 공급시 도관을 통한 압력을 관찰하면서 심폐기를 가동한다.

## 4. 정맥관 삽관

### A. 삽관정맥관의 수 및 삽관 위치

대정맥의 해부학적 구조 및 수술의 종류에 따라 정맥 삽관의 위치 및 수를 결정한다. 술 전 시행한 CT angiography를 이용하여 대정맥 및 삽관을 계획한 정맥의 해부학적 구조를 확인

한다. 대퇴정맥이나 내경정맥의 협착 혹은 선천성 하대정맥의 단절 등의 이상소견이 발견될 경우 정맥삽관의 위치를 조정한다. 우심방의 개방이 요하지 않는 승모판막, 대동맥 판막 수술의 경우 환자의 체중이 80Kg 이하인 경우라면 대부분 단일 대퇴정맥을 이용한 삽관으로 수술의 진행이 가능하다. 대퇴정맥을 통한 배액을 위해 사용되는 캐뉼라 중 국내에서 사용 가능한 것은 다음의 3 종류이다. Fem-Flex II (Edwards Lifesciences, Irvine, CA), DLP and Bio-Medicus (Medtronic, Minneapolis, MN)

우심방의 개방이 요하는 삼첨판막 수술과 심방중격 결손증의 수술등에서는 상대정맥의 배액을 위해 추가적인 삽관이 요하는데, 이러한 경우 저자는 경피적 우측 내경정맥을 이용한 삽관 보다는 수술 시야에서 직접 상대정맥에 삽관하는 것을 선호한다.

### B. 우측 내경정맥을 이용한 삽관

마취과 의사에 의해 기도 삽관 및 전신마취를 시작한 후 우측 내 경정맥을 이용하여 경피적(Seldinger technique)으로 정맥관을 삽관한다. 환자의 체표면적에 따라 14Fr에서 17Fr 사이의 동맥용 캐뉼라를 사용한다. 삽관 방법은 일반적은 중심정맥 삽관 방법과 동일하나, 캐뉼라의 크기가 굵어 삽관과 관련된 혈관손상의 발생시 그 위험도가 크다. 따라서 경피적 삽관시 항상 혈관 초음파로 확인하며 혈관을 천자 하고, Guide-wire가 정맥내에 위치함을 다시 한번 확인한다. 삽입된 캐뉼라의 끝이 상대정맥-우심방의 경계부위에 위치할 수 있도록 경식도 초음파로 확인하면서 조절한다. 삽관된 정맥관의 혈전생성을 예방하기 위해 삽관 직전에 20U/Kg용량의 헤파린은 정주하고, 삽관 후에 캐뉼라를 통해 30U/Kg 용량의

헤파린은 1시간 동안 투여한다. 우측 내 경정맥을 통해 삽관된 캐뉼라는 수술 시야의 밖에 존재하므로, 마취과의가 캐뉼라의 고정 위치 및 꺽임 등을 면밀히 살펴야 한다. 삽관을 위해 사용되는 캐뉼라의 종류는 대퇴동맥을 통해 삽입되는 동맥 캐뉼라와 같고, 15 혹은 17Fr 를 주로 사용한다.

### C. 상대정맥 직접 삽관

수술 전 단일 대퇴정맥 삽관 후 수술을 진행하였으나, 정맥혈 배액이 원활하지 않은 경우나, 우심방 절개가 요하는 수술에서 우측 내경정맥 삽관을 대신하여 수술 시야에서 상대정맥에 직접 삽관을 시행할 수 있다. 삽관에 사용되는 정맥 캐뉼라는 14~16Fr 의 작은 크기의 캐뉼라이면 충분하고, 수술 창이나, 독립적인 포트를 통해 체외로 배액 한다. 최근 많은 보고에서 최소 침습심장수술을 시행 후 수술장에서 인공 호흡관을 발관하는 경우가 많은데, 상대정맥을 통한 직접 삽관 하는 경우 우측 내경정맥 부위의 지혈을 위한 압박이 불필요하여 수술장내 인공호흡기 발관을 용이하게 한다.

## 5. 심근보호법

### A. 대동맥 겸자

우측 개흉술을 이용한 최소 침습적 개심술의 경우 Chitwood clamp를 이용한 경흉부 대동맥 겸자를 이용하여 차단한다. 경흉부 대동맥 겸자는 3번 늑간의 후방 액와선상으로 삽입하며, 겸자의 한쪽 날은 상행대동맥의 전면이 위치하고 나머지 한쪽 날을 transverse sinus로

진입하여 폐동맥 및 좌심방이의 손상에 유의하면서 상행대동맥을 겸자한다. 최근 다양한 모양의 대동맥 겸자가 개발되어 사용이 가능하므로, 각각의 술자의 선호도에 맞는 겸자를 이용하는 것이 바람직하다.

### B. 심정지액의 주입 방향

국내에서는 최소침습 심장수술 중 역행성 심정지액의 주입을 위해 개발된 ProPlege sinus catheter (Edwards Lifesciences, Irvine, CA)의 이용이 불가능한 실정이다. 따라서 우측개흉술 및 제한적 흉골절개술을 통한 최소침습 심장수술시 대동맥 근부에 캐뉼라를 직접 삽입하고 전향적 심정지액을 주입하는 것이 유일한 심정지액 투여 방법이다.

### C. 심근 보호액의 선택:

최소침습 심장 수술 시 심근 보호액의 선택은 수술자의 선호에 따라 결정된다. 최소 침습 심장수술을 일반적으로 수술 중 대동맥 차단시간이 길고, 수술 중 추가적인 심근 보호액의 투여가 곤란한 경우가 많아 Custodiol 심정지액이 가장 널리 사용되고 있다. 하지만 Custodiol 심정지액의 경우 다량의(2L) 세포 내액성 수액이 비교적 빠른 속도로 주입됨에 따라 혈액희석, 응고장애, 전해질 불균형 등의 부작용을 초래한다. 이에 저자들은 Custodiol 심 정지액을 투입하는 경우 관상정맥동으로 배출되는 심 정지액을 흡입하여 제거하고 있다. 또한 저자들은 대동맥 겸자 시간이 50분이내로 예상되는 비교적 간단한 수술의 경우 저제온 법(29℃)과 동반하여 혈성 심 정지액을 사용하고 심방중격결손증의 교정수술의 경우 심근 보호액의 투여 없이 중등도의 저 체온 하에서 심실세동을 유발하여 수술을 시행한다.

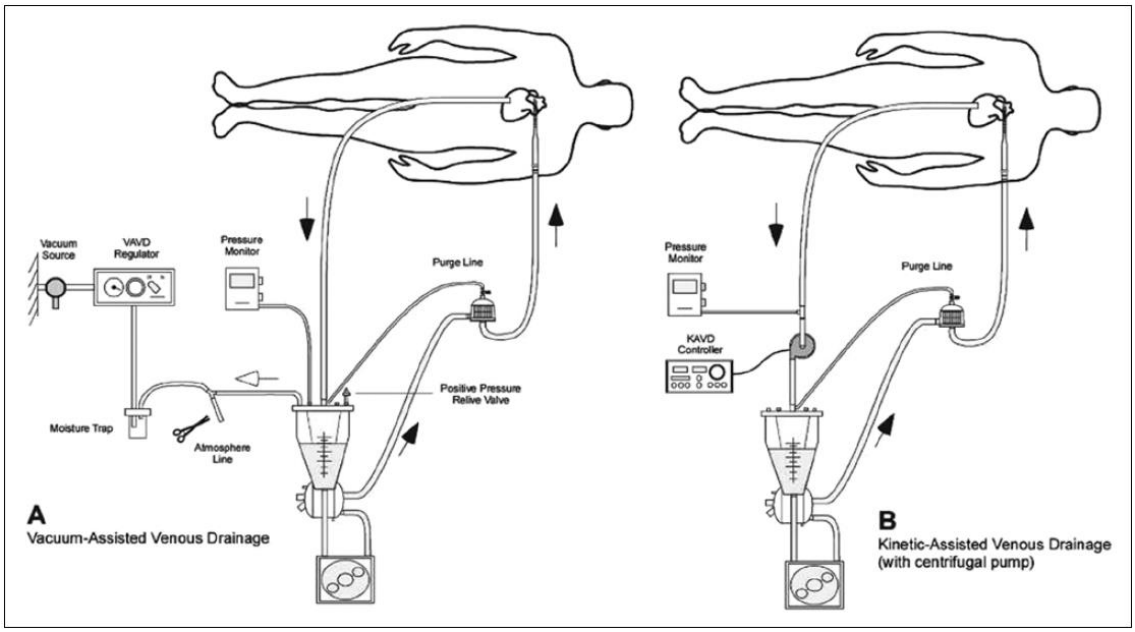
일반적으로 최소침습 삼첨판막에 재수술을 시행하는 경우 박리를 최소화 하기 위하여 말초 삽관으로 심폐기를 가동 후 정상 체온을 유지하면서 심 박동하에서 판막수술을 시행한다. 최근에는 성인에서 점차 안정성을 확보해 가고 있는 Del Nido 심 정지액을 사용하기 위해 병원 내에서 협의 중이다.

## 6. 심폐기 가동 원칙

### A. 음압 보조 정맥환류법

최소침습적 심장수술에 사용되는 정맥관들은 고식적인 개심술시 사용되는 캐뉼라에 비해 작은 내경을 가지고 있다. 따라서 다양한 방법으로 정맥환류를 최대화 하기 위해 노력한다.

**Figure 1. Schematic of vacuum assisted-venous drainage (VAVD) and centrifugal-assisted venous drainage (CAVD).**



이를 위해 가장 흔하게 사용되는 방법은 음압 보조 정맥환류법 (Fig1. A) 이며, 외국의 일부 병원에서는 원심성펌프 보조 정맥환류법을 (Fig1. B)를 사용한다. 국내에서는 비용적인 측면과 연질재질의 정맥 저혈소 (soft reservoir)의 사용이 불가능한 관계로 원심성펌프 보조 정맥환류법을 사용하는 기관이 없는 것으로 알고있다. 음압 보조 정맥환류법은 공인된 음압 조절기를 이용하여 적절한 음압을 저혈소에 형성하여 정맥환류를 증대시키는 방법으로, 정수압에 추가하여 20-60mmHg 정도의 음압 보조를 통해 정맥환류를 극대화 한다. (Figure 1. A) 이는 15년 이상의 임상경험이 보고된 비교적 안전한 방법이지만, 몇몇 주의점이 있는데, 저혈조 및 정맥도관에 -100mmHg 이상의 음압이 걸리게 되면 혈구 손상으로 용혈을 유발하며, 심한 경우 정맥 저혈조의 균열을 유발할 수도 있다. 따라서 최소한의 음압을 적용하는 것이 권장된다. 또한 심폐기 가동 초기에 적절하게 음압이 적용되지 않은 상태에서 pump sucker 와 vent를 가동하면, nonvented-reservoir 내부에 갑작스런 양압이 발생하여, 정맥도관을 통한 air-lock이 발생할 수 있다. 이를 예방하기 위해서 5 mmHg를 초과하는 양압이나 -150 mmHg 이하의 음압이 발생시 작동하는 감압밸브가 설치 되어있는 저혈조를 사용하여야 한다. 음압보조 정맥환류법에서 주의할 점은 아래와 같다.

가) 공인된 음압 조절기를 이용한다.

나) 정수압과 합한 음압의 최대가 −100 mm Hg을 초과하지 않게 조절한다.

다) 적절한 정맥배액이 가능한 최소한의 음압을 적용한다.

라) 저혈조에 음압 및 양압 알람을 모니터 한다.

마) 심폐기 가동 직후 정맥도관 내에 air-lock의 발생에 주의한다.

### B. 이산화 탄소

우측 개흉술을 이용한 최소침습 심장수술 시 수술의 후반부에 대동맥 근부 캐뉼라를 이용하여 심장 내부의 잔존 공기를 제거함에 어려움을 겪을 수 있다. 이는 대동맥 근부의 캐뉼라를 최적의 위치에 삽입하기 어렵고, 잔존공기의 배출을 위한 심장 마사지를 적용하기 어렵기 때문이다. 이에 산소 및 질소에 비해 혈액에 용해도가 높은 이산화 탄소를 수술 중 지속적으로 수술 부위에 분사함으로써 공기 색전증의 빈도를 줄일 수 있다.

### C. 저 체온 법

저자들은 최소침습 심장수술 중 일상적으로 중등도의 저 체온증을 유도하고 있다. 이는 심근보호에 유리하고, 주요 수술 술기를 시행하는 도중 심폐기의 혈류를 낮게 유지하여 수술 시야의 확보에 도움을 준다. 비교적 긴 심폐기 가동시간이 요하는 수술에서 저체온의 유도 및 정상체온으로의 회복은 혈액응고 기전에 장애를 초래할 수 있으므로 수술 진행 중 심폐기사와 밀접한 대화를 통해 심폐기 가동시간을 최소화 하기 위한 체온 조절 전략이 필요하다.

### D. 수혈 최소화를 위한 노력

최소침습 심장수술시 절개를 최소화함으로써 실혈량을 줄이는 점은 수혈을 최소화하는데 도움이 되지만, 비교적 긴 심폐기 가동시간은 오히려 수혈의 요구량을 증가시킨다. 최근

여러 문헌을 살펴보면 낮은 수혈 빈도는 최소침습 심장수술의 장점 중 하나로 꼽히고 있다. 이를 위해 저자들이 시도하고 있는 처치로는 다음과 같다.

가) Priming 용액을 줄여 혈액희석을 최소화

A. 환자의 체표면적에 적합한 산화기의 선택

B. 심폐기의 위치를 대퇴동정맥 근처로 이동하여 동정맥 튜브의 길이를 최소화

C. 3/8 inch 정맥 튜브 사용

D. Retrograde autologous priming

나) Autologus blood donation:

수술 전 환자의 혈액검사를 바탕으로 Priming 후 예상되는 Hct 이 25%를 초과할 경우, 적절한 자가 헌혈의 양을 계산하고 삽관된 동맥 캐뉼라 이용하여 자가 헌혈을 시행한다. 자가 헌혈된 혈액은 심폐기 가동을 완료하고 헤파린을 중화하는 시기에 환자에게 재주입한다.

다) 수술 중 혈액여과 필터의 사용:

최소침습 심장수술시 이용되는 Custodiol solution 심정지액, 판막 검사와 메이즈 술식시 냉동절제를 위해 사용된 카테터를 녹이기 위해 사용되는 생리식염수가 정맥혈 저혈조로

배액됨에 따라 일시적인 혈압강하와 혈액희석이 발생할 수 있다. 이를 극복하기 위하여 심폐기 가동을 시작함과 동시에 지속적으로 혈액투과를 실시한다.

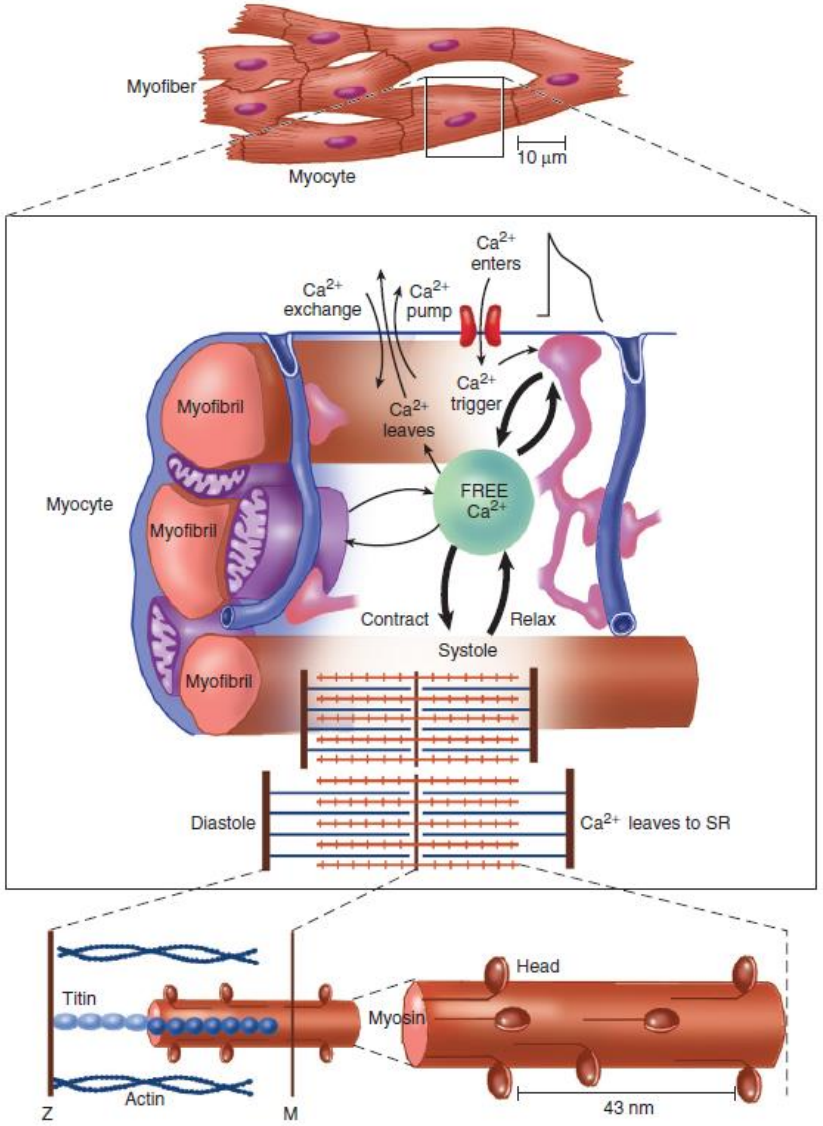
## 맺음말

최근 최소침습 심장수술을 보다 활발하게 적용할 수 있게 만든 가장 큰 변화는 수술 기법의 변화나 수술 로봇의 발전이 아니라 말초 삽관을 비롯한 다양한 심폐기 가동방법의 변화라고 생각한다. 흉골을 절개하지 않고도 심폐기의 가동 및 안정적인 심근보호가 가능해진 체외순환 방법의 발전은 최소침습 심장수술의 결과를 예측 및 재현이 가능하게 만들고 있다. 본 강의에서 다룬 최소침습 심장수술의 체외순환법은 다양한 임상상황에서 적용이 가능하며, 무봉합 대동맥 판막 치환술(Sutureless AVR, Rapid deployment AVR) 등의 최근 빠르게 발전하는 심장수술의 여러 영역에서 유용하게 적용될 수 있을 것이다. 최근 진일보한 다양한 장비의 국내 도입과, 이를 이용한 보다 안전하고 효율적인 심폐기 가동이 가까운 미래에 가능하리라 기대해 본다.

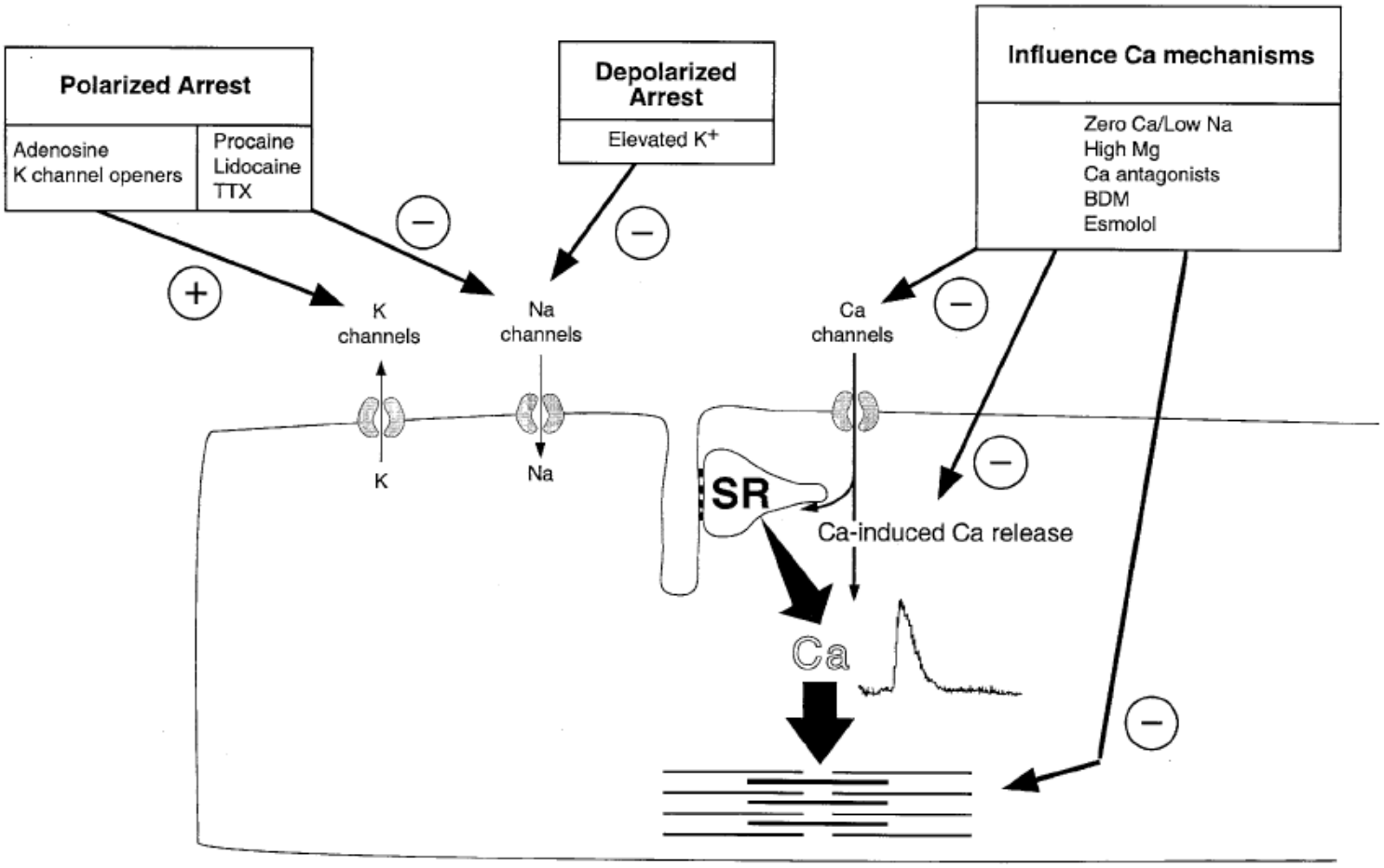
# 심근보호액의 종류와 장단점

전남대학교 이교선

# The Crux of the Contractile Process



# Excitation-Contraction Coupling



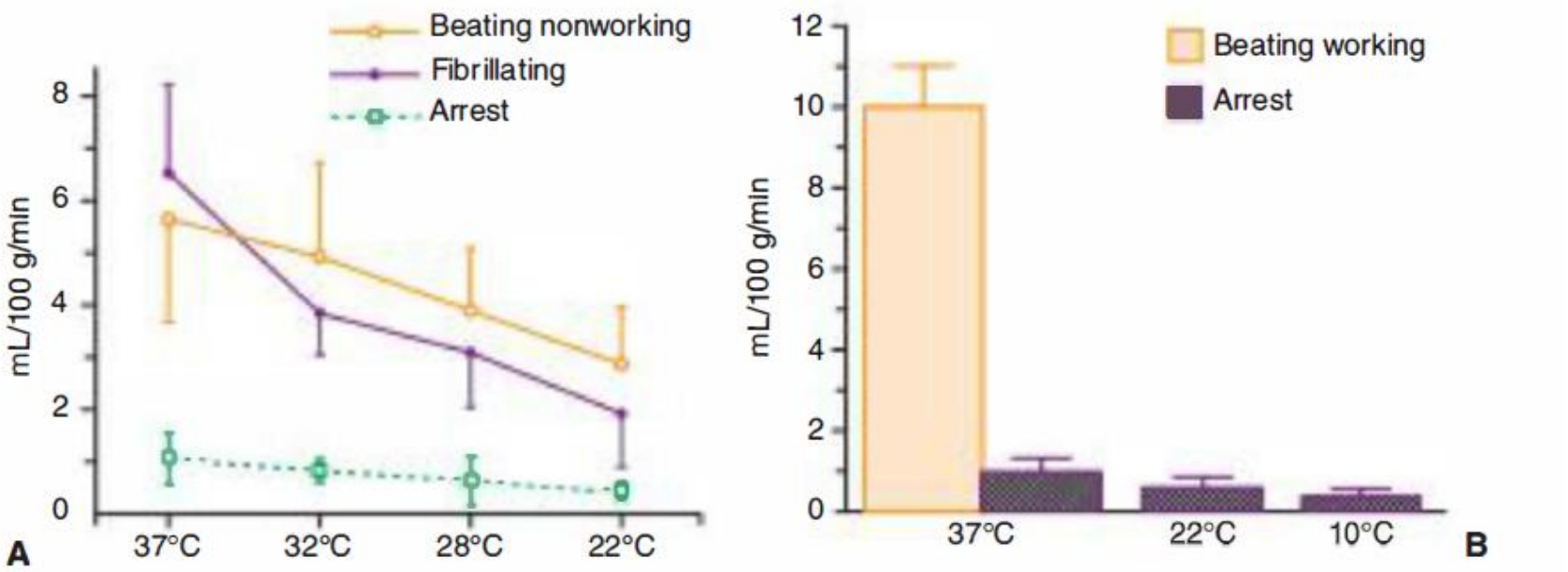
# Basic Concepts of Cardioplegia

- Rapid chemical arrest to conserve energy and create a still operative field
- Hypothermia to reduce metabolism
- Agents that provide additional protection

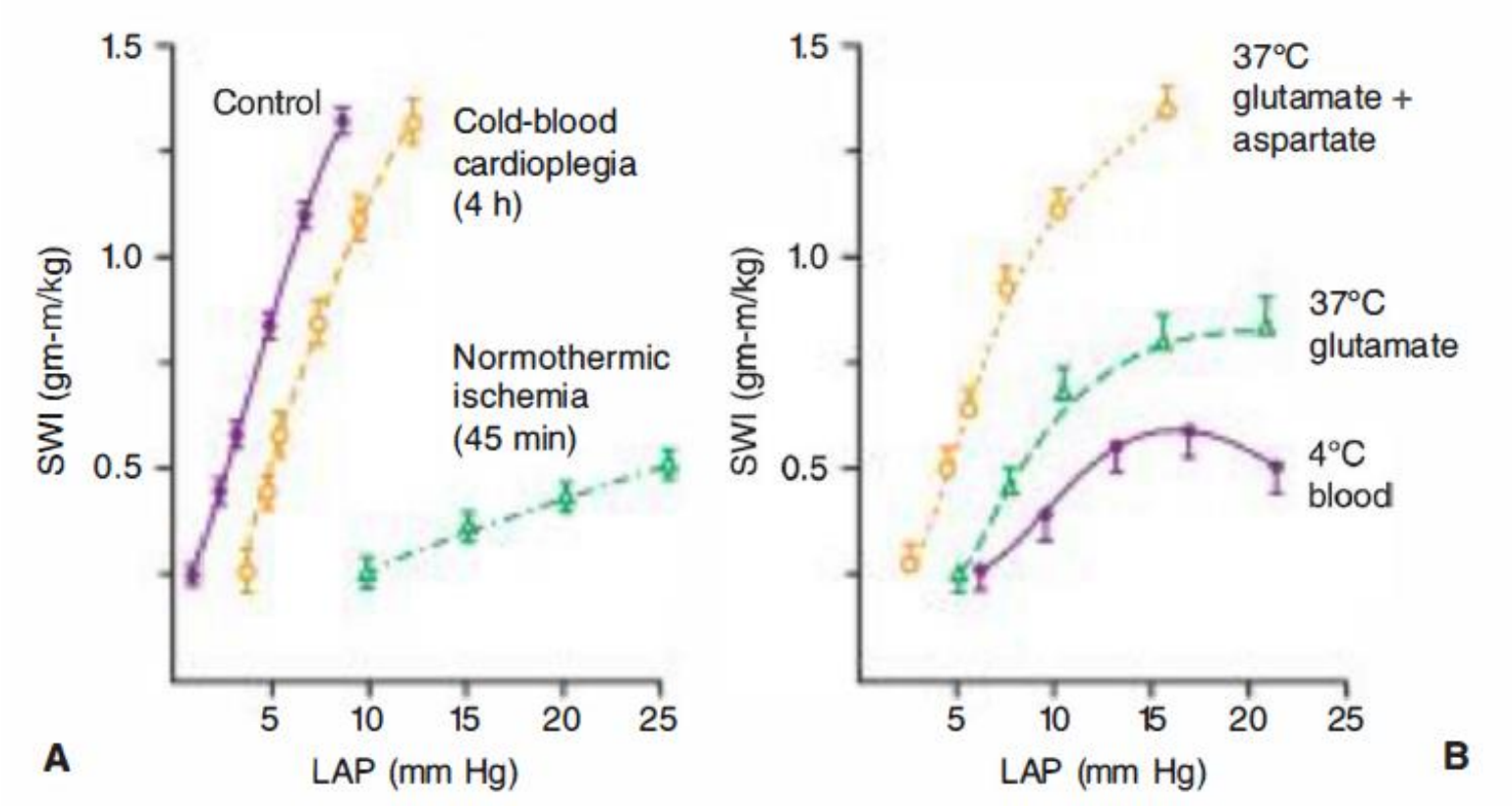
# Principles of Cardioplegic Protection

- Arrest
  - A rapid and effective induction of diastolic arrest to keep the myocardium relaxed and minimize cellular use of ATP
- Myocardial protection
  - Protective effects to delay the onset of irreversible injury caused by global ischemia and limit the extent of reperfusion injury
- Reversibility
  - Readily reversible cardioplegic effects on washout of prompt resumption of heart function
- Low toxicity
  - A short half-life with no toxic effects on other organs after cessation of CPB

# LV Oxygen Requirements

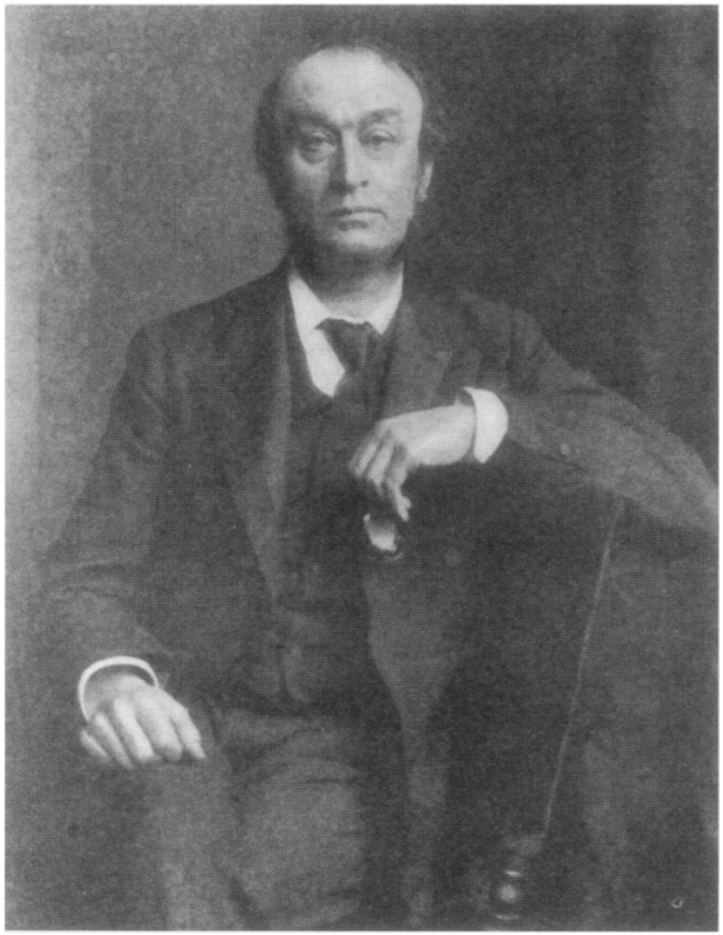


# Hypothermia only ?



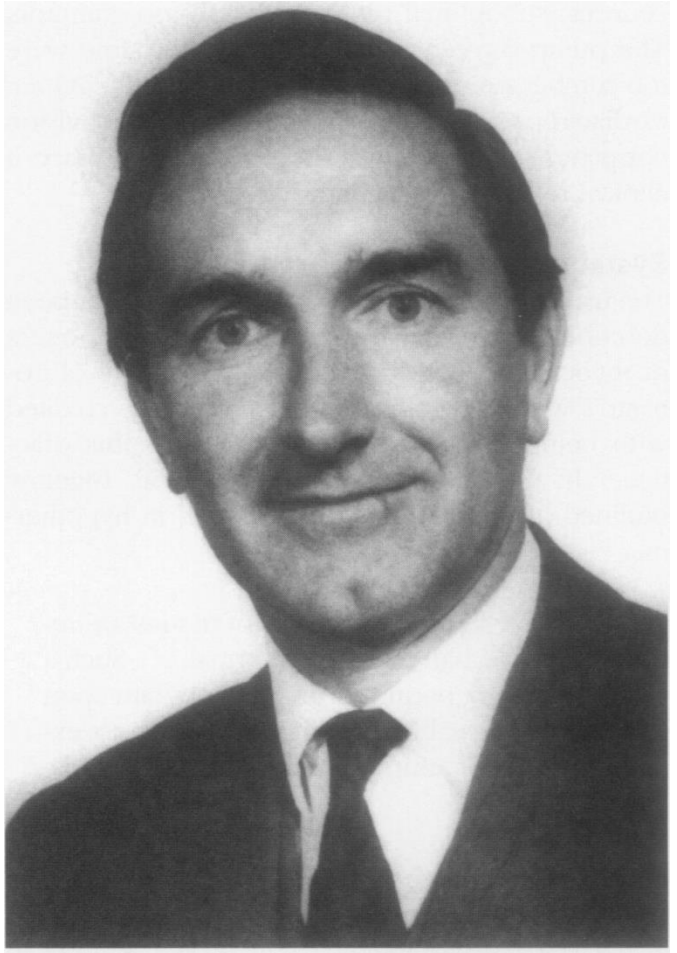
# Ionic Theory of Cardiac Activity

- Syndey Ringer
  - Calcium was left unopposed by potassium salts, contractions strengthened until fusion of beats occurred and ventricular tetani ultimately resulted



# Potassium Citrate Arrest

- Denis G. Melrose
  - *The oxygen consumption of the quiescent heart is very low, and at normal body-temperature, cessation of the coronary circulation for over fifteen minutes does not endanger such a heart. Although a great deal of further work remains to be done, this method may offer an opportunity for useful surgery on the motionless heart, without the danger of air embolism*

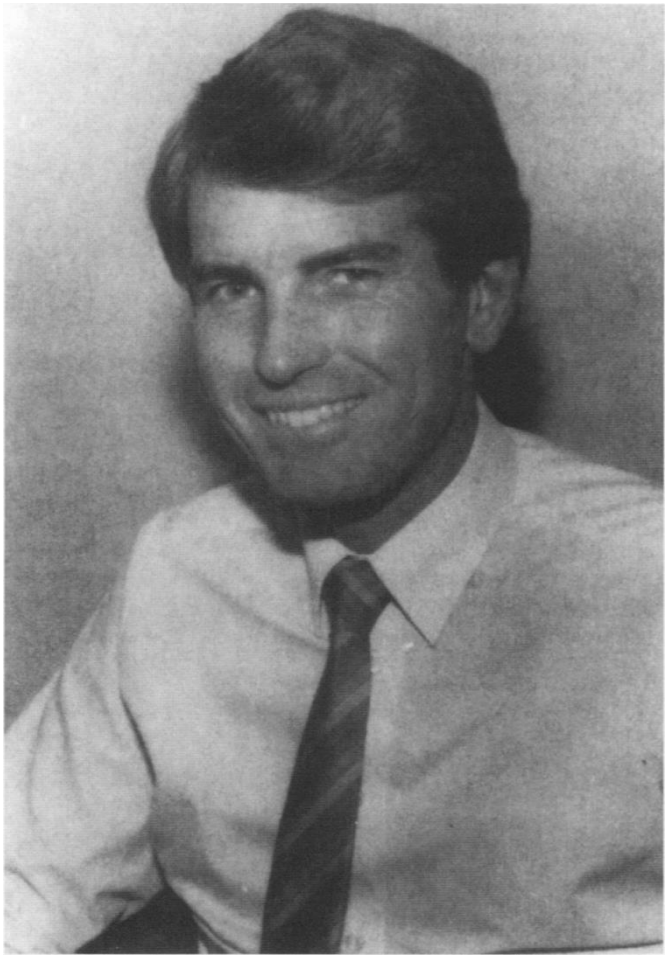


# Bretschneider's solution

- Hans J. Bretschneider
  - Sodium concentration
    - the same as the intracellular concentration of sodium
    - Prevent the excitation potential and thus prevent myocardial contraction
  - Calcium-free environment
    - Prevent contraction
  - Procaine
    - Provide membrane stabilization
  - Mannitol
    - Maintain ideal osmolarity

# St. Thomas' Hospital Solution

- David J. Hearse
  - Extracellular cardioplegic solution



# Evolution of Cardioprotective Methods and Techniques

| Reference | Year | Innovation |
|---|---|---|
| Bigelow WG et al | 1950 | Studied the application of hypothermia to cardiac surgery in canines |
| Swan H et al | 1953 | Showed that hypothermic arrest (26°C) in humans provided a bloodless field for operating |
| Melrose DG et al | 1955 | Introduced the concept of reversible chemical cardiac arrest in canines |
| Lillehei CW et al | 1956 | Heart was protected by retrograde coronary sinus perfusion of oxygenated blood |
| Lam CR et al | 1957 | One of the earliest known uses of the term ‘cardioplegia’ |
| Gerbode F, Melrose D | 1958 | Used potassium citrate to induce cardiac arrest in humans |
| McFarland JA | 1960 | Challenged the safety of the Melrose technique; changed from potassium arrest to intermittent aortic occlusion or coronary artery perfusion for myocardial protection |
| Bretschneider HJ et al | 1964 | Developed a sodium-poor, calcium-free, procaine-containing solution to arrest the heart |
| Sondergaard KT | 1964 | Adopted Bretschneider’s solution for clinical use |
| Gay WA, Ebert PA | 1973 | Credited with revival of potassium-induced cardioplegia; demonstrated that potassium solution could arrest a canine heart for 60 minutes without cellular damage |
| Roe BB et al | 1973 | Demonstrated that ‘the modalities of cardioplegia, hypothermia, and capillary washout’ provided effective myocardial protection |
| Tyres GF | 1974 | Demonstrated in preclinical studies that an infusion of cold blood to maintain myocardial temperature < 4°C provided 90 minutes of protection |
| Hearse DJ et al | 1975 | Emphasized preischemic infusions to negate ischemic injuries in rats; this formula becane known as St. Thomas solution no. 1 |
| Braimbridge MW et al | 1975 | One of the first to use St. Thomas solution no. 1 clinically |
| Effler DB et al | 1976 | Simple aortic clamping at room temperatures recommended |
| Buckberg GD | 1979 | Blood is an effective vehicle for infusing potassium into coronary arteries |
| Akins CW | 1984 | Hypothermic fibrillatory arrest for coronary revascularization without cardioplegia |
| Murry CE et al | 1986 | First to report that brief periods of ischemia (preconditioning) and reperfusion enable the heart to withstand longer periods of ischemia |
| Lichtenstein SV et al<br>Salerno TA et al | 1991 | Reported warm antegrade and retrograde blood cardioplegia safe |
| Ikonomidis JS et al | 1995 | Combined normothermic continuous retrograde cardioplegia with intermittent antegrade infusions |
| Teoh LK et al | 2002 | Introduced concept that intermittent cross-clamp fibrillation in CABG surgery patients confers cardioprotection via ischemic preconditioning and adenosine receptor activation |
| Quinn DW et al | 2006 | Phase II human trial demonstrated efficacy of cardoprotective effects of systemic glucose-insulin-potassium (GIK) when administered peroperatively |
| Mentzer RM et al | 2008 | Phase III myocardial protection trial in humans demonstrated proof of concept that perioperative MI can be reduced with IV infusion of a pharmacologic agent in CABG surgery patients |

# Commercially Prepared Cardioplegic Solutions

| Components | Plegisol St. Thomas II | CAPS[a] Buckberg | Bretschneider | ViaSpan UW | Units |
|---|---|---|---|---|---|
| $K^+$ | 16 | 60 | 10 | 125 | mmol · $L^{-1}$ |
| $Na^+$ | 110 | [b] | 15 | 30 | mmol · $L^{-1}$ |
| $Cl^-$ | 128 | [b] | 50 | 41.5 | mmol · $L^{-1}$ |
| $Ca^{2+}$ | 1.2 | — | — | — | mmol · $L^{-1}$ |
| $Mg^{2+}$ | 16 | — | 4 | 2.5 | mmol · $L^{-1}$ |
| $PO_4^{2-}$ | — | — | — | 25 | mmol · $L^{-1}$ |
| Histidine | — | — | 198 | — | mmol · $L^{-1}$ |
| Tryptophan | — | — | 2 | — | mmol · $L^{-1}$ |
| Ketoglutarate | — | — | 1 | — | mmol · $L^{-1}$ |
| Glucose | — | 4 | — | — | g · $L^{-1}$ |
| Mannitol | — | — | 30 | — | mmol · $L^{-1}$ |
| THAM (0.3 mol) | — | 200 | — | — | mL |
| CPD | — | 50 | — | — | mL |
| Raffinose | — | — | — | 30 | mmol · $L^{-1}$ |
| K-Lactobionate | — | — | — | 100 | mmol · $L^{-1}$ |
| Allopurinol | — | — | — | 1 | mmol · $L^{-1}$ |
| Adenosine | — | — | — | 3 | mmol · $L^{-1}$ |
| Hydroxyethyl starch | — | — | — | 50 | g · $L^{-1}$ |
| Glutathione | — | — | — | 5 | mmol · $L^{-1}$ |
| pH | 7.8 | 7.65 | 7.1 | 7.4 | |
| Osmolarity | 280 | –350 | 310 | 320 | mOsm/L |
| *Additives*[c] | | | | | |
| $NaHCO_3^-$ | 10 | — | 25 | — | mmol · $L^{-1}$ |
| 0.46 mol aspartate glutamate[d] | — | — | 250 | — | mL |
| Insulin | — | — | — | 40 | units · $L^{-1}$ |
| Dexamethasone | — | — | — | 16 | mmol · $L^{-1}$ |

[a]This formulation is intended for dilution by two or four parts blood (perfusate) to solution.
[b]Concentration is diluent dependent.
[c]Added to the commercially prepared solutions.
[d]For warm induction and reperfusion strategies only.

# Crystalloid Cardioplegic Solution

- Intracellular type
  - Abscent or low concentrations of sodium and calcium
  - Bretschneider's solution
- Extracellular type
  - Higher concentrations of sodium, calcium, and magnisium
  - St. Thomas' Hospital solution

# Types of Cardoplegia

- Blood cardioplegia
  - Natural buffering agent
  - Maintain oncotic pressure
  - Advantageous rheologic properties
  - Free-radical scavenger

- Cold-crystalloid cardioplegia
  - Systemic hemodilution
  - Shifts the oxyhemoglobin disassociation curve leftward
  - Retarding Na/K adenosine triphosphatase
  - Produces edema and activation of platelets, leukocytes, and complement

# Components of Blood Cardioplegia

- Four parts blood to one part crystalloid solution
- High level of potassium
  - Maintains cardiac arrest and prevents sudden intracellular calcium accumulation
- Low level of calcium
  - To limit calcium loading during the conditions of impaired ionic balance in the early period of reperfusion
- Aspartate and glutamate
  - Increase the energy-depleted heart's ability to use oxygen and hasten ionic recovery
- Hyperosmolarity
  - Reduce edema
- THAM(tromethamine)
  - To limit the evolution of acidosis during ischemia
  - Hasten enzymatic recovery

# Blood vs Crystalloid ?

| Authors | Title | Year | Intervention | Patients included | Study design | Study endpoints |
|---|---|---|---|---|---|---|
| Øvrum et al. | A prospective randomized study of 1440 patients undergoing coronary artery bypass grafting | 2004 | Blood versus crystalloid | 1.440* | Prospective randomized | Operative variables[1], inotropic support, ICU/hospital stay, arrhythmias, stroke, mortality |
| Øvrum et al. | A prospective randomised study of 345 aortic valve patients | 2010 | | 345* | Prospective randomised | |
| Guru et al. | Is blood superior to crystalloid cardioplegia? A meta-analysis of randomized clinical trials | 2006 | | 5.044* | Meta-analysis | LOS, MI, CKMB at 7 h, 24 h, 48 h |

# Is Blood Superior to Crystalloid Cardioplegia?

## A Meta-Analysis of Randomized Clinical Trials

Veena Guru, MD; John Omura, BHSc; Abdullah A. Alghamdi, MD;
Richard Weisel, MD; Stephen E. Fremes, MD

***Background***—Many small, randomized, controlled trials have evaluated the effectiveness of blood as compared with crystalloid cardioplegia for myocardial protection during cardiac surgery. Blood cardioplegia provides a closer approximation to normal physiology, which may translate into measurable clinical benefits. This meta-analysis describes the effectiveness of blood cardioplegia in lowering adverse postoperative outcomes.

***Methods and Results***—MEDLINE, EMBASE, and the Cochrane registry of controlled trials were searched for clinical trials. The search was restricted to peer-reviewed English language publications of randomized controlled trials that primarily compared blood and crystalloid cardioplegia in adult patients. Each trial was blindly assessed and abstracted by 2 reviewers. The primary outcomes were: low output syndrome (LOS), myocardial infarction (MI), and death. Surrogate outcomes included postoperative creatinine kinase MB (CKMB) increase. Random effects summary odds ratio (OR) for binary outcomes, and weighted mean difference for continuous outcomes were calculated. A total of 34 trials were included. The majority of trials were conducted in patients undergoing elective CABG surgery (n=18). The incidence of LOS was decreased significantly with blood cardioplegia (OR, 0.54; 95% confidence interval [CI], 0.34 to 0.84; $P$=0.006; 879 patients, 10 trials). The incidence of MI and death were similar between treatment groups (MI: OR, 0.78; 95% CI, 0.54 to 1.13; 4316 patients, 23 trials) (death: OR, 0.80; 95% CI, 0.46 to 1.40; 4022 patients, 17 trials). CKMB release after surgery at 24 hours was reduced with blood cardioplegia (5.9 U/L; 95% CI, 1.6 to 10.2; $P$=0.007; 821 patients, 7 trials).

***Conclusions***—Blood cardioplegia provides superior myocardial protection as compared with crystalloid cardioplegia, including lower rates of LOS, and early CKMB increase, whereas the incidence of myocardial infarction and death are similar. (***Circulation***. **2006;114[suppl I]:I-331–I-338.**)

**Key Words:** cardioplegia ■ meta-analysis

# Is Blood Superior to Crystalloid Cardioplegia?

## A Meta-Analysis of Randomized Clinical Trials

Veena Guru, MD; John Omura, BHSc; Abdullah A. Alghamdi, MD;
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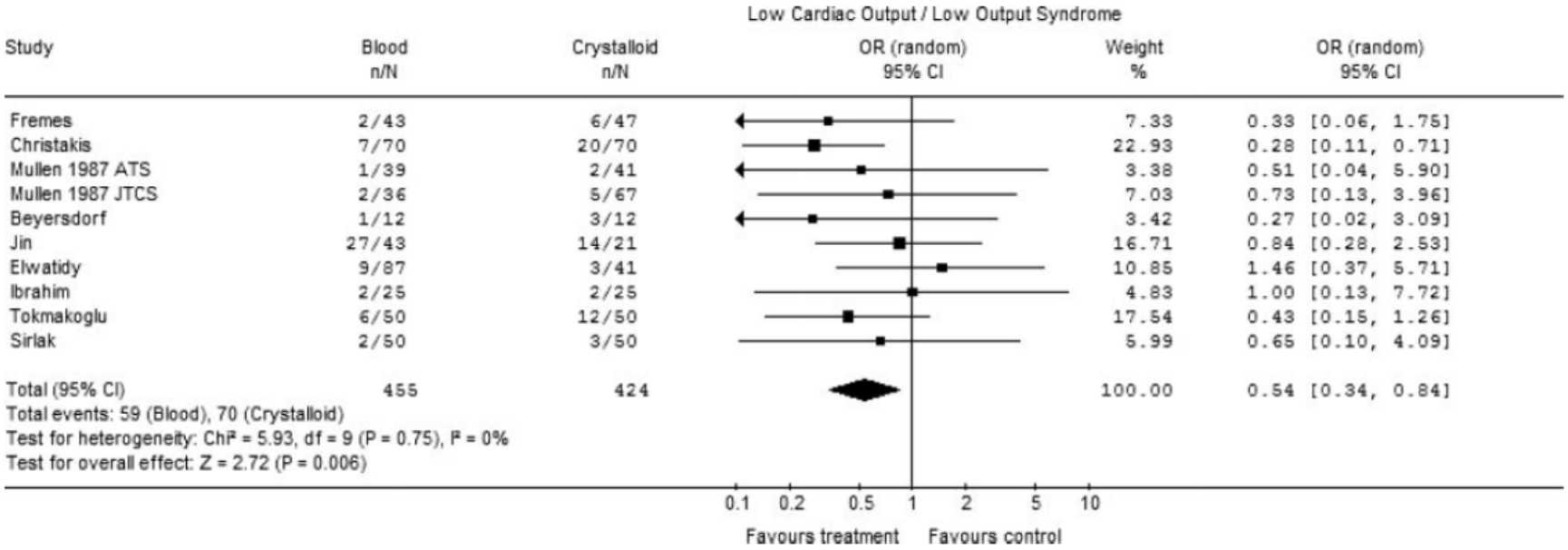

# del Nido Cardioplegic Solution

| | |
|---|---|
| ***Crystalloid Components*** | |
| Plasma-Lyte A | 1000 mL |
| Mannitol 20% | 16.3 mL |
| Mg sulfate 50% | 4.0 mL |
| Sodium bicarbonate 1 mEq · $mL^{-1}$ | 13 mL |
| Lidocaine 1% | 13 mL |
| KCl 2 mEq · $mL^{-1}$ | 13 mL |
| Plasma-Lyte A | Electrolyte-balanced and pH-adjusted carrier solution |
| Sodium bicarbonate | Buffers crystalloid solution closer to a pH of 7.4 |
| Mannitol | Used to decrease myocardial edema and serve as an oxygen free radical scavenger |
| ***Arresting Agents*** | |
| Potassium chloride | Depolarizes cell membrane |
| Lidocaine | Sodium channel blocker; serves to maintain arrest in a hyperpolarized state, counteracting negative effects of potassium |
| Magnesium | Used as a calcium channel blocker and competitive inhibitor of calcium interaction with contractile proteins, preventing contractile activation |

# Future Perspective

- Magnesium cardioplegia
- Esmolol cardioplegia
- Preconditioning and postconditioning

# 심근보호법(myocardial protection)의 종류

고려대학교 안산병원 신 재 승

## '심근보호'의 정의

넓은 의미의 '심근보호'란 심근보호액 뿐 아니라 좋은 수술결과를 얻기 위해 사용되는 수술 전후의 모든 환자관리를 포함한다. 그러나 일반적인, 좁은 의미의 심근보호법은 심장수술 시 심정지를 유도하고, 수술 후 심장의 기능 및 환자의 회복을 돕기 위해 행해지는, 심정지 기간중의 환자 및 심근처치법를 의미한다. 1950년대 이후 냉관류액 및 표면냉각요법을 이용한 저체온법이 심근보호의 중요한 방법이 되었다. 또한 심근세포의 물질대사율을 감소시키고, 허혈 기간 내 세포손상을 감소시키기 위하여 심근보호액을 사용하게 되었다.

이전의 심근보호법은 심장수술 시 심정지를 유도하고 손쉽게 수술하기 위하여 수술시야에서 혈액제거가 주목적이었으나, 최근에는 박동하 심장수술과 최소침습심장수술이 발전하며, 그 개념이 수술 전후의 좋은 결과를 위한 모든 환자관리를 의미한다. 즉, 협심증 환자에서 술전에는 심근의 산소요구량/공급량의 균형을 위한 투약, 항응고제, 혈전용해제 및 대동맥풍선의 사용 등이 포함된다. 심근정지/보호액을 사용한 수술 중에는 심근에 산소와 영양소의 공급, 산증(acidosis)에 대한 완충제, 세포부종의 예방, 심근보호액을 심근에 골고루 공급하는 방법, 산소 자유라디칼의 제거법 등을 포함한다. 박동하 수술 시에는 관상동맥 문합 중 허혈을 최소화 하기 위한 전처치(pre-conditioning)방법이나 관상동맥내 도관(shunt)의 사용과 혈류역학적 감시와 처치 등이 포함된다.  또한 허혈-재관류 손상을 최소화하기 위한 모든 처치들이 포함된다. 그리고 수술 후 회복기의 심장 후부하 감소, 심박수 조절, 심근의 산소전달능력 향상 및 산소소모량을 감소시키는 모든 것이 포함된다.

# 허혈-재관류손상을 감소시키는 연구

허혈-재관류손상을 최소화하는 방법은 가능한 허혈을 피하고, 재관류 시 낮은 관류압을 유지하며, 재관류액의 저농도 칼슘을 유지한다. 또한 재관류액에 산소자유라디칼 제거제를 첨가하고 중성구를 제거하는 방법이 사용되기도 한다.

## 1. Modification of ischemia-reperfusion injury by cardioprotective interventions

심근허혈-재관류에 따른 심근세포의 손상은 심장수술 시 심정지 후뿐 아니라, 혈관성형술, 관상동맥우회술, 혈전용해술 등의 상황에서 발생된다. 이러한 손상을 초래하는 원인은 칼슘의 과부하, 산소 자유라디칼의 과생성, 여러가지 효소의 활성도 변화 등인 것으로 알려져 있으며, 심근세포의 사멸, 심근수축력 저하, 부정맥 등을 유발한다. 따라서 이 과정에 작용하여 심근손상을 줄이기 위하여, preconditioning, antioxidants, $Ca^{++}$ blocker, phospholipase $A_2$ inhibitor, $Na^{+}$-$H^{+}$exchanger inhibitor, $P_{38}$ MAP kinase inhibitor, protein phosphatase inhibitor, phosphodiesterase inhibitor-phentoxifylline, 5-HT receptor antagonist 등에 관한 연구가 진행되고 있다.

## 2. Myocardial protection during acute myocardial infarction and angioplasty

급성 심근경색에 이은 재관류 시 심근에 발생하는 손상은 부정맥, 심근 수축력 약화 혹은 심근혼절(myocardial stunning), 관상동맥 및 모세혈관의 재관류 손상 및 가역적 손상세포내의 괴사침전 등이 발생한다. 심근세포의 허혈성 손상에 대한 저항력을 증가시키기 위하여, 허혈전처치, Glucose-insulin-potassium, ATP, potassium channel agonist, hypothermia, fatty acid oxidant inhibitor, reducing oxygen requirement, angiotensin-blocker, beta-adrenergic blocker, IABP, CPB support, coronary retro-perfusion법 등이 사용된다. 또한 재관류손상을 감소시키기 위하여 antiplatelet IIb-IIIa inhibitor, Sodium-

hydrogen exchanger, magnesium, adenosine, leukocyte receptor monoclonal antibody, complement inhibitor등이 사용된다.

## Continuous coronary perfusion with ordinary, normokalemic blood

체온을 약간 감소시킨 상태 (32-34℃)에서, 박동상태 혹은 심실세동 상태의 심장에 지속적으로 혈액을 공급하는 방법이다. 대동맥을 겸자로 차단하고 대동맥간 혹은 관상동맥에 직접 혈액을 공급하는 방법으로 관상동맥우회술, 좌심실기능이 좋지 않은 대동맥 판막 수술이나, 우측 개흉술 후 대동맥 차단 없이 시행하는 승모판 재수술의 경우 사용될 수 있다. 주의할 점은, 세동하 수술의 경우 전기적으로 유도된 심실세동은 자발적 세동에 비하여 심내막하 관류가 부족하므로 심근비대가 심한 경우 주의하여야 한다. 또한 관상동맥질환이 있는 경우 허혈부위의 측행혈류에 변화가 발생할 수 있다. 그리고 과다한 관상동맥 혈류량 (>300 mL/min)은 심근세포손상과 부종을 유발할 수 있다.

## Cross-clamp fibrillation

체외순환 후, DC 전류를 사용하여 심실세동을 유도한 후, 대동맥 차단을 시행한다. 주로 관상동맥우회술시 많이 사용되며, 정맥환류가 좋고, 심실이 팽창되지 않는다면 심내막하 허혈은 발생하지 않는다. 세동 하에서 관상동맥 문합을 완성하고, 제세동을 시행한 후 이식편의 대동맥 문합을 시행한다. 이 방법은 관상동맥과 정맥의 구별 및 이식편의 혈류측정이 용이하고, 심근내 관상동맥의 경우 유용하다. 또한 수술 중 관상동맥을 통하지 않는 측행혈류의 차단이 없다는 장점이 있다.

## Moderate hypothermic intermittent global ischemia

흔히 Intermittent aortic cross-clamping으로 알려진 방법으로 평이한 관상동맥우회술에 사용된다. 이 방법은 “저체온에서는 심근의 산소소모량이 감소하고 20분 미만의 허혈성 손상은 혈액의 재관류시 빨리 회복된다”는 개념에 토대를 둔다. 1986년 Dr. Murry는 허혈성 전처치(Ischemic preconditioning)를 통해 허혈에 대한 심근의 저항성이 증가하고, 재관류로 인한 부정맥이 감소하고, 수축기능부전을 감소시키며, 허혈성 경축을 예방되고, 물질대사상태를 개선하여 산증(acidosis)을 예방되며, 심근 ATP가 보존되는 것을 발표하였다. 대동맥차단 초기에 adenosine, achetylcholine, catecholamine, angiotensin II, bradykinin, opioids등의 내인성 물질들이 분비되는데 이중 adenosine이 심근보호 효과를 가진다.

체외순환이 시작되면, 체온을 32℃까지 낮추고, 심실세동을 유도한 후 대동맥 차단을 시행한다. 3-4분간 대동맥을 차단하고 관상동맥 문합을 시행한다. 3-4분간의 대동맥 차단 후에 대동맥 겸자를 제거하고 1분간 재관류를 시행하는 것을 반복한다. 이때 만일, 10분 이내에 문합이 완성되지 않으면, 문합을 중단하고, 겸자를 제거한 후에 3-4분간의 충분한 재관류를 시행한다. 마지막 문합 도중 체온을 상승시켜 대동맥 겸자를 마지막으로 제거할 때에는 정상 체온이 되도록 한다.

이 방법의 장점은 매 순간 심근의 기능을 확인할 수 있으며, 관상동맥 이식편의 길이와 위치를 확인하기 쉽다는 점이다. 그러나, 반복적으로 대동맥을 차단함으로 인해 대동맥의 손상 및 색전이 발생할 단점이 있으며, 심실이 팽창되지 않도록 대동맥 차단 전에 확인하여야 한다.

## Profoundly hypothermic global ischemia

이 방법은 초저체온법과 함께 대동맥/대동맥궁 수술 시 사용된다.

# Cardioplegic arrest

심정지액을 이용한 방법으로 심근세포 내외의 전해질 농도차이에 따른 전위를 변화시켜서 이완기 심정지를 유도하는 방법으로, 흔히 세포외액의 칼륨을 증가시켜 탈분극을 방지하는 방법이 흔히 사용된다. 간혹 세포외액의 나트륨의 농도를 감소시켜 재분극을 막는 방법이 사용되기도 한다.

## 심근보호액의 전달법

### 1. Antegrade, Retrograde, or Both?

| | Antegrade | Retrograde |
|---|---|---|
| 장점 | ① Easy, natural<br>② Rapidity of administration<br>③ Rapid cardiac arrest | ① Uniform, homogenous distribution<br>② Less invasive<br>③ Possibility of continuous delivery<br>④ Without interruption of surgical procedure<br>⑤ Allows arterial grafts to be de-aired in retrograde fashion in CABG<br>⑥ Prevent distal migration of emboli in redo CABG |
| 단점 | ① Potential traumatization of the coronary arteries<br>② Inadequate distribution of the perfusate in the presence of coronary disease | ① Bicaval cannulation and complete bypass<br>② Enormous volume of cardioplegia<br>③ Longer time to achieve complete cardiac arrest<br>④ Part of cardioplegia is lost into the lungs<br>⑤ Edema formation (Pr > 45-50 mmHg)<br>⑥ Inadequate protection of RV |

해부학적으로 관상정맥 및 정맥미세순환은 관상동맥계보다 분포가 풍부하고 정맥판막이 없다. 알려진 바와 같이, 관상정맥은 심혈류량의 73%가 환류되며 관정맥동을 통해 우심방

으로 배액된다. 테베지우스정맥(Thebesian vein)은 심혈류량의 27%를 담당하며 각 심방/실로 배액된다. 관상정맥의 해부학적인 특징으로 인해 심근보호액의 역행성 공급을 할 경우, 우심실 전벽과 심실중격에는 잘 공급되지 않는다. 따라서 전향성 공급과 병행하거나, 관정맥동 차단법을 혼합한 방법이 많이 쓰인다.

### 2. Intermittent or Continuous?

심근의 산소요구량/공급량의 균형을 위하여는 지속적인 심근보호액의 공급이 이상적이나 관상동맥을 통해 지속적인 공급을 할 경우 수술 시야의 지장을 초래한다. 따라서 전향성 간헐적 공급법이나, 지속적 역행성 공급법을 사용한다.

### 3. Hypothermia or Normothermia?

Warm heart surgery 참조

## Combined use of antegrade and retrograde cardioplegia

최근에는 빠른 심정지와 심근온도저하가 가능한 전향성 전달법과 심근전반에 걸쳐 골고루 전달이 가능한 역행성전달법의 장점만을 택한 혼합법을 흔히 사용한다.

예를 들면, 혈액:심근보호액=4:1의 냉혈성 심근보호액을 전향성으로 70 mmHg이하의 압력으로, 300 mL/min의 속도로 2분간 주입한 후에, 역행성으로 35 mmHg 이하의 압력으로, 200 mL/min의 속도로 2분간 주입하여 심정지를 유도한다. 이후 심정지의 유지는 4:1의 냉혈성 심근보호액을 15-20분마다 역행성으로 35 mmHg 이하의 압력으로, 200 mL/min의 속도로 2분간 주입하여 유지한다. 이후 수술이 종료되면 마지막으로 정상체온의 심정지액을 주입하는데 (final warm shot) 37℃의 심근보호액을 전향성 혹은 역행성으로 300 mL를 200 mL/min의 속도로 1.5분에 걸쳐 주입한 후에, 37℃의 혈액을 주입한다.

## Controlled aortic root reperfusion

심장수술 후 재관류를 시행할 때 관류액의 조성과 압력을 의도적으로 조절하여 심근의 회복을 향상시키는 방법이다. 재관류의 목적은 심근세포의 빠른 에너지 회복이다. 에너지 회복을 위해서는 재관류시 심근이 전기생리적으로 안정화되어 있어야 한다. 이를 위하여 혈액의 재관류 전에 칼륨을 포함한 37℃의 심근보호액으로 마지막 관류를 시킨다. 수술 중 심근보호액의 사용량이 적었으면, 칼륨 농도 20-30mEq/L, 사용량이 많았으면 15 mEq/L의 심근보호액을 역행성으로 주입한다. 총 주입량은 500mL X 체표면적/1.5로 한다. 이후 37℃ 혈액으로 재관류를 시행하는데, 관상동맥 내막의 손상을 최소화 하기 위하여 관류압을 조절한다. 처음에는 대동맥 차단을 유지한 상태에서 혈액을 역행성으로 30mmHg미만의 압력으로 주입하면서 심장의 박동이 회복되면, 대동맥간 캐눌라를 통해 공기를 제거한다. 이후 대동맥간 캐눌라를 통한 전향성 혈액 재관류를 시행하는데 처음 3분간은 30mmHg 미만의 압력으로, 이후에는 술전 이완기 혈압과 75mmHg중 낮은 압력으로 혈액관류를 시행한다.

## Warm Heart Surgery

1970년대까지의 심근보호법은 Bigelow에 의한 저체온법과 Melrose에 의한 Potassium 심근보호액이 주된 방법이었다. 이후에 심근보호액에 혈액, 산소, 영양분 및 완충제가 추가되었다. Warm heart surgery는 1957년 Gott가 처음으로 제안하였으나 임상적으로 사용되지 않았다. 그 후 Buckberg 등에 의해 심근허혈과 재관류손상의 기전이 밝혀지고, 15℃ 미만의 차가운 심근보호액의 주입 시, 산소-해리 곡선이 좌측으로 이동됨에 따라 산소의 이용이 제한된다는 개념에 따라, ‘substrate-enhanced warm cardioplegia induction’과 대동맥 겸자 제거 전의 ‘terminal hot shot’의 개념이 도입되었다. 이러한 개념을 발전시켜 1989년 Salerno등은 37℃의 심근보호액을 사용하게 되었다.

차가운 심근보호액 대신 정상체온의 심근보호액을 사용하게 된 이론적 배경은 다음과 같다. 정상체온의 박동중인 심근의 산소소모량을 100%로 보았을 때 정상체온, 정지상태의

심근 산소소모량은 10%로 감소한다. 이 상태에서 추가로, 체온을 감소시킬 경우 산소요구량이 50%이상 감소한다. 따라서 체온과 관계없이 정지 상태의 심근산소 요구량은 박동상태의 5-10%에 불과하다. 그런데, 37℃의 심근보호액을 지속적으로 주입하는 경우, 정상적 상태의 물질대사에 필요한 산소 및 기질 요구량의 30-50%까지 공급이 가능하다. 따라서, 37℃의 심근보호액은 심근물질대사에 필요한 산소와 기질 등을 상당히 안전하게 공급하는 방법이다. 더욱이, 냉 심정지액 주입 시 발생하는 부작용, 즉, 미토콘드리아와 세포의 부종, 세포막 불안정화, sarcoplasmic reticulum의 칼슘대사이상 등으로 인한 심근 에너지원 공급부족과 회복이상을 예방할 수 있다. 반면, 지속적 37℃ 심근보호액 주입의 단점으로는 고칼륨혈증, 고혈당, 혈액희석 등이 있다. 또한 정상체온에서의 혈관확장 효과로 인해 혈압유지를 위하여 혈관수축제의 사용량이 증가하여, 관상동맥이식편의 수축을 초래할 수 있다.

초기에는 37℃의 심근보호액과 37℃의 체관류액을 사용하였는데 뇌졸중 발생률이 상당히 높았다. 그 원인은 확실하지는 않으나, 37℃ 이상의 관류액 온도 및 고혈당의 심근보호액이 중추신경계 합병증을 일으킨 것으로 판단된다. 따라서 현재는 대뇌보호와 정상체온으로 인한 혈관확장 및 혈관수축제 사용을 감소시키기 위하여, 체온을 32-34℃로 유지한다.

체외순환을 시작한 후에 체온을 32-34℃로 유지하고, 37℃ 고칼륨 심근보호액(혈액:고칼륨 Fremes' 용액=4:1)을 전향적으로 주입하고 대동맥을 차단한다. 심장이 정지되면, 저칼륨 심근보호액(혈액:저칼륨 Fremes' 용액=4:1)을 역행성으로 지속적으로 주입한다. 이때 역행성 도관의 압력이 40mmHg이하로 유지하면, 약 122mL/min의 심근보호액이 주입된다.

### Miniplegia

논란의 여지가 있지만, 혈성 심근보호액의 우수성을 주장하는 연구자들은 그 장점으로 대동맥차단 중 호기성 물질대사를 활성화시키고, 심근 산소소모량을 증가시키며, 호기성 대사 산물인 젖산 생성을 감소시키며, 고에너지 ATP를 보전하는 것을 주장한다. 또한 수술 후 수축기/이완기 심근 기능이 우수하다고 한다. 이러한 혈성 심근보호액을 사용할 때는 저

온에서 점도증가 및 적혈구의 연전형성(rouleaux formation)을 방지하고, 첨가물에 의한 심근보호효과를 증가시키며, 염증반응 매개물을 약화시키기 위하여 희석을 하여 사용한다. 그러나 90년대에 Menasche등은 혈액희석에 따른 부작용을 최소화하기 위하여 칼륨과 마그네슘 만을 사용하였다. 일반적인 심근보호액의 구성은 심정지를 유발하는 칼륨, 칼슘 키일레이트제인 CPD(citrate-phosphate-dextrose), 완충제인 THAM(tris-hydroxymethyl aminomethane)과 영양성분(aspartate, glutamate, glucose)등으로 구성된다. 이중에서 칼륨 및 칼슘 키일레이트 대용으로 마그네슘 만을 사용한 것이다.

Miniplegia의 구성은 칼륨 16 mEq, 마그네슘 6 mEq가 포함된 증류수 20 mL 앰플로 되어 있다. 대동맥 차단 후 대동맥간을 통하여 정상체온의 혈액을 300 mL/min으로 관류하며 주사기펌프를 사용하여 miniplegia 20 mL 앰플을 30초이상에 걸쳐 주입한다. 심장이 정지되면, 관상정맥동을 이용하여 역행성으로 혈액을 150-200 mL/min로 관류하며 miniplegia 3앰플(60 mL)을 45 mL/h (36 mEq/h)의 속도로 주입한다. 이때 심전도의 활성이 나타나면 주입속도를 60 mL/h로 증가시키고, 안정화되면 30 mL/h로 감소시킨다. 이때 1시간 평균 주입량은 심정지 유도량 20 mL와 평균 1시간 주입량 45 mL로 총 칼륨양은 52 mEq가 된다.

Miniplegia의 사용은 수액의 과부하와 혈관이완을 예방할 수 있으며, 칼륨의 주입을 조절할 수 있고, 사용하기 편리하며, 경제적인 장점과 함께 술 후 부정맥의 감소화 심근보호효과가 긍정적이나, 혈관내막의 손상을 초래하여 혈관이완제에 대한 이상 반응이 문제가 되기도 한다.

## 참고문헌


1. Salerno TA. *Warm Heart Surgery*. Boston: Edward Arnold, 1995
2. Salerno TA, Ricci M. *Myocardial protection*. Blackwell publishing, Inc. 2003

3. Engelman RM, Levitsky S. *A textbook of cardioplegia for difficult clinical problems*. New York: Futura publishing company, Inc. 1992
4. Keogh BE. *Myocardial preservation.* In: Ohri SK, Tang A, Stephenson LW. *Key topics in cardiac surgery.* London and New York: Taylor & Francis. 2004
5. Buckberg GD. *Myocardial temperature management during aortic clamping for cardiac surgery. Protection, preoccupation, and perspective.* J Thorac Cardiovasc Surg 1991;102:895-903.
6. Buckberg GD. *Myocardial protection: an overview.* Semin Thorac Cardiovasc Surg 1993;5:98-106
7. Buckberg GD. *Update on current techniques of myocardial protection.* Ann Thorac Surg 1995;60:805-14
8. Buckberg GD. *Myocardial protection: entering the new millennium.* J Card Surg 2002;17:447-50.
9. Barner HB. *Blood cardioplegia: a review and comparison with crystalloid cardioplegia.* Ann Thorac Surg 1991;52:1354-67
10. Krunkenkamp IB, Levitsky S. *Myocardial protection: modern studies [key references].* Ann Thorac Surg 1996;61:1581-2

# CPB for Brain, Spinal cord and Kidney protection

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# Cerebral Function

- Independent of cerebral perfusion pressure
  - Range of 50-150 mmHg
  - Outside of range
    - CBF is directly related to cerebral perfusion pressure
  - Variables
    - the methods of acid-base management, mean arterial pressure, flow rate, and type of perfusion

# Cerebral Blood Flow

- Determinants
  - Brain
    - 2% of total Bwt. 14% of CO, and 20% of total $O_2$ consumption
    - High metabolic rate and limited energy stores
    - Extremely vulnerable to ischemia
  - Threshold cerebral blood flow at normothermia
    - under 30ml/100g/min; brain acidosis occurs
    - less than 20ml/100g/min; loses electrical activity
    - less than 10ml/100g/min; loses further cellular membrane integrity

# Cerebral Blood Flow

- Cerebral blood flow during deep hypothermia (20℃)
  - < 7ml/100g/min ; reduction of cerebral O2 metabolism
  - 9 ml/100g/min is necessary for aerobic metabolism (25-30% of normal)

- Full-flow perfusion at hypothermia
  - Metabolic rates for oxygen lower than those with 40ml/kg/min perfusion
  - Paradoxical acidosis & brain embolism at extreme velocity

# Cerebral Blood Flow

- Mean arterial blood pressure
  - 50 mmHg : minimal acceptable arterial blood pressure during CPB for cerebral autoregulation
  - Dependent on collateral perfusion
  - Reductions in $Sjvo_2$, occur in 17-23%
    - Associated with impaired tissue oxygenation and cognitive dysfunction

Schell RM, Anesth Analg 1993;76:849–65.
Taylor KM. Sem Thorac Cardiovasc Surg 1990;2:300–12.
Newman MF, Circulation 1996;94:353–7.
Mutch WA, J Cereb Blood Flow Metab 1994;14:510–8.
Schwartz AE, Ann Thorac Surg 1995;60:165–9.

# Cerebral Blood Flow

- Low-flow& intermittent perfusion
  - Prevent anaerobic glycolysis, intracellular acidosis, and prolong cerebral tolerance to ischemia
  - Minimal flow rate : 5-30 ml/kg/min at 18℃
  - Metabolic homeostasis is maintained
    - Every 20 min circulatory arrest at 18℃ for 2 min perfusion
- Pulsatile flow
  - Hemodynamic advantages over non-pulsatile

# Cerebral Blood Flow

- Pulsatile CPB benefits

**Table 2.** Putative Benefits of Pulsatile CPB Flow Compared with Nonpulsatile Flow

- Increased capillary patency
- Less venous "sludging"
- Enhanced lymphatic drainage reducing edema
- Enhanced nitric oxide and attenuated endothelin-1 release reducing cerebral vascular resistance
- Attenuation of inflammatory response to CPB
- Increased regional CBF after hypothermic circulatory arrest leading to increased tissue oxygenation and metabolism
- Increased CBF when blood flow is pressure dependent (i.e. impaired autoregulation)
- Lower neuropathologic score in ischemic penumbra after experimental stroke
- Less neuronal cell loss to CA1 hippocampal region and caudate nucleus after global cerebral ischemia
- Decreased number of $Sjvo_2$ desaturations

CPB = cardiopulmonary bypass; CBF = cerebral blood flow; $Sjvo_2$ = jugular venous oxygen saturation.

Anstadt MP, Ann Surg 1991;214:478–88.
Shepard RB, J Thorac Cardiovasc Surg 1969;58:694–702.
Champsaur G, J Thorac Cardiovasc Surg 1997;114:738–45.

# Open Heart Surgery

- Neurologic injury
  - 2nd common reason for death
  - Significant neurologic injury : 2% to 5% of patients
  - Including mild cognitive dysfunction: 70% of patients

  – Hemodilution, ↓ oncotic pressure
  – Microemboli or macroemboli, systemic inflammatory response, and cerebral hypoperfusion

# Cardiopulmonary Bypass

- Cerebral vulnerability
  - Microcirculatory dysfunction after TCA
  - Increased capillary permeability
  - Increase metabolic rate after TCA (hyperthemia)
  - Decreased substrate delivery (hypoglycemia)
  - Worsening right ventricular function (↑ venous pressure)

# Cardiopulmonary Bypass

- Brain injury in adults
  - Atheromatous emboli
  - Fixed cerebrovascular stenosis
  - Moderate hypothermia is used.
  - Relative vasodilation by PH-stat
    - Increased cerebral delivery of embolic material
    - Steal blood flow away from post-stenotic area

# Cardiopulmonary Bypass

- Brain injury in infants
  - Hypoperfusion during low or no blood flow
  - Deep hypothermia is used.
  - Cerebral oxygen supply will be enhanced .
  - High incidence of air embolism
    - Presence of intra- and extracardiac communication between systemic and pulmonary circulation
    - Increased amount of intracardiac surgery

# Optimal Neurologic Protection

- Variables
  - Perfusion pressure
  - Flow rate
  - Duration of cooling
  - Duration of circulatory arrest
  - Hematocrit
  - Ultrafiltration
  - Blood gas strategy
  - Presence of collateral flow
  - Impact of age

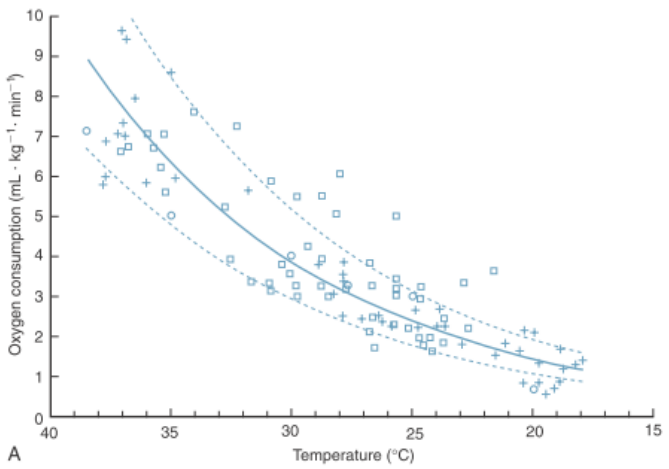
# Brain protection

| | Documented | Possible | Hypothetical |
|---|---|---|---|
| Slow cooling & Rewarming | V | | |
| Ice-Packing of the head | V | | |
| Wait for electrical silence | V | | |
| Continuous anterograde perfusion | V | | |
| Intermittent anterograde perfusion | V | | |
| Continuous retrograde perfusion | | V | |
| High Hct | | V | |
| Pharmacologic blockade of neurotransmitter | | V | |
| Pharmacologic enhance of vascular function | | | V |
| Pharmacologic prevention of reperfusion injury | | | V |

# Cerebral temperature

- Determinants of changes
  - Cerebral blood flow
  - States of metabolic rate
  - Heat exchange with environment

# Temperature & Oxygen consumption



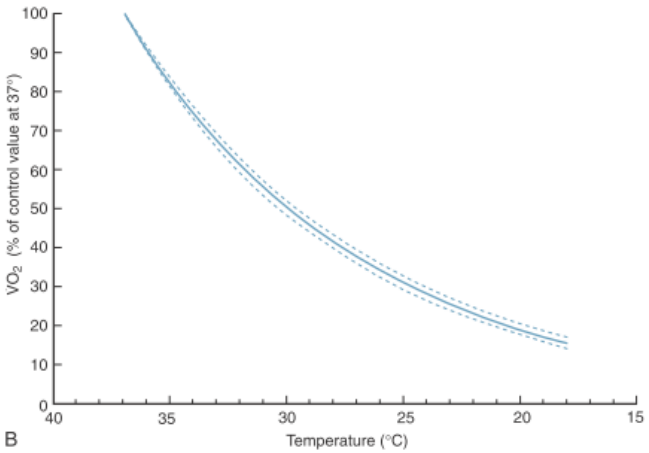




**Figure 2-1** Temperature and oxygen consumption. (Note reversal of temperature scale from normothermia on the left to hypothermia on the right.) **A,** Figure contains two depictions. One is a group of symbols representing data points relating measured whole-body oxygen consumption ($\dot{V}O_2$) to body temperature in dogs made hypothermic by surface cooling. (Crosses are data points from Ross[R22]; circles from Bigelow and colleagues[B31]; squares from Penrod.[P12]) From these, a regression equation, the second depiction, was derived, showing the van't Hoff relation between $\dot{V}O_2$ and temperature (Appendix Equation 2A-1). Solid line (representing the point estimates) and dashed lines (70% confidence band) are nomograms of the equation. Slope indicates a $Q_{10}$ of 2.7. **B,** Nomogram of the same equation, with oxygen consumption expressed as percentage of control value at 37°C.

$Q_{10}$

Bigelow WG, Am J Physiol 1950;160:125.
Penrod KE. Am J Physiol 1949;157:436.

# Temperature & Oxygen consumption

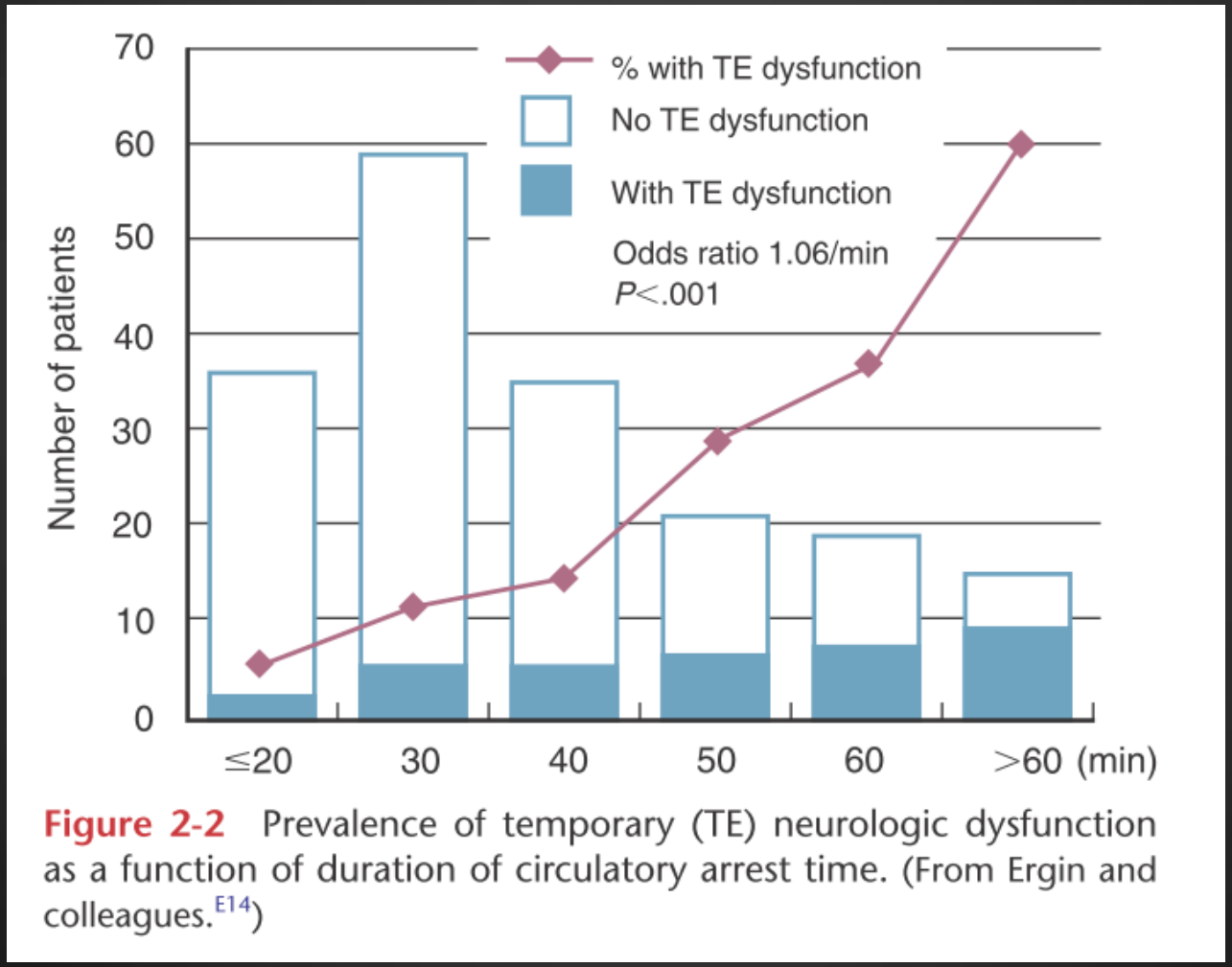



**Figure 2-2** Prevalence of temporary (TE) neurologic dysfunction as a function of duration of circulatory arrest time. (From Ergin and colleagues.[E14])

Ergin MA, J Thorac Cardiovasc Surg 1994;107:788.

# Temperature & Oxygen consumption

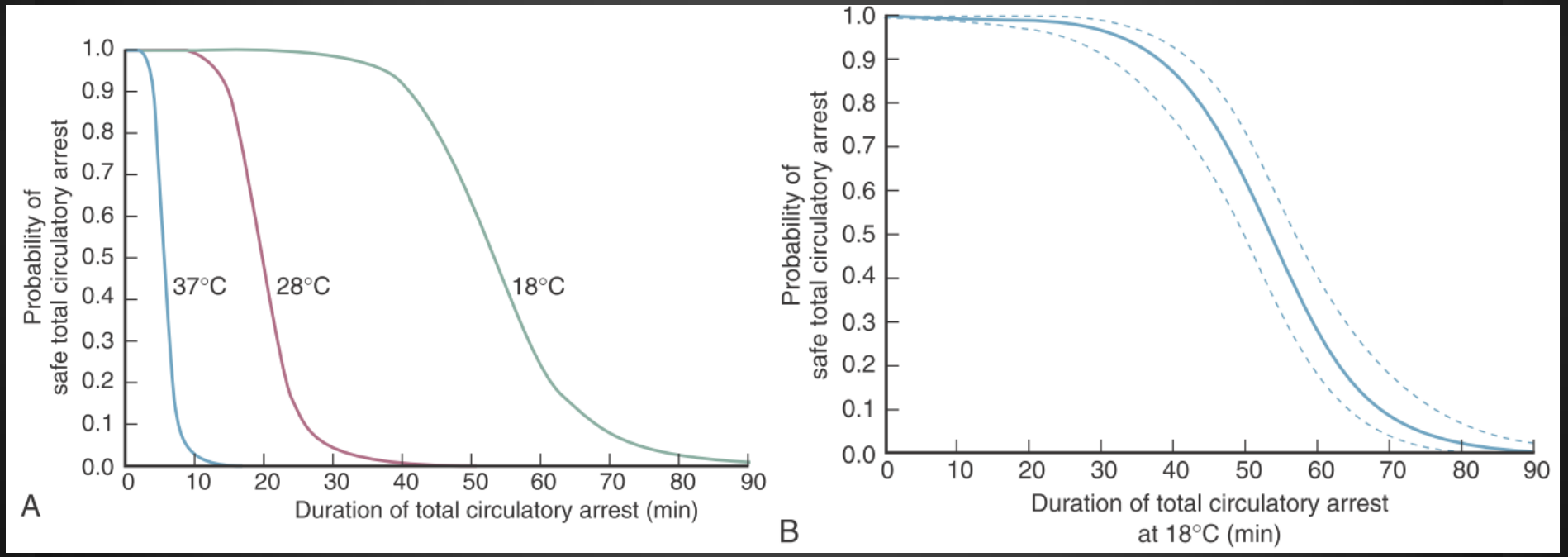
**Table 2-2** Major Neurologic Events after Hypothermic Circulatory Arrest

| Method | No. of Patients | Circulatory Arrest (min) | Major Neurologic Events[a] | | |
|---|---|---|---|---|---|
| | | | No. | % | CL |
| Surface cooling to 28°C, then core cooling | 80 | 42.5 ± 13.6 | 0 | 0 | 0-2 |
| Core cooling only | 138 | 42.8 ± 15.4 | 8 | 6 | 4-9 |
| TOTAL | 218[b] | | | | |
| *P* | | | | .03 | |

Data from Stewart and colleagues.[S31]
[a]Excludes seizures followed by uneventful convalescence.
[b]Repair of ventricular septal defect, tetralogy of Fallot, transposition of the great arteries, and atrioventricular septal defects. Mean temperature ± standard deviation during arrest for both groups was 19.7 ± 1.76°C.

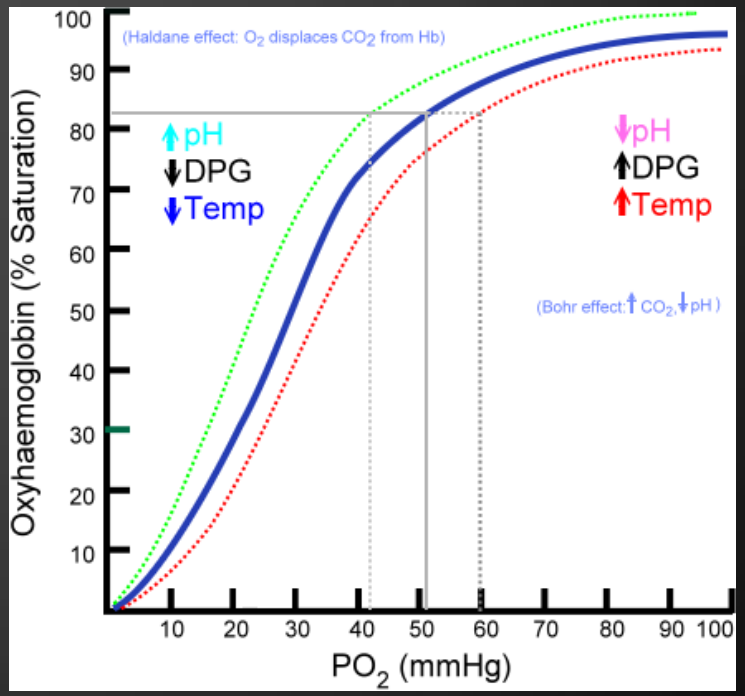
Stewart RW Congenital heart disease in the first three months of life. Medical and surgical aspects. Bologna, Italy: Patron Editore, 1981, p. 431.

# Temperature & Oxygen consumption



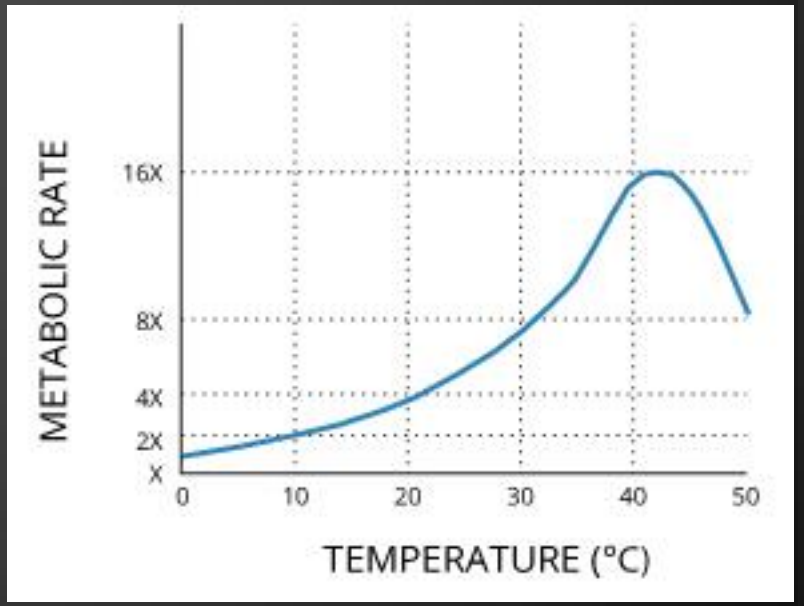
# Basic effects of Hypothermia

- Gas transport
  - ↓temperature →↓gas unloading from Hb
  - ↑carrying power of blood for $CO_2$



# Basic effects of Hypothermia

- Reduce the metabolic rate of the CNS
- Greater drop at high temperature
  (about 6 % for 1℃ around 37℃)




- ↑ flow/metabolism ratios

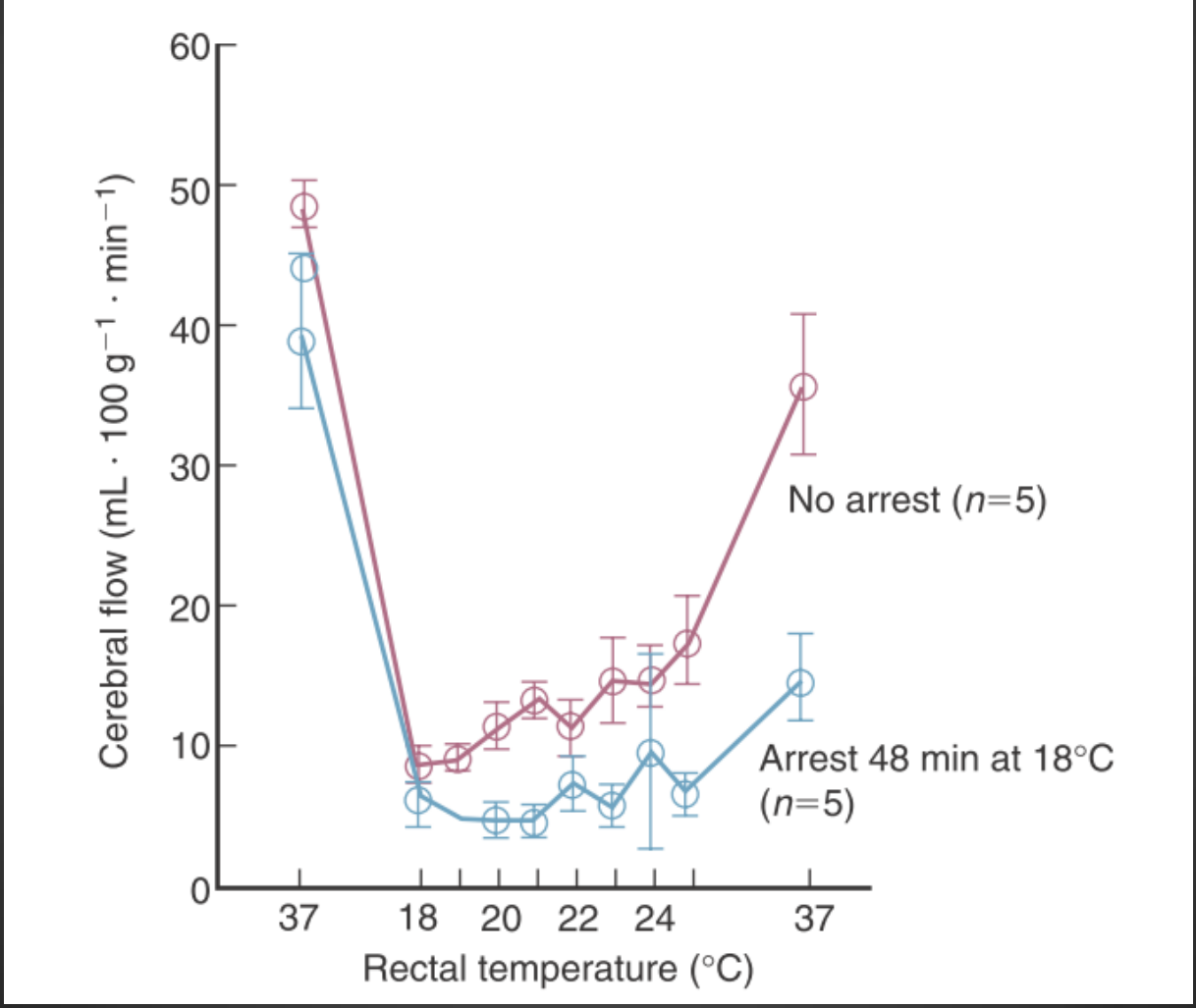
# Temperature management

- Cooling
  - Slow rate of cooling or rewarming
  - High blood flow
    - Two factors ensuring homogenous changes of the BT
  - Reduced oxygen availability & parallel decrease in metabolic rate
    - Balance between availibility & requirement of oxygen
    - Increased Hct
      - Compensate for decreased oxygen availibility
    - **Slow cooling & Adequate Hct !**
      - **Washout metabolites, buffers free radicals, and provides substrates before cerebral electrical activity**

# Temperature management

- Rewarming
  - Slow rewarming for optimal hemodynamic conditions and avoiding cerebral hyperactivity
  - Impaired cerebral vascular resistance & energetic metabolism
  - vulnerable period can last for 6-8 hours after reperfusion, and hyperthermia exacerbates cerebral activity & disturbs cellular metabolism, so a relative hypothermia is beneficial

# Temperature management




Kirklin JW. Perspectives in pediatric cardiology. Vol. 2. Pediatric cardiac surgery, part 1. Mount Kisco, N.Y.: Futura, 1989, p. 3.

Strauch JT, Eur J Cardiothorac Surg 2003;24:807-16.

# Hypothermic Circulatory Arrest

- Effects on brain
  - Global brain ischemia followed by ischemic-reperfusion injury
  - Loss of wall integrity in microvasculature
  - Fluid leakage
    - Brain edema, ↑ ICP, ↓brain tissue perfusion
  - Adherent neutrophils and microvascular thrombosis
    - Impairment of cerebral blood flow

# Hypothermic Circulatory Arrest

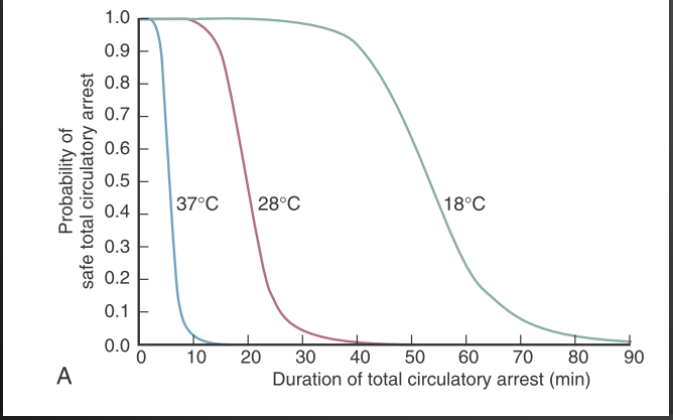
- Focal neurologic injury
  - Interruption of blood in a terminal vascular territory d/t embolic or gas
  - Localized necrosis (Watershed lesion)
  - Age, atherosclerosis, and manipulation of aorta
  - Not duration of circulatory arrest

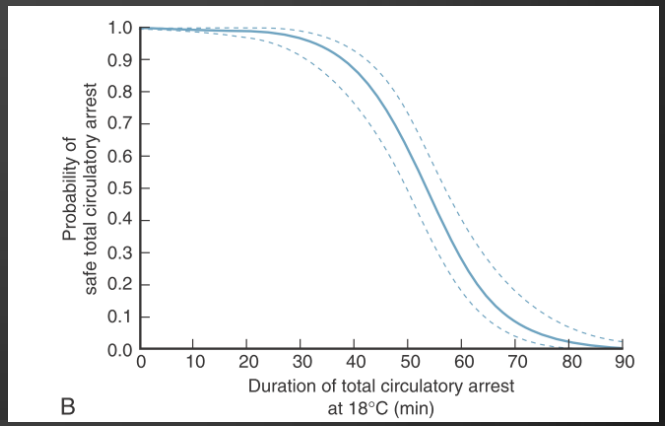
# Hypothermic Circulatory Arrest

- Diffuse neurologic injury
  - Global cerebral ischemia
    - Various levels of cellular dysfunction
    - Areas with reduced perfusion (atherosclerosis)
    - Increased metabolic activity (hyppocampus)
  - Age, improper conduct of CPB, prolonged duration of circulatory arrest

# Hypothermic Circulatory Arrest

- Limitations
  - No clear cut of safety duration
  - Recovery of oxygen consumption is already impaired after 15 minutes of ischemia at 18 ℃
  - Cerebral-produced lactate is detectable after 20 minutes of ischemia



# Intermittent Circulatory arrest

- Rationale & advantages
  - High energy demand organ
  - Brain oxygenation steadily decrease during retrograde cerebral perfusion and insufficient supply
  - Prevent anaerobic metabolism to reduce ischemic brain damage
  - Aerobic metabolism is maintained during the 1st 20 minutes of DHCA but rapidly changed over to anaerobic metabolism after the 1st 30minutes of DHCA.

# Low-flow CPB

- Low-flow CPB was superior to DHCA with respect to
  - High-energy phosphate preservation
  - Cerebral oxygen metabolism
  - CBF
  - Cerebral vascular resistance
  - Brain lactate levels.

# Blood Gas Management

- pH-stat strategy
  - Aim; constant pH
  - Total CO2;  increased
  - Intracellular state; acidosis
  - Alpha-imidazole & buffering ; excess(+) charge& ↓
- Alpha-stat strategy
  - Aim; constant OH/H,
  - Total CO2; constant
  - Intracellular state; neutral
  - Alpha-imidazole & buffering ; constant net charge&→

# pH STAT

- Advantages
  - Enhance cerebral blood flow
  - Enhance cerebral oxygenation
  - Maintain normal intracellular pH during cooling
  - Improve brain cooling & faster recovery of intracellular pH, cerebral high energy metabolites and oxygenation after HCA
- Disadvantages
  - Detrimental to cardiac & brain function
  - Increase the risk of cerebral embolism
  - Increase the regional ischemia  (steal through collateral)

# Alpha STAT

- Advantages
  - Maintain cerebral autoregulation
  - Maintain cerebral flow/metabolism coupling
  - Less neuropsychological damage
  - Reduction of global cerebral perfusion in low temperature is disadvantageous
- Disadvantages
  - Less metabolic suppression in hypothermia
  - Intracellular alkalosis during cooling
  - Need of higher hematocrit
  - Disturbed cerebral oxygenation during fast rewarming

# Acid-Base Management

**Table 3.** Prospectively Randomized Clinical Trials of the Effects of Acid-Base Management During CPB on Neurologic Complications After Cardiac Surgery

| Study | n | Findings |
|---|---|---|
| Murkin et al (134) | 316 | Frequency of cognitive impairment no different between α-stat and pH-stat management using primary endpoints. Subsequent analysis suggested a benefit with α-stat when CPB duration >90 min ($P$ = 0.047 versus pH-stat). Whether there was correction for multiple comparisons is not clearly stated. |
| Bashein et al (154) | 86 | No difference in psychometric endpoints 7 mo after CABG surgery for patients undergoing CPB with α-stat or pH-stat management. |
| Stephan et al (155) | 65 | Neurologic deficits (mostly cerebellar and cranial nerve deficits) more common 7 days after surgery with pH-stat versus α-stat management. Psychometric testing was not performed and long-term results were not reported. |
| Patel et al (156) | 70 | Frequency of cognitive dysfunction 6 wk after CABG surgery was not different between groups undergoing CPB with pH-stat versus α-stat management using predefined endpoints. Patients with cerebrovascular disease or diabetes were excluded from study. A benefit of α-stat management was found when the definition of cognitive decline was changed during *post hoc* data analysis from >2 SD decline from baseline on >2 tests to decline on >3 tests. |

CPB = cardiopulmonary bypass; CABG = coronary artery bypass graft.

Bashein G, Anesthesiology 1990;72:7–15.
Stephan H, Br J Anaesth 1992;69:51–7.
Patel RL, J Thorac Cardiovasc Surg 1996;111:1267–79.

# Perfusion Strategies

- Non-pulsatile vs pulsatile perfusion
- Aortic and venous cannulation
  - Venous obstruction by large, stiff venous cannulas
  - Preferential flow with aortic cannula location
- Airembolism
  - Cannulation
  - Aortic cross clamp off
  - High pump flow rate
  - Use of agents that increase perfusion pressure

# Hematocrit

- Hemodilution
  - Necessary during hypothermia to reduce blood viscosity and ensure microcirculatory flow (?)
  - Reduced oxygen-carrying capacity of diluted blood
  - Cerebral microcirculatory flow is not impaired during experimental hypothermic CPB with Hct as high as 30%
  - Higher Hct reduce white cell/endothelial activation
  - Hct < 10% resulted in inadequate tissue oxygenation

# Hematocrit

- Hemodilution
  - Strong relationship between lower Hct level and operative mortality
  - Low Hct level increase the risk for neurologic outcomes

Kirklin JW Cardiac surgery. New York:Churchill Livingstone, 1993:62–73.
Duebener LF. Circulation 2001;104:260–4.
Fang WC, Circulation1997;96(Suppl II):II194–9.
DeFoe GR, Ann Thorac Surg 2001;71:769–76.

# Glucose management

- Hyperglycemia
  - Detrimental effect
  - Potential cerebral injury
    - ATP utilization
    - Lactic acidosis by inhibiting the phophofructokinase
- Hypoglycemia
  - Alterations in cerebral autoregulation
  - Culminate in increased cortical injury
- No difference (?)

Nedergaard M, J Neurosci 1991;11:2489–97.
Li PA, Acta Physiol Scand 1997;161:567–80.
Leigh R, Stroke 2004;35:1903–7.
Parsons MW, Ann Neurol 2002;52:20–8.
Parsons MW, Ann Neurol 2002;51:28–37.

# Anti-inflammatory Therapy

- Dexamethasone administration before CPB
  - Reduction in the post-CPB inflammatory response
- Ultrafiltration
  - Removes some anti-inflammatory mediators
- Leukocyte filtration
  - Improve neurologic outcomes after DHCA

# Pharmacologic neuroprotection

- Agents such as barbiturates, propofol, volatile anesthetics, lidocaine, benzodiazepines, and calcium channel blockers have been shown experimentally to attenuate the neurologic injury from CPB and DHCA.

- Volatile agents, barbiturates, and propofol reduce ischemic neuronal injury after a short postischemic recovery period.

**Table 4.** Randomized, Placebo-Controlled, Trials of Pharmacologic Neuroprotection for Adults Undergoing Cardiac Surgery

| Drug | Proposed primary mechanism | Author | *n* | Type of surgery | Main findings |
|---|---|---|---|---|---|
| Thiopental | ↓ $CMRO_2$ | Nussmeier et al (222) | 182 | Valvular | Thiopental ↓ cognitive complications 10 days after surgery. |
| | | Zaidan et al (223) | 300 | CABG | No difference in neurologic outcomes thiopental versus placebo. |
| Propofol | ↓ $CMRO_2$ | Roach et al (224) | 225 | Valvular | No difference in cognitive complications 5–7 days or 50–70 days after surgery propofol versus controls. |
| Nimodipine | $Ca^{++}$ channel blocker | Legault et al (225) | 150 | Valvular | Study terminated early due to higher mortality in treated versus control group; no evidence of benefit with nimodipine on cognitive outcomes. |
| Prostacylin | ↓ platelet aggregation, ↓ inflammation | Fish et al (226) | 100 | CABG | No difference in cognitive outcomes 2 wk after surgery between treated and control patients. |
| GM1 ganglioside | ↓ EAA signaling | Grieco et al (227) | 29 | CABG ± valvular | Pilot study finding no difference cognitive outcomes between treated and control patients. |
| Remacemide | NMDA receptor antagonist | Arrowsmith et al (228) | 171 | CABG | Remacemide led to better performance on 3 of 10 psychometric measures and better global cognitive function. |
| Pegorgotein | Antioxidant | Butterworth et al (229) | 67 | CABG | Study stopped before completion; no drug benefit in reducing the rate of neurocognitive dysfunction. |
| Aprotinin | Mechanism(s) unknown; maybe due to ↓ inflammation/ ↓ pericardial aspirate | Levy et al (230) | 287 | CABG | No strokes in "high" and "low" dose aprotinin groups versus controls ($n = 5$) and "pump" prime only ($n = 1$) groups ($P = 0.01$). |
| | | Harmon et al (231) | 36 | CABG | Cognitive deficits 6 weeks after surgery lower in aprotinin versus placebo group (23% versus 55%, $P < 0.05$). |
| Lidocaine | Na+ channel blockade; membrane stabilization/ ↓ EAA release | Mitchell et al (232) | 55 | Valvular | Neurocognitive outcome better 10 days and 10 wk after surgery in lidocaine versus placebo group but not at 6 mo. |
| | | Wang et al (233) | 42 | CABG | Improved neurocognitive function 9 days after surgery with lidocaine versus placebo. |
| Clomethiazole | GABA receptor agonist | Kong et al (234) | 219 | CABG | No difference in neurocognitive function 4–7 wk after surgery in clomethiazole versus placebo groups. |
| Pexelizumab | ↓ C5a and C5b-9 | Mathew (235) | 800 | CABG | Pexelizumab had no effect on global cognition but did lower decline in the visuo-spatial domain compared with placebo. |

$CMRO_2$ = cerebral metabolic rate for oxygen; CABG = coronary artery bypass grafts; EAA = excitatory amino acid; NMDA = *N*-methyl-D-aspartate; GABA = gamma-aminobutyric acid.

# Brain monitoring

- Real-time neurologic monitoring should be an integral part of neuroprotective strategies .
- Several monitoring modalities are available.

# Electroencephalographic monitoring

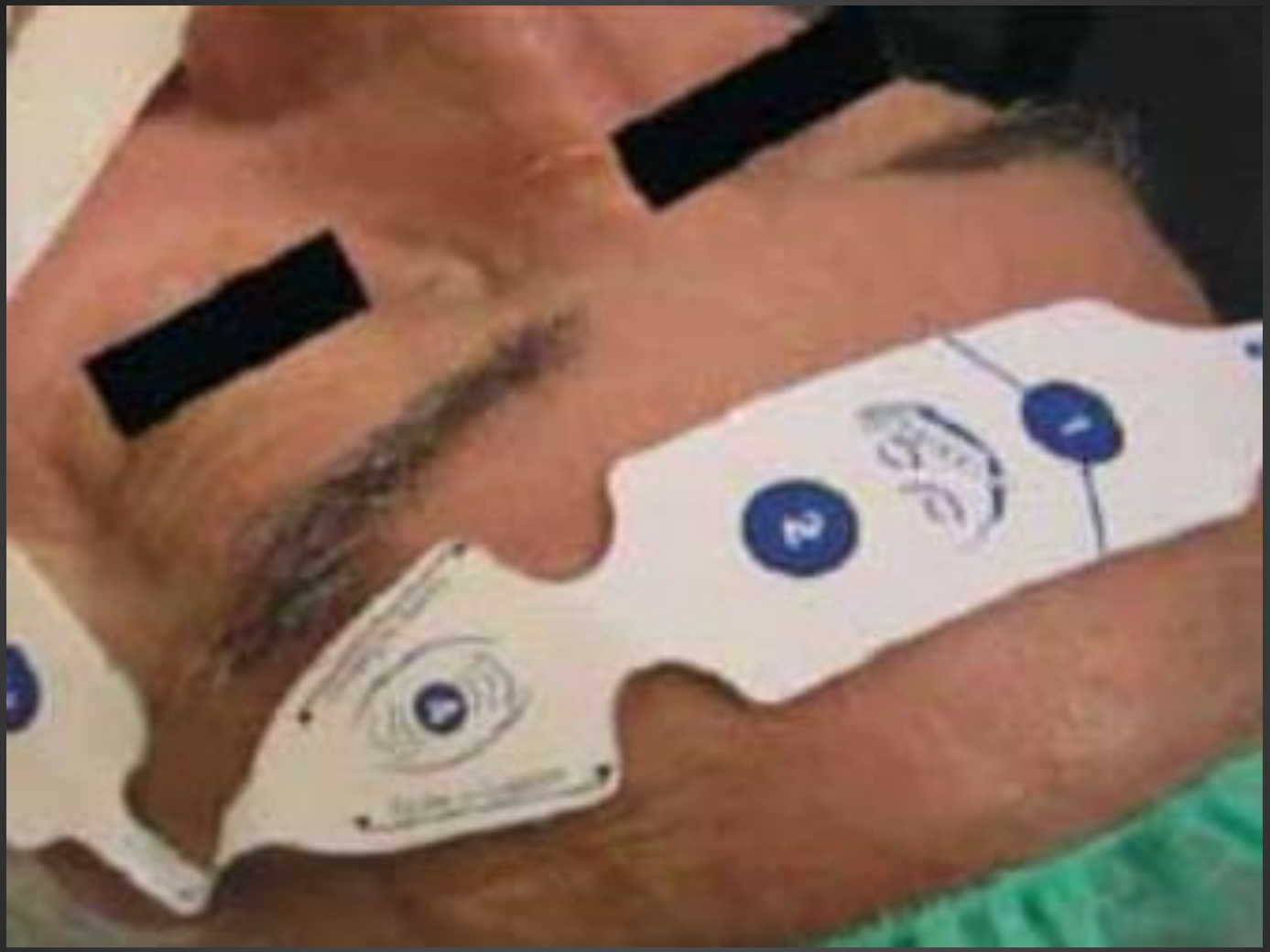
- Signal is affected by electrical interference, patient temperature, anesthetic agents, and CPB.

- Newer devices  use processed EEG technology .

# The Bispectral Index (BIS)

- BIS is used to detect electrical silence during deep hypothermia.
- BIS values
- BIS  monitoring is reported to detect cerebral hypoperfusion and cerebral air embolism.
- EEG monitoring is best combined with other neurologic monitoring modalities.


58



# Near infrared spectroscopy (NIRS)

- A new clinical monitor
- The NIRS displays a numeric value, the regional cerebral saturation index (rSO2i)
- rSO2i reflects brain tissue oxygen content influenced by cerebral oxygen delivery, oxygen consumption, and arterial/venous blood volume ratio

# Transcranial Doppler Ultrasound

- Sensitive, real-time monitor of cerebral blood flow velocity (CBFV) and emboli .
- CBF autoregulation is lost at profound hypothermia.
- Transcranial Doppler ultrasound is used to determine the threshold of detectable cerebral perfusion during low-flow CPB

# Management of atherosclerosis

**Table 1.** Proposed Strategies for the Management of Atherosclerosis of the Ascending Aorta

- Epiaortic ultrasound guidance to avoid atheroma during aortic manipulations
- Avoid partial aortic occlusion cross-clamp ("single cross-clamp" technique)
- Internal mammary artery for proximal bypass graft anastamosis (Y graft) to avoid aortic manipulation
- Axillary artery, innominate artery, or distal aortic arch cannulation rather than ascending aorta cannulation for CPB
- Modified aortic cannula (e.g., low-velocity jetting profile or deployable intra-aortic filter)
- Conversion to "off-pump" CABG with Y graft anastamosis for "no-touch technique"
- Replacement of the ascending aorta under circulatory arrest when atherosclerosis is severe and widespread

CPB = cardiopulmonary bypass; CABG = coronary artery bypass grafts.

Hammon JW JR, Ann Thorac Surg 1997;63:1613–7.
Royse AG, Ann Thorac Surg 2000;69:1431–8.
Sabik JF, J Thorac Cardiovasc Surg 1995;109:885–90.
Gold JP, Ann Thorac Surg 2004;78:1579–85.
Hedayati N Thorac Cardiovasc Surg 2004;128:386–90.
Duda AM, J Vasc Surg 1995;21:98–109.

# Etc

- Surgical filed $CO_2$ insufflation
  - 50 times heavier and 25 times more soluble in blood than air
  - Decrease the nitrogen content of gaseous emboli
- Anticoagulation during CPB
  - Influence platelet-thrombus microemboli formation

Mitz MA. Theor Biol 1979;80:537–51.
Webb WR, Ann Thorac Surg 1997;64:1489–91.
Martens S, J Thorac Cardiovasc Surg 2004;127:51–6.
Martens S, Ann Thorac Surg 2001;72:1940–4.
Persson M, l J CardiovascAnesth 2003;17:329–35.
Svenarud P, Circulation 2004;109:1127–32.
Despotis GJ Thromb Hemost 1996;76:902-8

# Spinal Cord Protection

- Spinal Cord Function
  - Less susceptible to ischemic injury than the brain
  - Evidence by absence of sensory or motor deficits who have been subjected to intervals of hypothermic circulatory arrest of up to 60 minutes.

Kouchoukos NT, Ann Thorac Surg 2001;72:699.

# Spinal Cord Protection

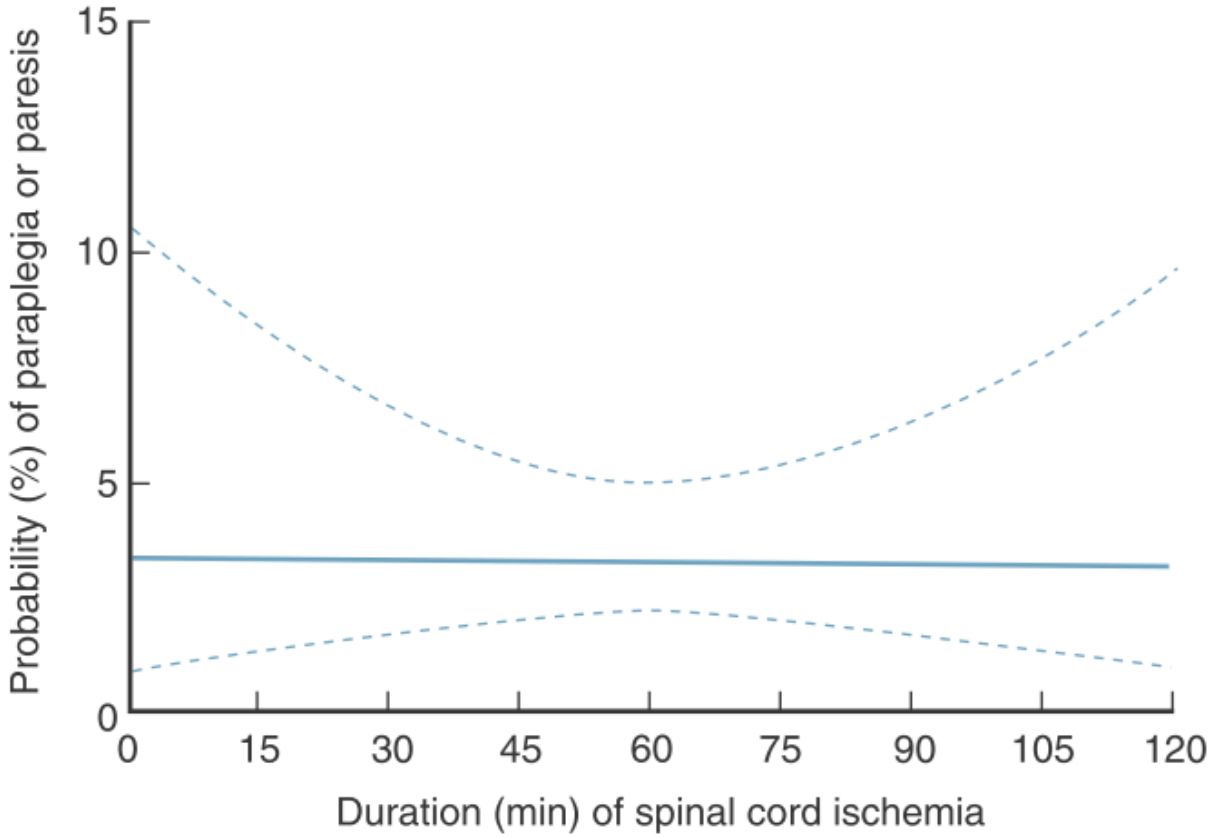
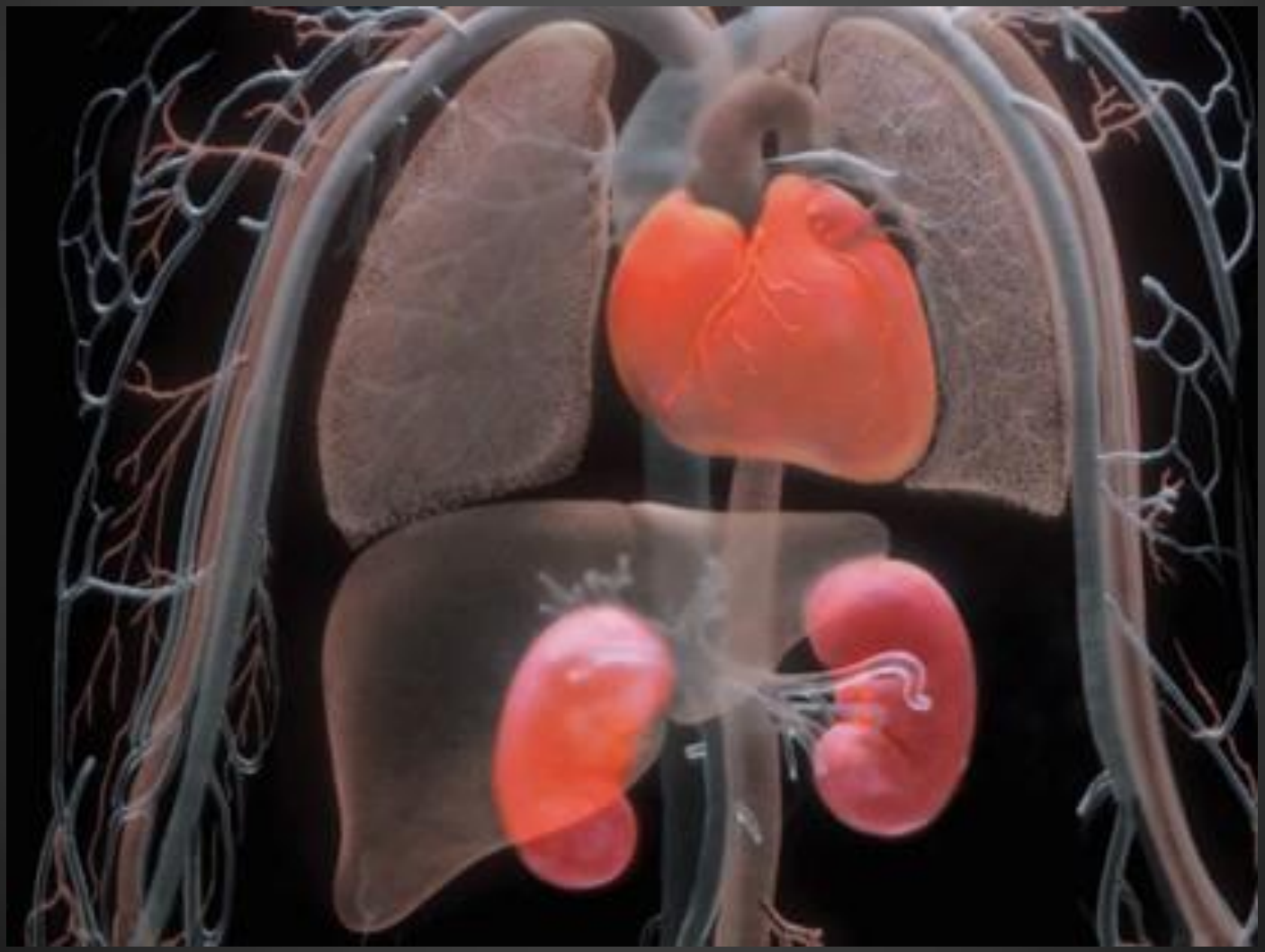


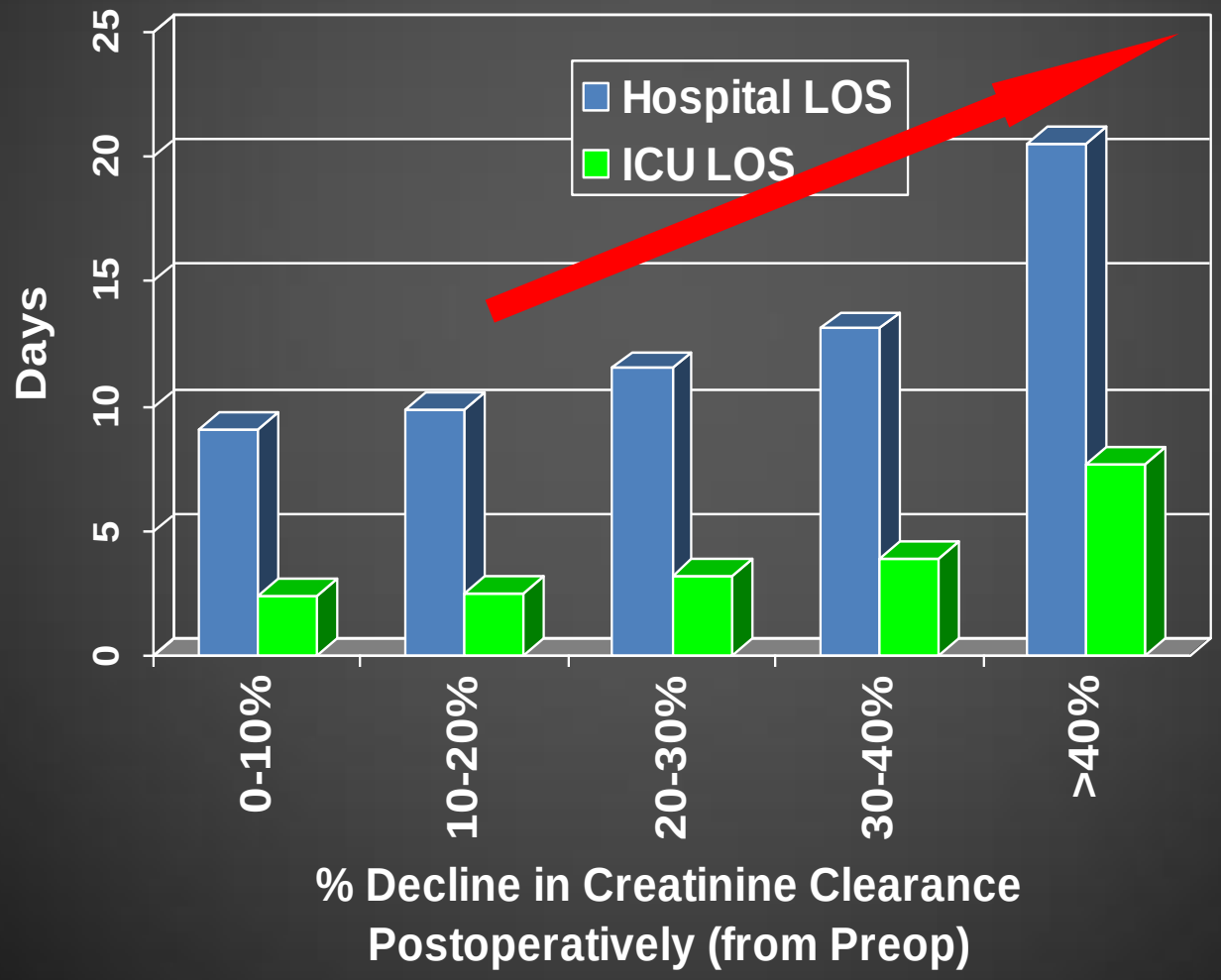

**Figure 2-7** Risk of paraplegia or paresis according to duration of spinal cord ischemia. Dashed lines represent 70% confidence limits. *P* value for relationship is .98. (From Kouchoukos and colleagues.[K20])

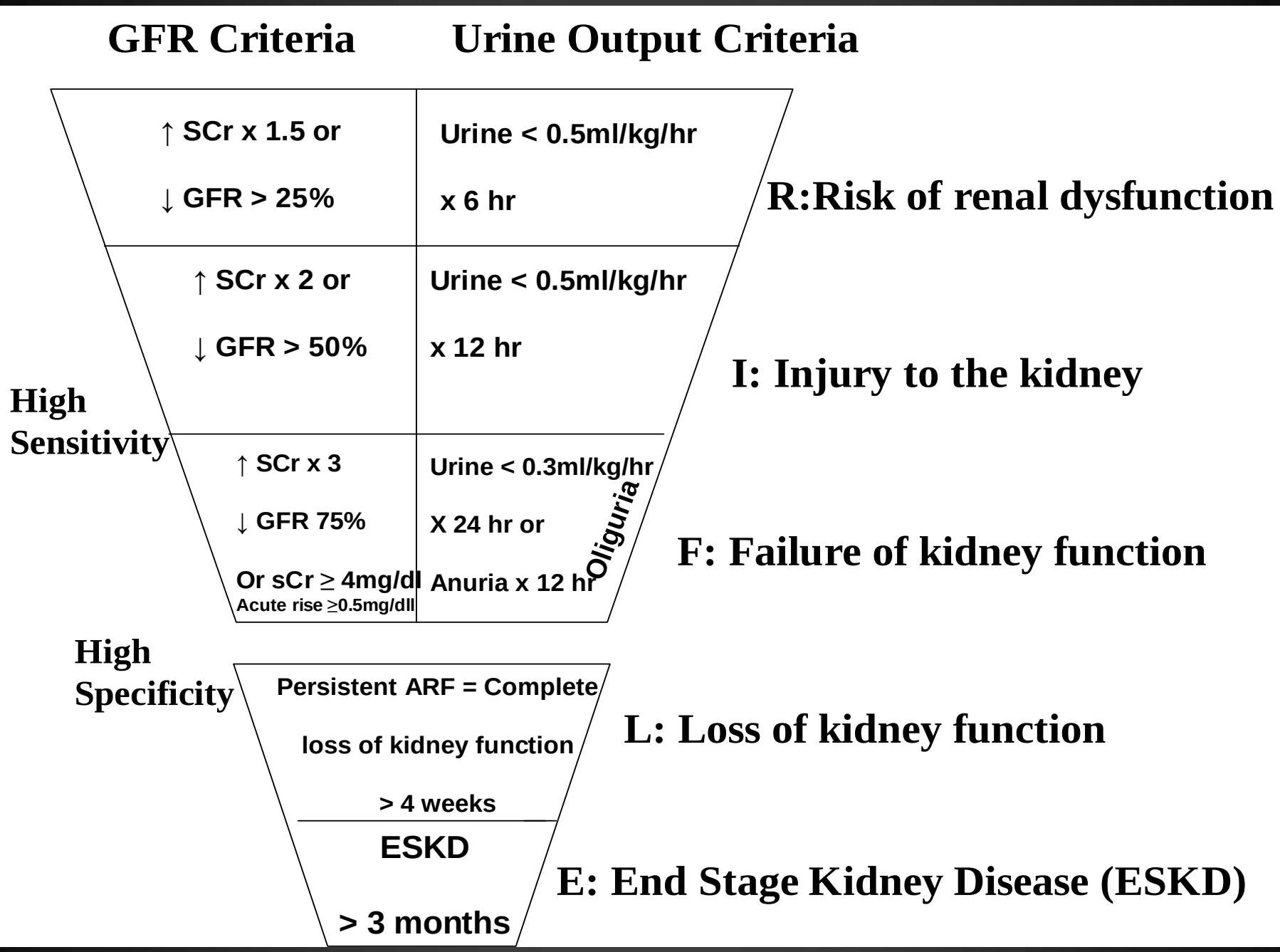
# Perioperative renal protection



# Small Reductions in Renal Function Following CABG Predict Prolonged Hospitalization

Mora-Mangano, et al. Anesth Analg 2000; 90, SCA 35






2547 Acute Dialysis Quality Initiative (ADQI) group

# Acute Kidney Injury (AKI)

- AKI assessment
  - Decrease in eCCr after surgery based on RIFLE criteria
  - eCCr = 0.413 x height (cm) / serum creatinine

| | Estimated CCr | Urine output |
|---|---|---|
| Risk | eCCr decrease by 25% | < 0.5 ml/kg/h for 8 h |
| Injury | eCCr decrease by 50% | <0.5 ml/kg/h for 16 h |
| Failure | eCCr decrease by 75% or eCCr < 35 ml/min/1.73 $m^2$ | <0.3 ml/kg/h for 24 h or anuria for 12 h |
| Loss | Persistent failure > 4 weeks | |
| End stage | End-stage renal disease (persistent failure > 3 months) | |

# Perioperative

# AKI

**Mortality > 50%**

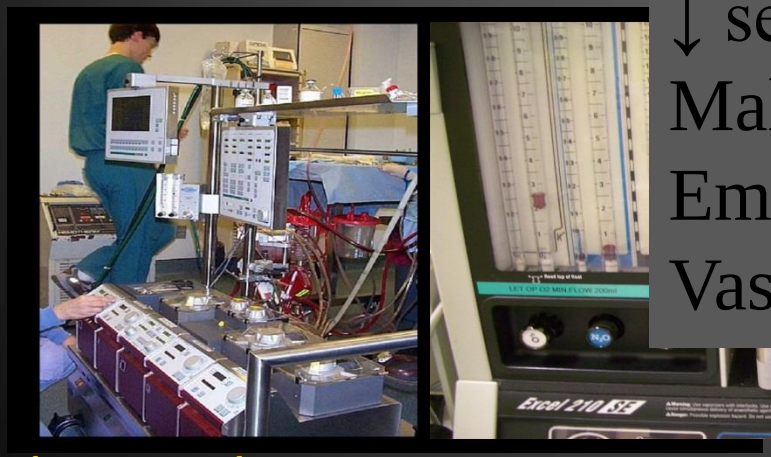
***Patients at Risk***

## Pre-op Risk

↑ SCr/BUN
↓ cardiac performance
Past history renal dysfunction

**Other**

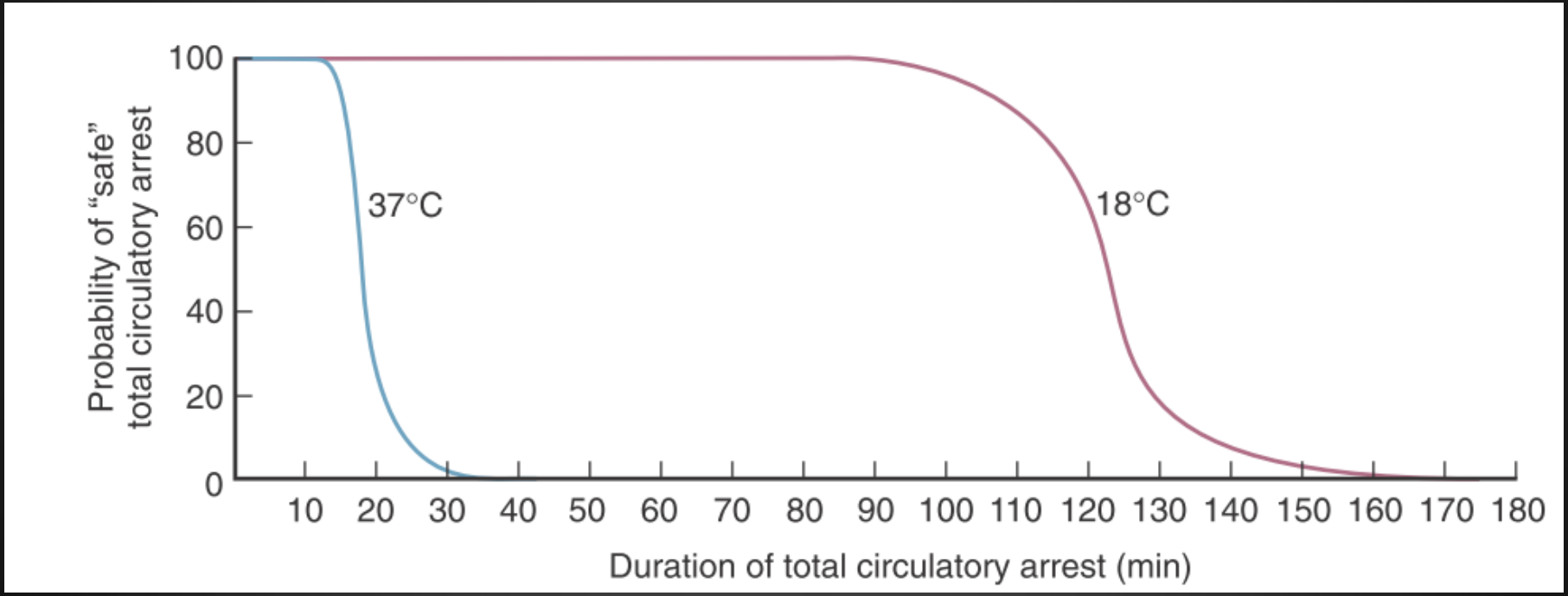
Advance age
Active bacterial endocarditis
↓ serum albumin
Malignancy
Emergency
Vascualr disease





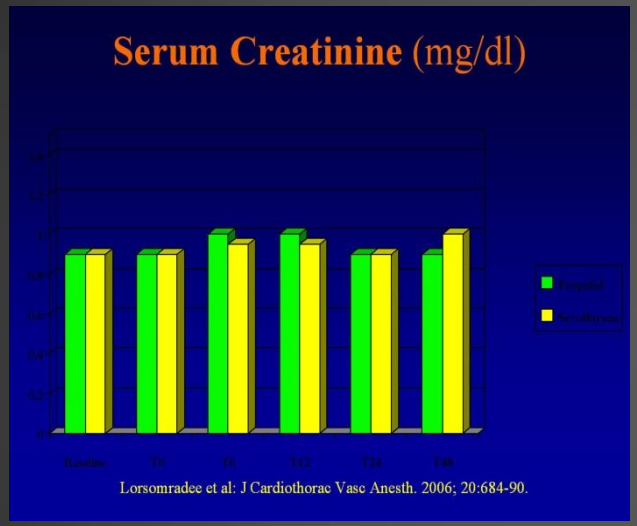
Suraphong Lorsomradee
Asian Cardiovasc Thorac Ann June 2008;16:256-264.

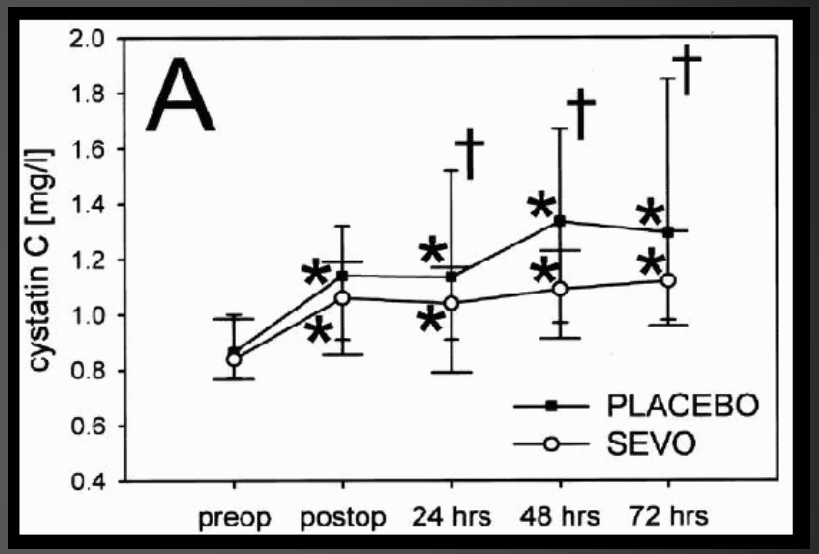
# Safety time for the kidney

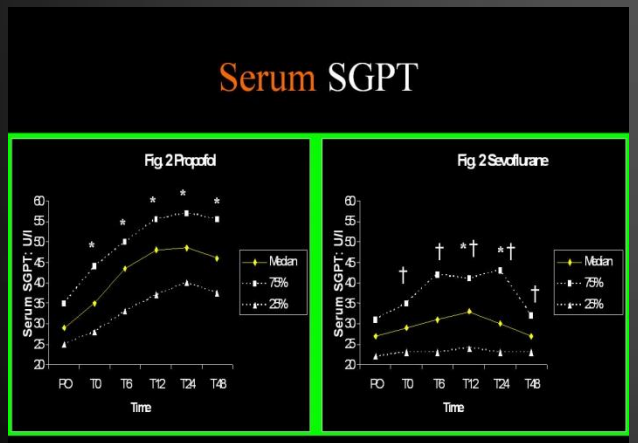


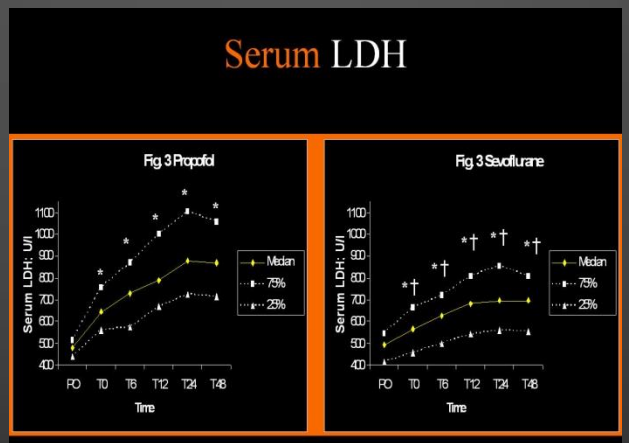

Vogt MT Am J Pathol 1968;53:1.

# Cystatin C *VS* Creatinine
## After Cardiac Surgery



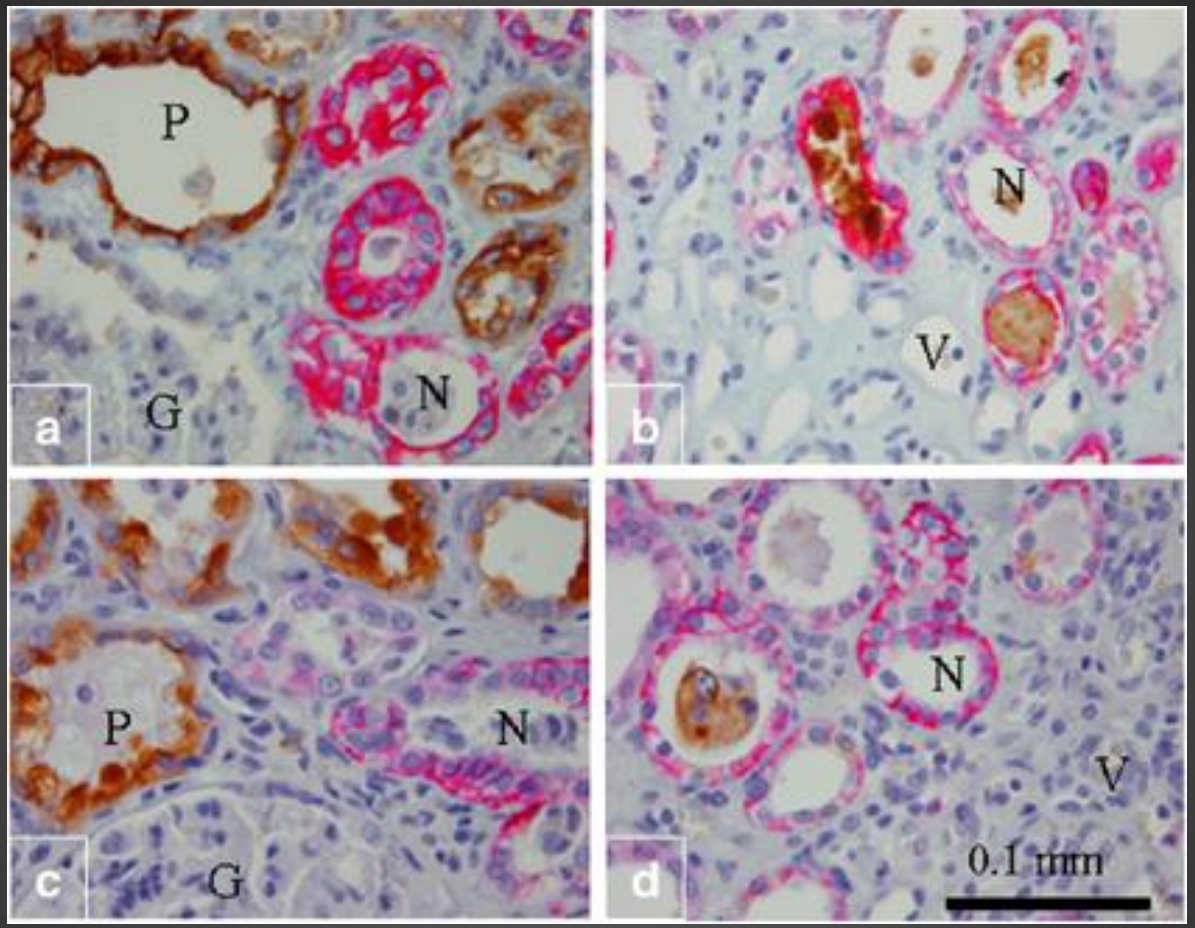


Lorsomradee S. J Cardiothorac Vasc Anesth. 2006 ;20(5):684-90
Julier K. Anesthesiology .2003;98:.1315-1327

# Biomarker

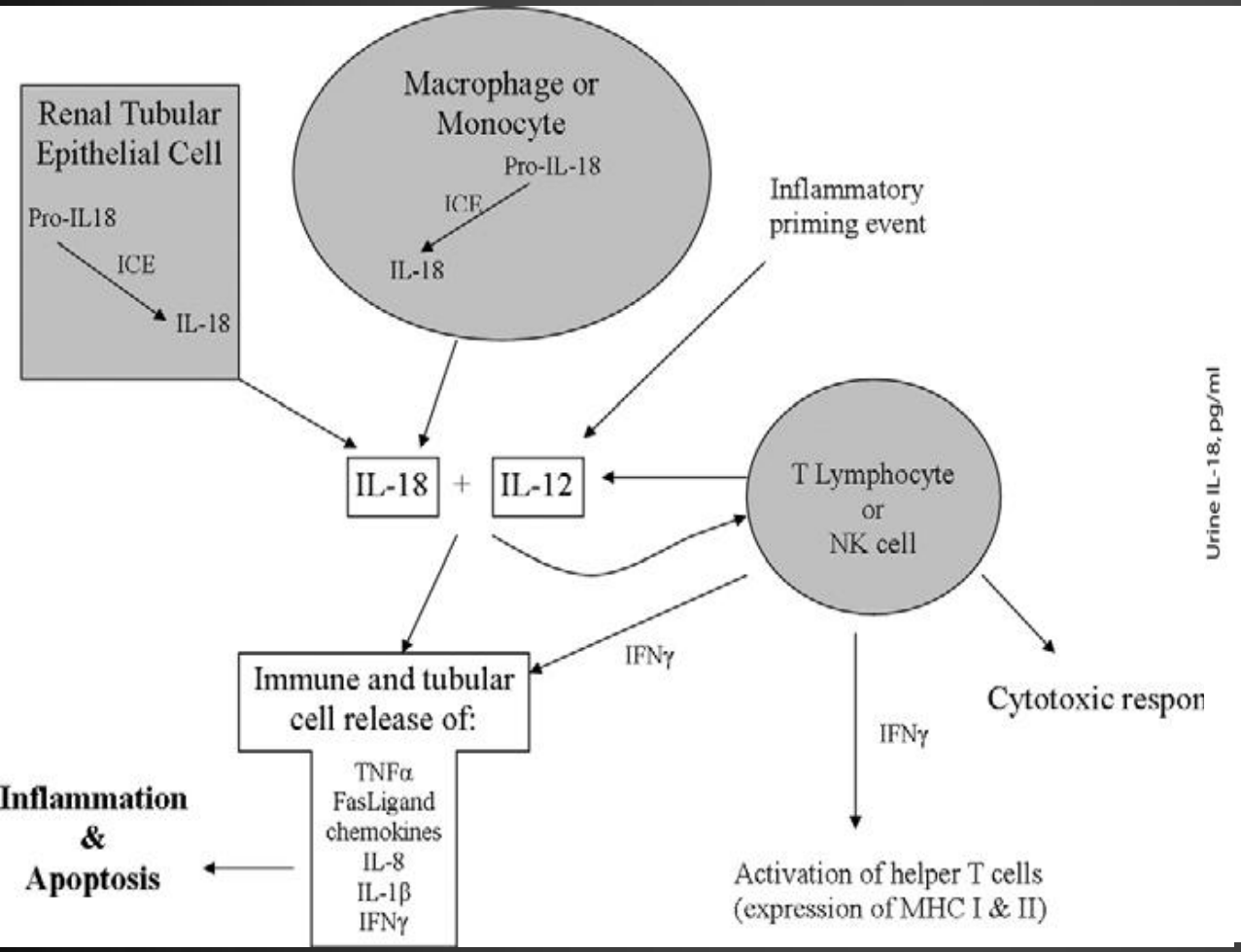

- Cystatin C
- KIM-1 (kidney injury molecule 1)
- IL-18 (interleukin 18)
- NGAL (neutrophil gelatinase associated lipocalin)

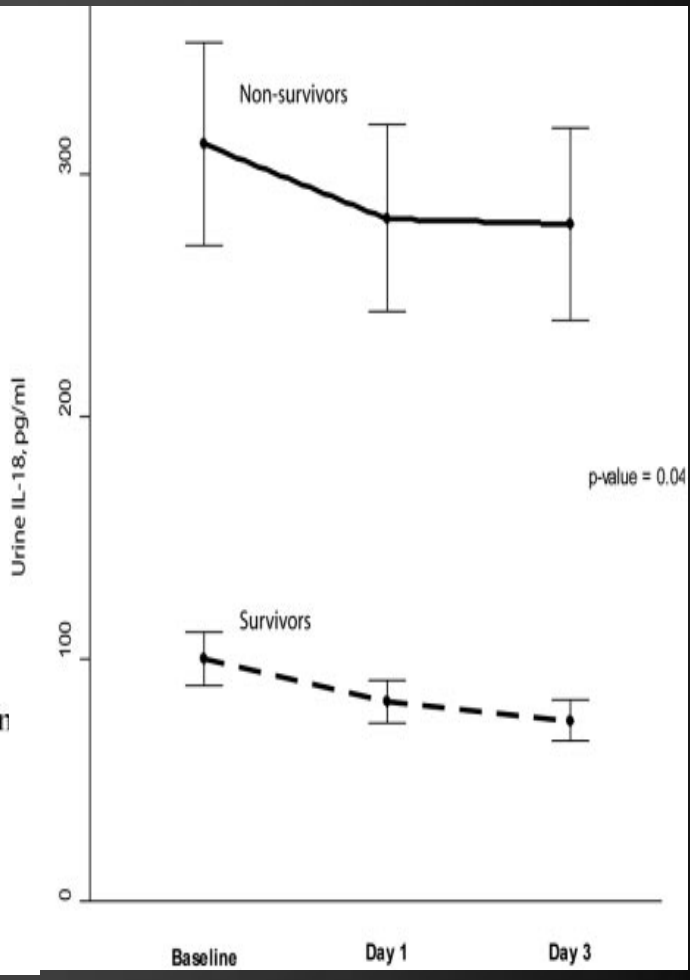
# Kidney Injury Molecule-1 (KIM-1)




Kidney International 2002; 62: 237–44.
Nature Clinical Practice Nephrology;2008;4:362-3

# Urine IL-18 Is an Early Diagnostic Marker for Acute Kidney Injury and Predicts Mortality in the Intensive Care Unit

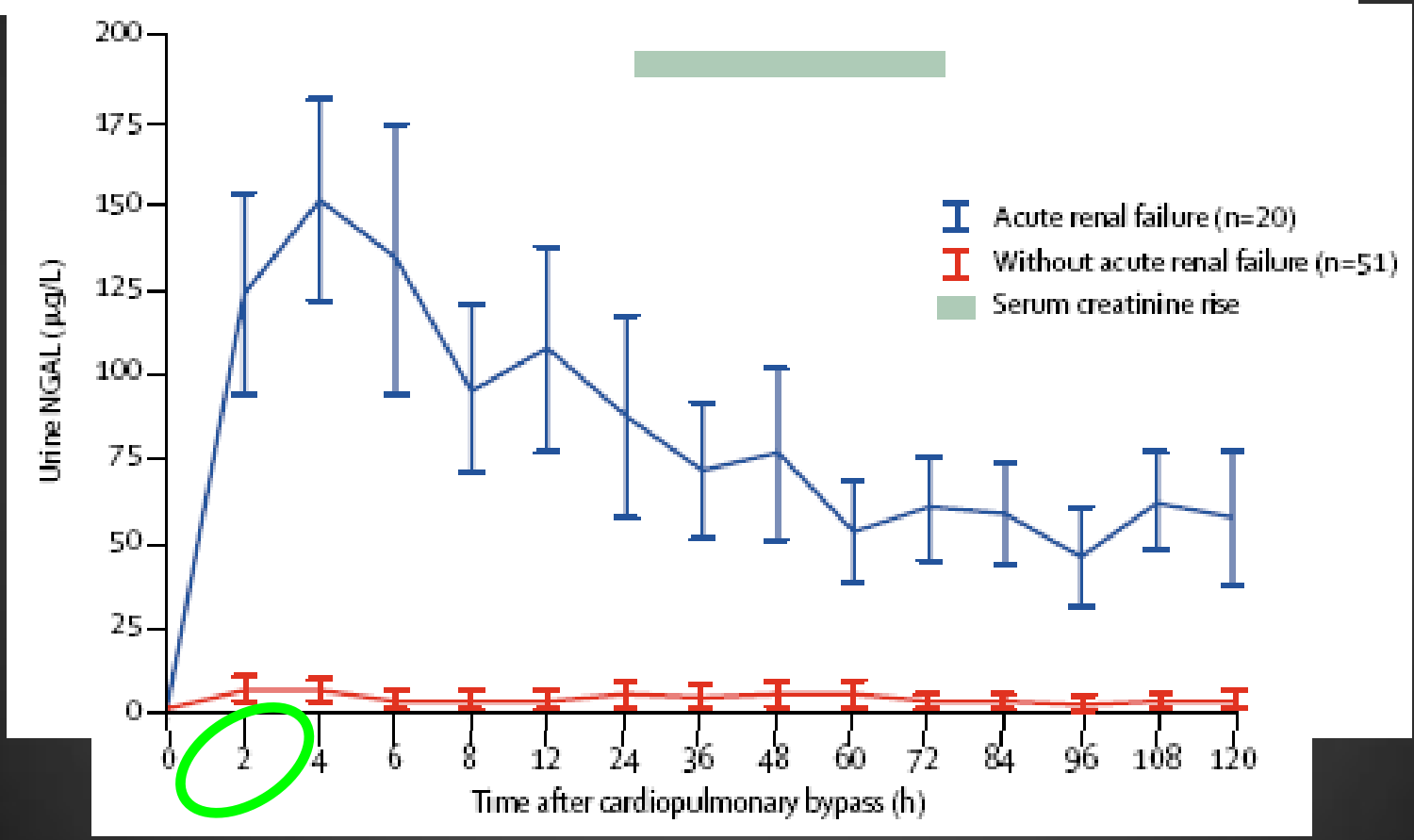



J Am Soc Nephrol 2005;16:3046-52

# Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery

*Jaya Mishra*, Catherine Dent*, Ridwan Tarabishi*, Mark M Mitsnefes, Qing Ma, Caitlin Kelly, Stacey M Ruff, Kamyar Zahedi, Mingyuan Shao, Judy Bean, Kiyoshi Mori, Jonathan Barasch, Prasad Devarajan*




Lancet 2005; 365:1231-8

# Interventions associated with a decreased risk of AKI after cardiac surgery

| Preoperative | Intra-operative | Post-operative |
|---|---|---|
| Adequate hydration & avoid loop diuretics<br>Surgery after 5 days of coronary angiography<br>Statin use<br>Anemia optimization | Avoid anemia<br>Avoid Hemodilution<br>Off-pump CABG<br>Use of ANP<br>Use of fenodopam<br>Shorter duration of CPB<br>Optimal glucose control | Start statin when feasible<br>Avoid nephrotoxic agents<br>Early RRT |

Vives M. et al. Peri-operative renal protective strategies in cardiac surgery. Nephrology 2013;1:9

# Management of Cardiopulmonary Bypass in Pediatric Patients

Sejong General Hospital

Department of Thoracic and Cardiovascular Surgery

Kwak Jae Gun

# History I

- 1934 Dr. DeBakey, hand-driven roller type pump, bubble or film oxygenator
- 1953 Dr. Gibbon, first successful human intracardiac operation using CPB

  → 5 consecutive death after first successful case → abandonment
- 1954 Dr. Lillehei, cross-circulation, using patient's parent as a pump/oxygenator

  → 18 death in 45 patients
- 1955 Dr. Kirklin, CPB machine (similar to Dr. Gibbon's) → 50% survival

# History II

- 3 types Oxygenators in 1950s
  - Mayo-Gibbon pump
  - Kay-Cross disc oxygenator
  - DeWall-Lillehei bubble oxygenator: most popular, by 1976
- Membrane oxygenator
  - Introduced in the mid 1940s
  - Vogue in the late 1970s to early 1980s (with the advent of microporous, hollow-fiber membranes)
    - Large surface area
    - Easy to produce, different sizes

# CPB in Infants vs. Adults

| Parameter | Adult | Pediatrics |
|---|---|---|
| Hypothermic temperature | Rarely < 25~32 ℃ | Commonly 15~20 ℃ |
| Circulatory arrest | Uncommon | Common |
| Pump prime | | |
| *dilution effect on blood volume* | *25~33 %* | *200~300 %* |
| *additional additives* | *Blood, albumin* | |
| Perfusion pressure | 50~80 mmHg | 20~50 mmHg |
| Influence of pH management | Minimal at moderate hypothermia | Marked at deep hypothermia |
| *measured $PaCO_2$ differences* | *30~45 mmHg* | *20~80 mmHg* |
| Glucose regulation | | |
| *hypoglycemia* | *Rare – requires liver injury* | *Common - ↓ glycogen stores* |
| *hyperglycemia* | *Frequent – insulin bolus or infusion* | *Less common – rebound ⇊ glucose* |

# Unique pediatric characteristics

- Smaller circulating blood volume
- Higher oxygen consumption
- Reactive pulmonary vascular bed
- Intra- and extracardiac shunting
- Altered thermoregulation
- Poor tolerance for microemboli

# Hypothermia I

- Reduction in metabolic rate and molecular movement
  - ATP consumption decreased, maintain cellular ATP store
  - Whole-body oxygen consumption decreased (32 ℃ → 45%), myocardium (12 ℃ →1%)
  - Cerebral metabolic rate decreased
  - Reducing excitatory neurotransmitter release
  - Preventing calcium entry into the cell
- Deep hypothermia (16~18 ℃)
  - 20~25 mL/kg/min of pump flow to maintain vital organ perfusion
  - Minimal return of blood into heart → good operative field
- Normothermia
  - When surgeon is able to use both vena caval cannulae “safely”
  - In small patients, cannulae may cause vena caval obstruction → impaired drainage from abdominal organs (IVC) or brain (SVC) may cause adverse effects

# Hypothermia II

- Neonates, infants, children → greater decrease in metabolic rate than adults → better brain and organ protection with hypothermia
- Cerebral blood flow auto-regulation: “lost” at deep hypothermia
  - Blood flow to cerebrum will return to normal with rewarming
  - Cerebral blood flow remain low up to 40 hours after CPB weaning despite adequate perfusion pressure

# Hypothermia III

- Hypothermia in Myocardium
  - Less important in myocardium than brain
  - 90% of myocardial protection at normothermia with electrical quiescence
  - Decrease in perfusion temperature: deleterious effect on myocardium?
    - Low temperature → Na/K ATPase inhibition → ↑ intracellular sodium → ↑ Na/Ca exchanger → ↑ intracelluar Ca → "rapid cooling contraction" & activation of calcium dependent degradative enzymes → damage to myocardium & free radical reaction

    ➨ post-bypass myocardium dysfunction
  - More rapid change in neonates or infants

# Neurological injury & protection I

- Neurodevelopmental impairment: 50% of children who have cardiac surgery as newborns or young infants
  - Increasing evidence of ‘pre-op’ reasons for neurodevelopmental impairment (structural CNS malformations)
  - Genetic abnormalities; Socioeconomic status; Maternal education
- Periventricular leukomalacia (PVL)
  - Necrosis of deep white matter adjacent to the lateral ventricles
  - Neonatal brain: susceptible to ischemia-reperfusion injury d/t fragile vascularity, high metabolic activity, immature autoregularation
  - During CPB running, hypoxia, hypoglycemia, meningitis
  - 16~25 % before CPB, 54~73% after CPB

# Neurological injury & protection II

- Pre-operative factors
  - Hypotension (diastolic hypotension d/t ductal dependent circulation)
  - Hyperthermia; Glycemic control
- Intra-operative
  - Emboli: air, particles (via intra-cardiac defect, ASD → filter)
  - CPB circuit: malposition of cannulae (poor flow), inflammatory response (steroids, heparin coating circuit, leukocyte depleting filters)
  - Steal by collaterals, ductal run-off
  - Deep hypothermic circulatory arrest → ischemic-reperfusion injury, uneven cerebral cooling
  - Hemodilution, Bleeding
  - pH stat management for any temperature

# Neurological injury & protection III

- NIRS: regional cerebral saturation index
  - ratio of oxyhemoglobin to total hemoglobin
  - A fall of 20% from baseline
  - Affected by cerebral perfusion pressure, blood flow, $PaCO_2$, cerebral metabolic rate; accuracy at low flow rates ???
  - 70% in acyanotic patients, 43~57% in cyanotic patients
  - More efficient in < 10kg babies because of skin or skull thickness
  - Guide for
    1. duration of deep hypothermic circulatory arrest
    2. proper placement of cannulae
    3. optimum flow during low-flow cerebral perfusion during arch repair
- EEG: affected by electrocautery, temperature, CPB itself (vibration)

# Neurological injury & protection IV

- Transcranial doppler (TCD): real time monitor of cerebral flow velocity and embolic events
  - Peak systolic, mean flow velocities
  - High-intensity transient signals by microemboli → audible click sound for each event, frequency > 1/min: significant
  - Drop of 60% (peak velocity) → moderate drop in perfusion; drop of 80% → significant drop in perfusion
  - Malposition of arterial cannula, arterial cannula occlusion, obstruction or mal-position of SVC cannula
- Jugular venous bulb saturation ($SjO_2$): measures of saturation of venous blood
  - 6.6% from extra-cranial sources (facial vein, frontal vein)
  - Temperature drops → metabolic rates fall → the brain extracts less oxygen from blood → higher jugular venous oxygen saturation

# Neurological injury & protection V

- pH Stat
  - Faster, much even cooling brain in pH stat by ↑ cerebral blood flow
  - ↑ EEG activity recovery , ↓ EEG-confirmed seizure
  - Better myocardial performance by even myocardial temperature during cooling d/t hypercapnia-induced vasodilation, ↑ oxygen-hemoglobin dissociation ➠ oxygen delivery ⇡ d/t $CO_2$ ⇡
  - Change in intracellular pH status ➠ prolonged depletion of high energy phosphates during “rewarming” ➠ cell damage
  - Loss of auto-regulation of blood flow by brain ➠ pressure dependent cerebral blood flow ➠ ↑ potential for an increased number of microemboli

# Neurological injury & protection V

- Alpha Stat: maintain intracellular pH status ➠ optimal enzyme activity ➠ preserve auto-regulation function of blood flow in brain
- In adult, because of microemboli problems, alpha stat showed superior outcomes in cognitive function after CPB ??
- pH stat during “cooling” & “deep hypothermic circulatory arrest” period, alpha stat during “rewarming” period

# Neurological injury & protection VI

- Post-operative factors
  - Low cardiac output
  - Acid-base unbalance
  - Hypoxia
  - Disrupted auto-regulation of cerebral blood flow by CPB: maintain adequate cerebral perfusion pressure
  - Hyperthermia, abnormal endocrine response

# Myocardial protection I

- Immature myocardium
  - Sensitive to extracellular Ca
    - Immature sarcoplasmic reticulum (SR): ↓ calcium storage capacity
    - Reduced $Ca^{2+}$-ATPase in SR (↓ re-uptaking calcium into SR)
  - Relies heavily on glucose as an energy source (fatty acid in adult)
- Preoperative condition
  - Cyanosis: bronchial collaterals → ↑ return of blood into the heart → insufficient myocardial protection by, 1. warming heart 2. washing cardioplegia
  - Hypertrophic myocardium → ↑ subendocardial ischemia
  - Volume or pressure overloading
  - Acidosis

# Myocardial protection II

- Hypothermia
- Cardioplegia
  - Rapid induction of cardiac arrest by membrane depolarization via hyperkalemia
  - Metabolic substrate: amino acids (aspartate, glutamate, ornithine) → ATP synthesis, generation
  - Warm induction
  - Appropriate pH
  - Membrane stabilization (low $Ca^{2+}$, $Mg^{2+}$, steroids, $O_2$ radical scavengers)
- Monitoring of function of cardioplegia
  - ECG only during operation
  - Myocardial function, inotropics requirements, troponin I level after bypass

# Myocardial protection III

- Del Nido solution
  - Low $Ca^{2+}$ level: high levels of intracellular $Ca^{2+}$ during ischemia and reperfusion → ↑ cellular injury
    - Normocalcemic or hypocalcemic cardioplegia → preservation of myocardium and vascular function in non-hypoxic hearts
    - Normocalcemia → ↑ cellular injury, myocardial & endothelial dysfunction in hypoxic hearts
  - High $Mg^{2+}$ level → ↓ arrhythmia in postop
  - Low $Ca^{2+}$ + High $Mg^{2+}$ :myocardial protection and functional preservation

# Myocardial protection IV

- 3 phases of cardioplegia
  - Induction: electrical silence
  - Maintenance: 1. maintenance of arrest, 2. restoring myocardial hypothermia, 3. buffering acidosis & washing away acidic metabolites, 4. replenishing high-energy phosphates, 5. counteracting edema
  - Reperfusion: spontaneous sinus rhythm, decreased inotropics use, improved lactate extraction
- Additional factors
  - Adequate distribution of coronary arterial flow: severe AR, severe hypertrophic ventricle
  - Delivery pressure: 30~50 mmHg (too high: injury to myocardium & vascular endothelium, increased edema, decreased ATP level)
  - Crystalloid vs. Blood cardioplegia
    - Blood cardioplegia: lower coronary sinus lactate level, better cardiac index & troponin I level after bypass

# Pulsatile vs. Nonpulsatile flow

- Hemodynamic energy generation ↑ in pulsatile flow: ↑ organ flow during CPB, ↑ organ function after CPB
  - Myocardial function ↑: ↓ inotropic dose
  - Cerebral flow: better in pulsatile flow
  - Pulmonary function: ↓ ventilator time, ICU stay in pulsatile flow
  - Renal function: ↑ urine output, ↓ ischemic change in renal tubule, ↑ renal cortical flow
  - Superior hormone response
- Pulsatile flow: ↑ microcirculation of vital organs
- Ideal, but not currently used yet

# Pulmonary effects of CPB

- Preoperative condition
  - Long time exposure to the increased pulmonary artery flow, pulmonary congestion (LR shunt with Down syndrome) → pulmonary artery media hypertrophy → reactive pulmonary vessels after CPB
- Inflammatory response during CPB
  - Capillary leakage by hemodilution, ischemic-reperfusion injury, decreased oncotic pressure, activated neutrophil, cytokines, complement, leukotrienes
  - extravasation of fluid into alveolar spaces: collapse of architectures, loss of wall stability of alveoli by decreased perfusion during CPB
- Modified ultrafiltration (MUF)
  - Reduction of total body water, lung water → improve lung compliance, decreased airway pressure
  - Decreased inflammatory markers → advantage on capillary leakage

# Renal function and protection

- Risk factors for AKI after CPB
  - Young age ( < 1 year)
  - Complexity of disease
  - Long bypass time, cross-clamp time, deep hypothermic circulatory arrest, ↑ use of blood products, low blood pressure on POD 1, low post-CPB cardiac output
- Neutrophil gelatinase-associated lipocalin (NGAL), IL-18: predictor for AKI in immediate postoperative period: ↑ 4~6 hours, peak at 12 hours, more sensitive than serum creatinine level (48~72 hours after injury)
- PD or CRRT

# Endocrine response during CPB

- Stress by surgery, inflammatory reaction by CPB
  - ➟ ↑ catecholamine, ↑ TNF, interleukin
  - ➟ hyperglycemia, ↑ hepatic glucose mobilization, ↓ peripheral insulin utilization, ↓ insulin deficiency ➟ insulin resistance
  - Hyperglycemia: ↑ morbidity and mortality
- Hypothermia: ↑ glucose level, ↓ insulin level
- Thyroid hormones: suppressed by surgery, CPB
  - ↓ T3, T4: lasts up to 5 days
  - Effects on entrance and extrusion of calcium to myocyte (via sarcoplasmic reticulum & cell membrane ) ➟ systolic & diastolic dysfunction, ↑ vascular resistance
- Growth hormone: increased by stressful situation, catabolic state

# Systemic inflammation

- Inflammatory cascade during open heart surgery due to
  - Blood exposure to foreign body (circuit surface)
  - Hypothermia
  - Ischemia/ reperfusion injury
  - Blood products administration
  - Artificial nature of perfusion (non-pulsatile flow)

  ➟ damage endothelium releases inflammatory markers (IL-8)

  - Mechanical sheer stress by suction or filter system

  ➟ cellular and humoral immune response ➟ activation of coagulation, complement, fibrinolytic pathway ➟ endothelial damage, capillary leakage, organ dysfunction

# CPB management I

- Hemodilution
  - Blood transfusion: effects on inflammatory cascade (↑ complement, inflammatory cytokines)
  - 20~25 % of Hct during CPB: diluted less than 20% → ↓ Psychomotor development index 1 year after CPB
- Circuit miniaturization
  - ↓ total surface area
  - Bloodless priming

  ← by 1. biocompatible coated circuit & oxygenator, 2. vacuum-assisted venous drainage, 3. placement of pump as close to the patient as possible, 4. exclusion of certain circuit components (arterial line filter, in-line cardioplegia)

# CPB management II

- Biocompatible circuits
  - Initiation of CPB → 5 proteolytic plasma systems activation, Cellular activation
    - Coagulation, Fibrinolysis, Complement activation, Kallikrein-kinin, Contact system
    - Leukocytes, Platelets, Endothelial Cells
  - Circuit surface modification
    - Coating: coat with another polymer to reduce protein adsorption
    - Chemical modification: using new chemical groups circuit surface
    - Attachment of macromolecules
    - Blending of polymers: combinations of hydrophilic/phobic, natural/synthetic polymers
      - Polymethoxyethylacrylate (PMEA): not react with platelet, clotting factors (maintaining the number or function of platelet) → decreasing inflammatory cascade
- Anti-inflammatory reaction: anti-fibrinolytic agents (aprotinine), steroid (adult coronary patients), modified ultrafiltration

# CPB management III

- Circuit design
  - Smaller circuit size → small prime volume → ↓ hemodilution → ↓ transfusion, inflammatory reaction → improved outcomes, hospital stay ↓
  - Low prime volume oxygenator, reservoir, arterial filter
  - Shorter extracorporeal circuitry, removal of parts of the classic circuit
  - Venous vacuum
  - Most important factor: oxygenator, arterial line filter
- Monitoring for transfusion
  - Hemoglobin concentration (<7 g/dL), regional cerebral oxygenation (< 50%), plasma lactate level (> 4 mmol/L), mixed venous saturation (< 70%)
- Donor blood neutrophil: one of the key factors in genesis of CPB related inflammatory cascade, capillary leakage leading to organ dysfunction

# CPB management IV

- Micro-emboli by
  - Pulsatile bypass
  - Field sucker, Venous line air
  - Low venous reservoir level
  - Vacuum assist venous drainage
  - Drug administration, Blood sampling

# CPB management V

- Anticoagulation
  - Vitamin K dependent clotting factors (II, VII, IX, X)
  - Contact factors (XI, XII)
  - Anticoagulant, inhibitory factors (antithrombin III, protein C & S, plasminogen)

  → all decreased in neonates (by ↑ clearance d/t ↑ metabolism, ↓ hepatic synthesis)
- Heparin induced thrombocytopenia (HIT): in repeated cardiac surgery
  - HIT 1: nonimmune-mediated ↓ platelet count, transient, not need to discontinue heparin
  - HIT 2: immune-mediated ↓ platelet count (> 50%)
  - Cautious in the decreasing platelet count by 50%, even still in normal range
  - Antibody formation to platelet factor 4 at endothelium surface, activated platelet surface in 50 % of adult cardiac surgery patients but only 1~3 % develop syndrome

# CPB management VI

- CPB weaning
  - Lung atelectasis: hypoxia, direct pulmonary bed compression → ↑ pulmonary arterial pressure
  - Hypothermia: ↓ atrial function (ventricular preload), bradycardia, heart block, ↓ ventricular fibrillation threshold, ↑ pacing threshold, ↓ platelet function, ↓ coagulation cascade, ↓ enzyme function for coagulation pathway
  - Heart rhythm
  - Bleeding control

# CPB management VII

- Modified ultrafiltration
  - ↓ unfavorable electrolytes, inflammatory mediator
  - ↓ total body water, inflammatory markers (TNF, IL-6, IL-8 ↔ SIRS, thromboxane B2, endothelin 1 ↔ pulmonary vascular hyperactivity, pulmonary hypertension)
  - ↑ lung compliance, ↑ ventilation, oxygenation, ↓ pulmonary arterial pressure
  - ↑ clotting factor, fibrinogen, ↑ hematocrit
  - ↑ LV systolic, diastolic function, ↑ RV function by ↓ pulmonary arterial pressure

  - Cooling during the procedure; hypotension by too much drawing from arterial line; air cavitating out of solution in the arterial line; exsanguination owing to unclamped oxygenator

# Future

- Functional survival
- Neurological outcomes
- Blood conservation
- Decreasing the inflammatory response to bypass
- Circuit miniaturization