

# Postoperative Cognitive Dysfunction after Cardiac Surgery

Wyoming Health Care Systems/University of Scranton  
Nurse Anesthesia

Ashley Fidler Parkinson RN BSN SRNA

# Objectives

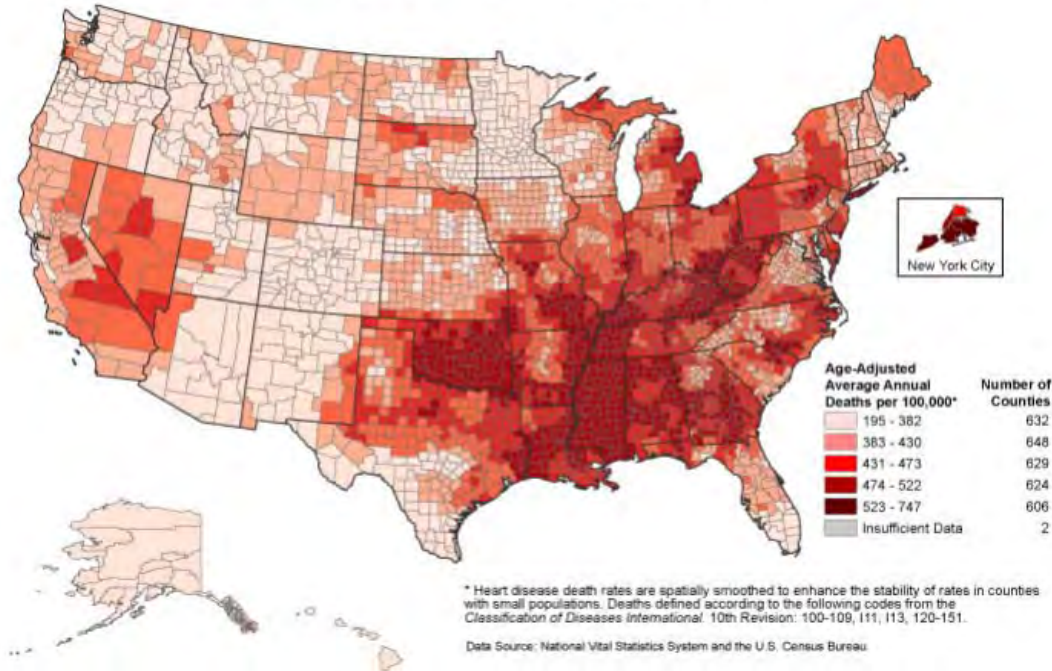
---

- ▶ Review cardiovascular disease history
- ▶ Define Postoperative Cognitive Dysfunction (POCD)
- ▶ Identify possible risk factors associated with POCD
- ▶ Analyze potential mechanisms for POCD
- ▶ Examine interventions on improving cognitive functioning
- ▶ Discuss POCD future research needs



# Cardiovascular Disease Statistics

Heart Disease Death Rates, 2000-2006  
Adults Ages 35 Years and Older, by County



- #1 health problem
- 70 million affected (34%)
- 25% of deaths (1/4 in U.S.)
- Leading cause of death
- Coronary heart disease
  - Most common type

Background

Etiology

Risks

Prevention

Review Questions

# Cardiac Surgery Background

---

## ▶ Historical Dates:

- ▶ 1952
  - ▶ 1<sup>st</sup> open-cardiac procedure
- ▶ 1953
  - ▶ Heart-lung machine
    - AKA - Cardiopulmonary Bypass (CPB)



## ▶ Cardiac Surgery:

- ▶ Coronary artery bypass grafting (CABG)
- ▶ Valves
- ▶ Abnormalities
- ▶ Transplantation
- ▶ Open-heart
  - ▶ On-pump
  - ▶ Off-pump
    - ▶ AKA - Beating heart

“Grandpa was never the same after his operation!”



Background

Etiology

Risks

Prevention

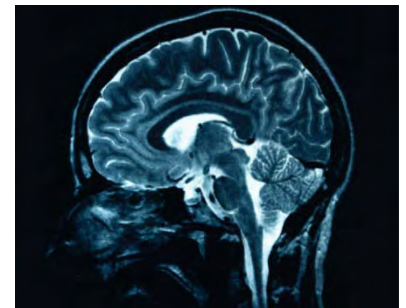
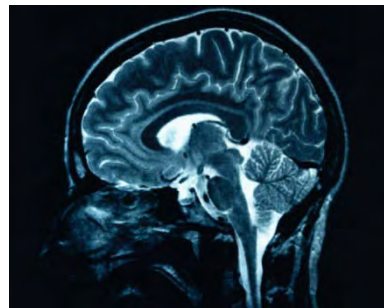
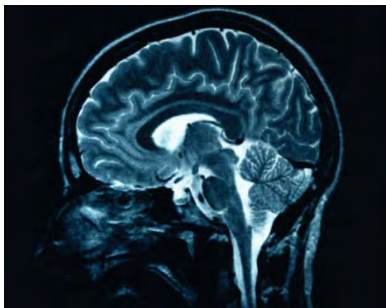
Review Questions

# Definition

---

## **Postoperative Cognitive Dysfunction (POCD):**

“A state of cerebral cognitive alterations following surgery and anesthesia that is characterized by impairment of attention, concentration, and memory that may have long-term implications.”



Background

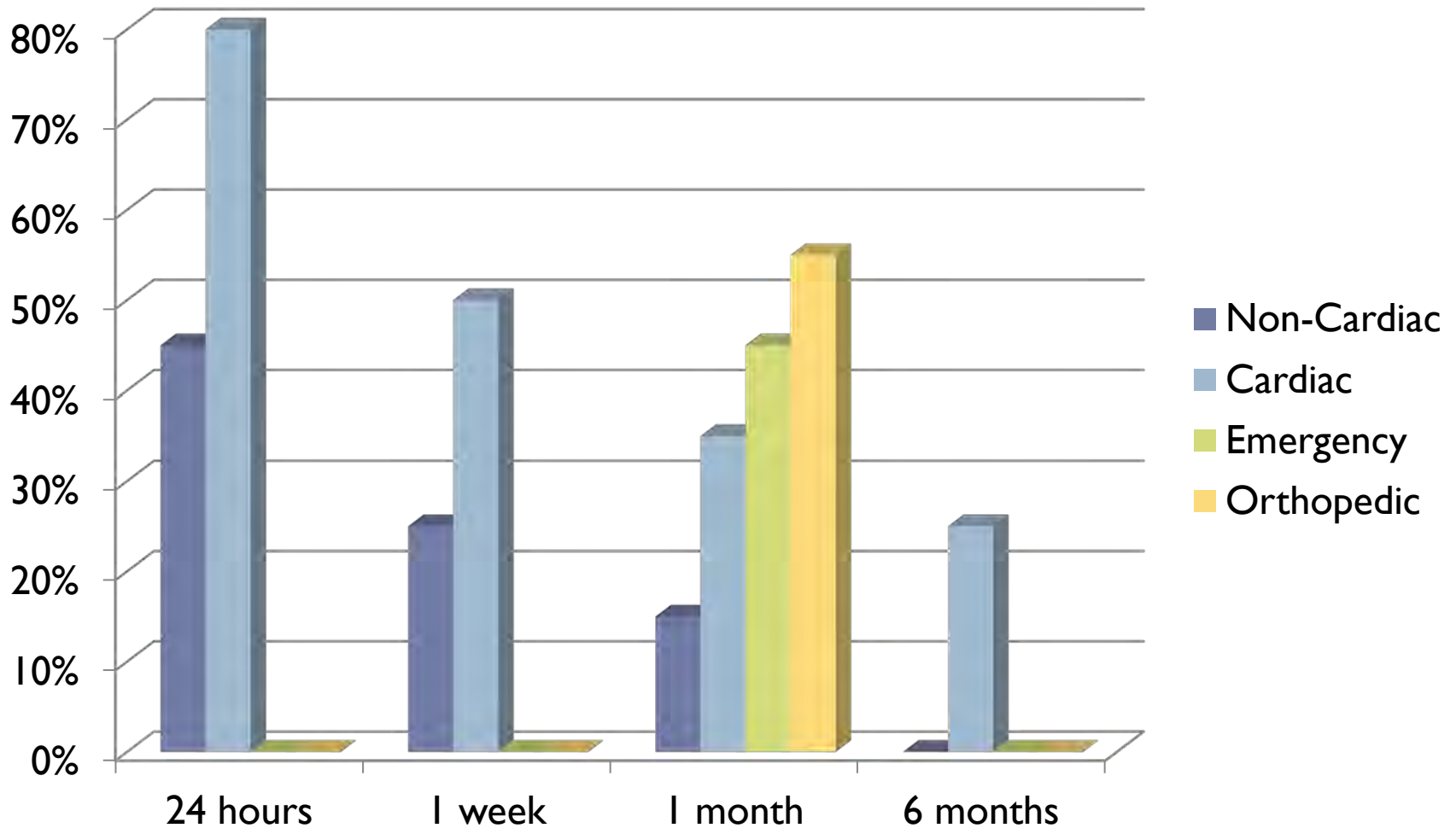
Etiology

Risks

Prevention

Review Questions

# POCD Incidence



Background

Etiology

Risks

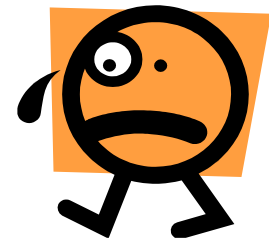
Prevention

Review Questions

# POCD: Significance

---

- ▶ Annoyance
  - ▶ Social integration
  - ▶ Loss of job
  - ▶ Relationship issues
  - ▶ Loss of independence
  - ▶ Quality of life
- ▶ Poor outcomes
    - ▶ Longer hospital stay
    - ▶ Long-term facility admission
    - ▶ Increased mortality
    - ▶ Poor cognitive & functional recovery



Background

Etiology

Risks

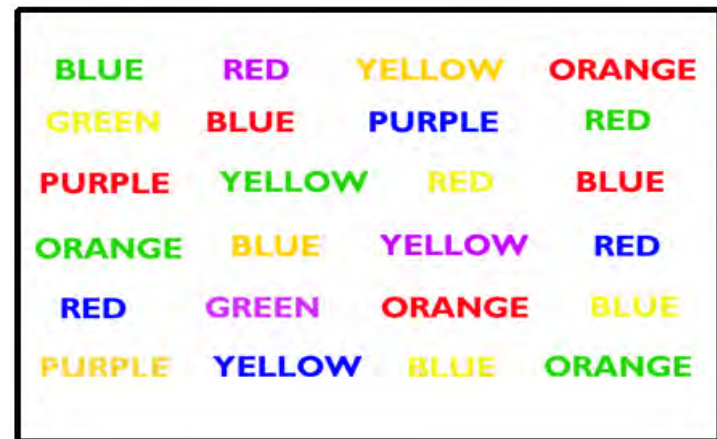
Prevention

Review Questions



# Neuropsychological Testing

- ▶ Immediate Memory:
  - ▶ Digit Span test of the Wechsler Memory Scale-Revised (WMS-R)
  - ▶ Rey Auditory Verbal Learning Test
  - ▶ Visual Memory Span Test of the WMS-R
- ▶ Learning & Recent Memory:
  - ▶ Rey Auditory Verbal Learning Test
- ▶ Attention & Psychomotor Speed:
  - ▶ The Bourdon – Vos Test
  - ▶ The Trail Making Test parts A and B of the Halstead-Reitan Neuropsychological Battery
  - ▶ The Stroop Color and Word Test
  - ▶ The Symbol Digit Modalities Test
- ▶ Verbal Fluency:
  - ▶ Stroop Test
- ▶ Assessing Mood:
  - ▶ Amsterdam Mood States Questionnaire



# Etiology

---

- ▶ **Unclear**
  - ▶ Genetic
  - ▶ Inflammation
  - ▶ Neurotransmitter function alteration
  - ▶ Stress response
  - ▶ Anesthesia
  - ▶ Cardiopulmonary bypass (CPB) technique
    - ▶ Off-pump
    - ▶ On-pump



# Etiology: Genetic

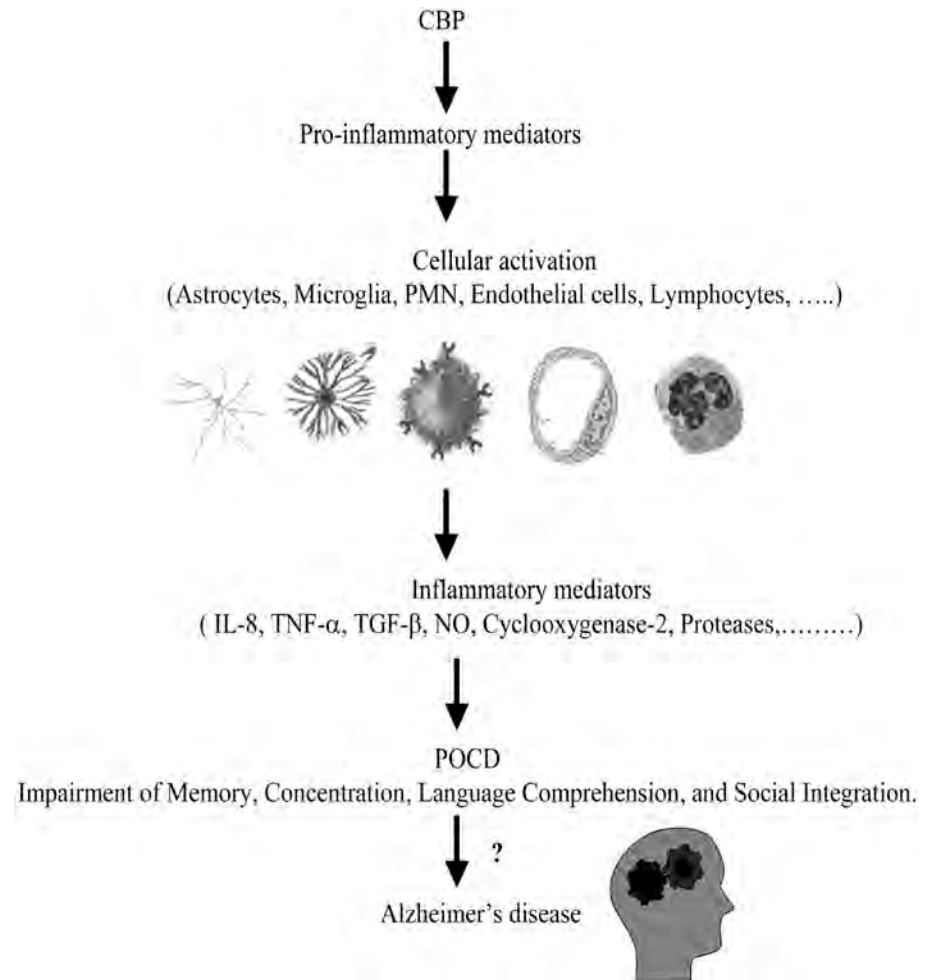
- ▶ **Apolipoprotein E**
  - ▶  $\epsilon 4$  allele
  - ▶ Alzheimer's disease
  - ▶ Neurodegenerative disorders
- ▶ **Phospholipases A2**
  - ▶ Lowers mental state scores
- ▶ **Interleukin-6**
- ▶ **C-reactive protein (CRP)**
- ▶ **Tumoral necrosis factor-alpha**



CPB inflammatory response

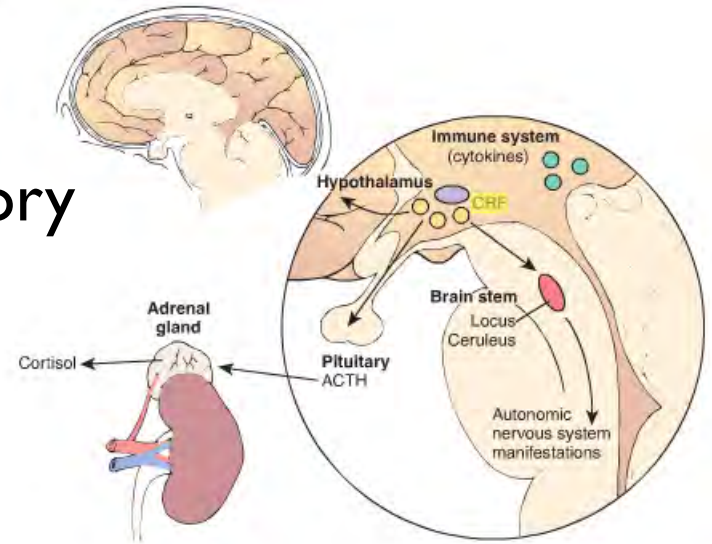
# Etiology: Inflammation

- ▶ CPB → Inflammatory response:
  - ▶ Contact activation
  - ▶ Aortic cross-clamp
  - ▶ Nonspecific activators
    - ▶ Surgical trauma
    - ▶ Blood loss
    - ▶ Transfusions



# Etiology: Stress

- ▶ Stress response
  - ▶ Increase cortisol
  - ▶ Increase catecholamines
- ▶ High stress levels → Inhibit memory
  - ▶ Altered hippocampal function
    - ▶ Organizing
    - ▶ Forming
    - ▶ Storing
- ▶ Surgery
  - ▶ Immune mechanisms
  - ▶ Inflammatory cascade

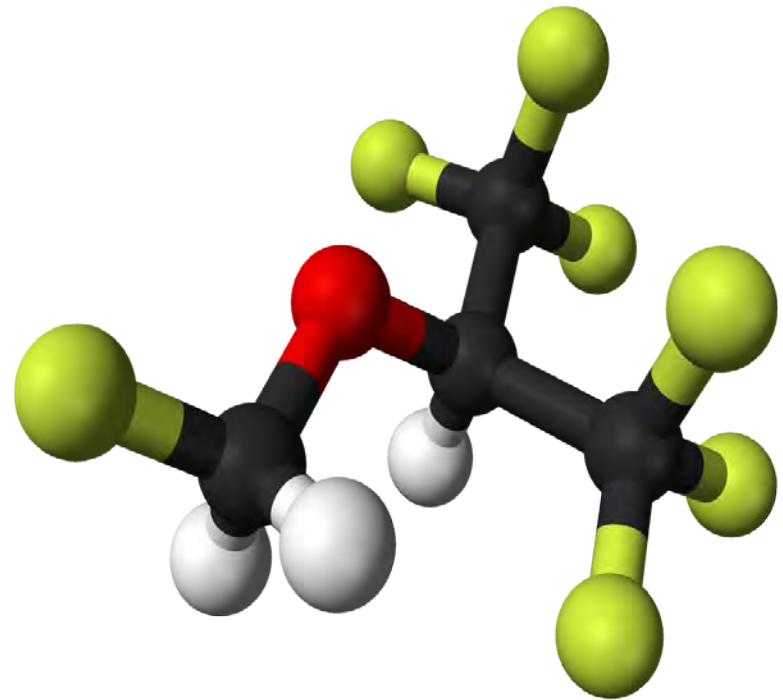


Corticotropin-releasing factor (CRF) →  
Adrenocorticotropic hormone (ACTH) release → Adrenal  
gland → Cortisol

# Etiology: Anesthesia

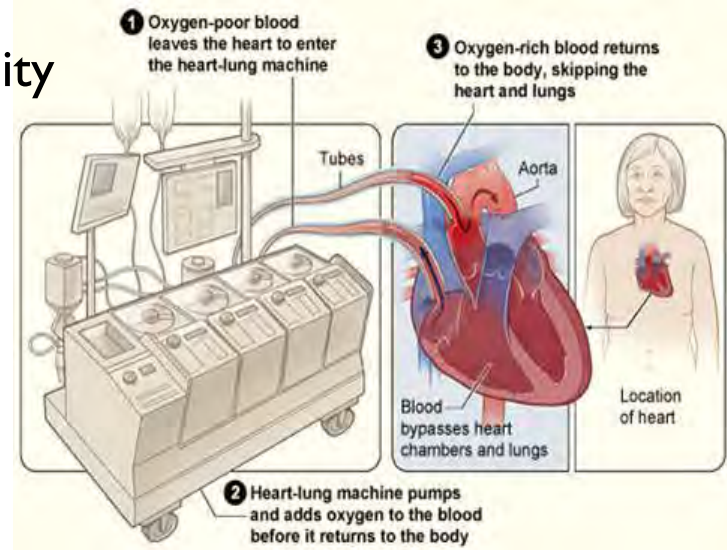
---

- ▶ Prolonged exposure →
  - ▶ Gene expression
  - ▶ Brain synthesis
  - ▶ Cognitive function
- ▶ Sevoflurane ≠ POCD



# Etiology: CPB Technique

- ▶ **Cardiopulmonary Bypass (CPB) technique:**
  - ▶ Off-pump
    - ▶ Immobilization
    - ▶ NO CPB
  - ▶ On-pump
    - ▶ Increases blood brain barrier permeability
    - ▶ Micro/Macroemboli
  - ▶ Duration
    - ▶  $\geq 114$  minutes  $\rightarrow$  Neurologic event



# Risk Factors

## ▶ Preoperative

- ▶ Age
- ▶ Education
- ▶ Previous Disease
- ▶ Lower socioeconomic status

## ▶ Intraoperative

- ▶ Embolization
- ▶ Surgical procedure duration
- ▶ Arterial pressure
- ▶ Inflammation
- ▶ Hyperglycemia
- ▶ Temperature
- ▶ Metabolic abnormalities
- ▶ Anemia
- ▶ Multiple transfusions

## ▶ Postoperative

- ▶ Hypoxia





# Preoperative Factors: Age

---

- ▶ Increased age
- ▶ Unknown mechanism
  - ▶ Atherosclerosis → Cardiovascular disease
  - ▶ Embolization
  - ▶ Vasculature alterations
  - ▶ Cerebral blood flow alterations
  - ▶ Pharmaceuticals (agents)
  - ▶ Cognitive function reduction



Background

Etiology

Risks

Prevention

Review Questions

# Preoperative Factors: Education

---

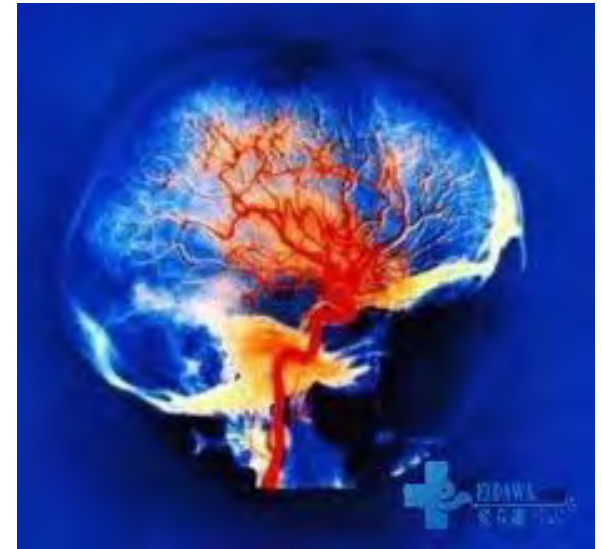
- ▶ **Protective effect**
- ▶ **Number of school years**
  - ▶ Cognitive reserve
  - ▶ Evaluation ability improvement
  - ▶ Increase neuronal homeostasis
  - ▶ Neuronal injury resistant
- ▶ **Unknown mechanism**
  - ▶ Education → Increase neocortex synaptic density → Increase neuronal communication → Minimize cognitive & functional impairment S/S



# Preoperative Factors: Previous Diseases

---

- ▶ **Diabetes Mellitus (DM)**
  - ▶ Cerebral blood flow alteration
- ▶ **Systemic Arterial Hypertension (SAH)**
  - ▶ Cerebral blood flow alteration
  - ▶ Cerebral artery hardening
  - ▶ Atherosclerotic disease
- ▶ **Chronic Renal Failure (CRF)**
- ▶ **Atrial fibrillation**
- ▶ **Left ventricular ejection fraction (EF)  $\leq$  30%**

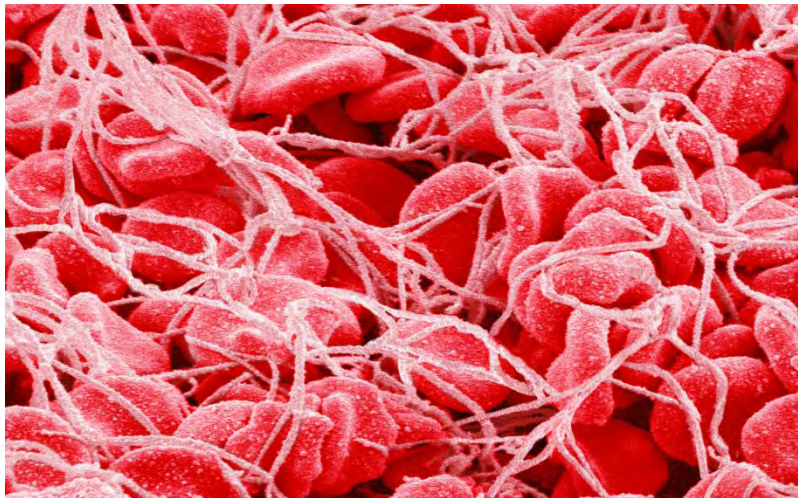


# Intraoperative Factors: Embolization

---

## ▶ Emboli formation:

- ▶ Aortic wall
- ▶ Aggregated platelets
- ▶ Air bubbles
- ▶ Heart chambers



## ▶ Micro vs. Macroemboli

- ▶ Microemboli → POCD
- ▶ Gaseous microemboli
  - ▶ Most probable source
  - ▶ Origin:
    - 1. Oxygenator
    - 2. Cooling process
    - 3. Opening heart chambers

# Intraoperative Factors: Surgical Procedure Duration

---

- ▶ **Cardiopulmonary bypass (CPB)**
  - ▶ Greater microvascular obstructions
- ▶ **Surgical procedure duration**
  - ▶ Greater microvascular obstructions



Background

Etiology

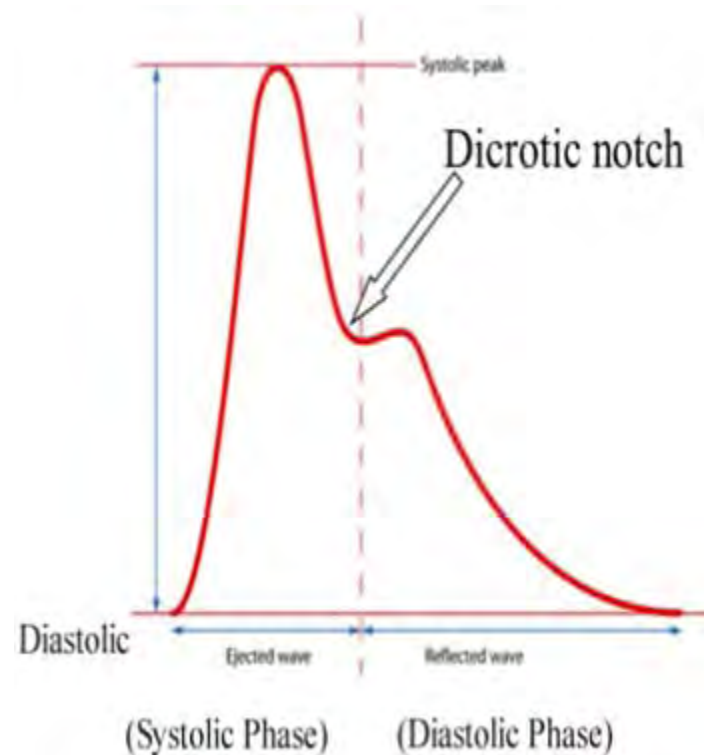
**Risks**

Prevention

Review Questions

# Intraoperative Factors: Arterial Pressure

- ▶ Hypertension
  - ▶ Neurological impairment
- ▶ Hypotension
  - ▶ Neurological impairment
- ▶ Mean arterial pressure (MAP)
  - ▶ Maintain



# Intraoperative Factors: Hyperglycemia

## ▶ Hyperglycemia

- ▶ Blood sugar > 200 mg/dL
- ▶ Cerebral metabolism
  - ▶ Anaerobic metabolism
    - Increase lactate production
    - Ischemic process
- ▶ Increase excitatory amino acids
  - ▶ Inflammatory response
  - ▶ Corticosteroid production

Alteration in:  
Glycolysis  
Protein Synthesis  
Homeostasis  
Enzymatic Functions  
Other cell processes



# Intraoperative Factors: Temperature

---

## ▶ Hyperthermia

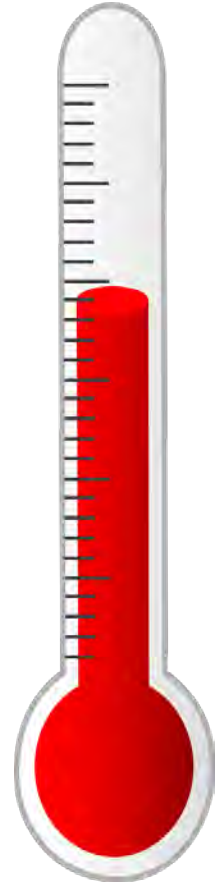
- ▶ Neurotransmitter release
  - ▶ Toxic amounts
- ▶ Free radical release
- ▶ Increase blood-brain barrier permeability
- ▶ Ischemic area enlargement
  - ▶ Increase ischemic depolarization
- ▶ Increase morbidity & mortality rates

## ▶ Hypothermia

- ▶ Reduces energy consumption → cell integrity
- ▶ Improves cerebral & myocardial tolerance

## ▶ Rewarming

- ▶ Speed → jugular desaturation

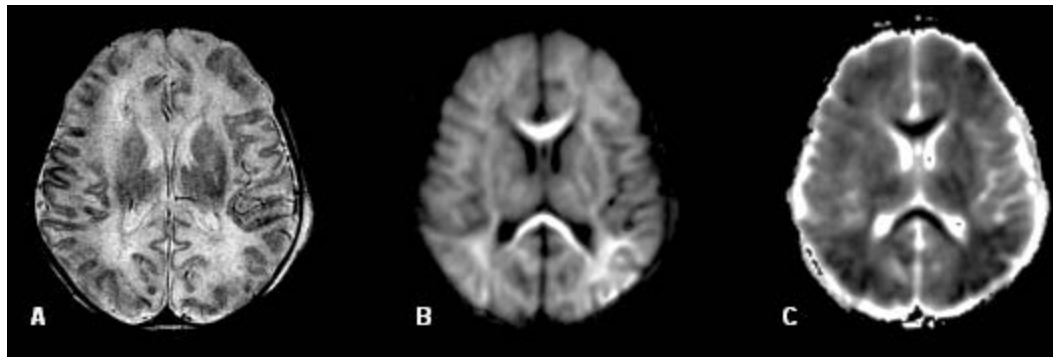




# Postoperative Factors: Hypoxia

---

- ▶ Cerebral hypoxia
  - ▶ Hippocampus alterations
  - ▶ CPB consequence



Background

Etiology

**Risks**

Prevention

Review Questions

# Prevention

---

- ▶ **Assessment:**
  - ▶ Hemodynamic stability
- ▶ **Temperature**
  - ▶ Hypothermia
  - ▶ Slow rewarming
- ▶ **Minimal surgical invasiveness**
- ▶ **Mechanical devices**
  - ▶ Intra-aortic filter
  - ▶ Ultrafiltration
  - ▶ Leukocyte depletion



# Pharmacotherapy

---

- ▶ **Aprotinin**
  - ▶ Serine protease inhibitor
  - ▶ Anti-inflammatory
- ▶ **Heparin**
  - ▶ Decrease inflammatory response
- ▶ **Barbiturates**
  - ▶ Neuroprotection
  - ▶ Controversial
- ▶ **Xenon**
  - ▶ Neuroprotection
  - ▶ N-methyl-D-aspartate (NMDA) antagonist
- ▶ **Steroids**
  - ▶ Inhibit ischemia-reperfusion injury
  - ▶ Anti-inflammatory



Background

Etiology

Risks

**Prevention**

Review Questions

# Future Research

- ▶ Quality of life
- ▶ Intervention strategies
- ▶ Reverse impact/incidence
- ▶ Treatment strategies
- ▶ Core neuropsychological testing
- ▶ Volatile anesthetics



Background

Etiology

Risks

**Prevention**

Review Questions

# Review Questions

---

1. Preoperative predisposing risk factors for POCD include all the following EXCEPT:
  - a. Increased age
  - b. Previous diseases
  - c. Increased education level
  - d. Diabetes
  
2. The use of the anesthetic gas, Sevoflurane, has been shown to increase the incidence of POCD.  
True  
False
  
3. Cardiopulmonary bypass (CPB) time greater than or equal to \_\_\_\_\_ minutes significantly increases the risk of a neurologic event.

114

# The End!



# References

---

- Alexander, L. P., Anstrom, K. J., Muhibaier, L. H., Grosswald, R. D., Smith, P. K., Jones R. H., & Peterson E. D. (2000). Outcomes of cardiac surgery in patients > 80 years: Results from the National Cardiovascular Network. *Journal of the American College of Cardiology*, 35(3), 731-738.
- Ancelin, M. L., DeRoquefeuil, G., Ledesert, B., Bonnel, F., Cheminal, J.C., & Ritchie, K. (2001). Exposure to anaesthetic agents: Cognitive functioning and depressive symptomatology in the elderly. *British Journal of Psychiatry*, 178, 360-366.
- Arrowsmith, J. E., Grocott, H. P., Reves, J. G., & Newman, M. F. (2000). Central nervous system complications of cardiac surgery. *British Journal of Anaesthesia*, 84, 378- 393.
- Baufreton, C., Allain, P., Chevaller, A., Etcharry-Bouyx, F., Corbeau, J. J., Legall, L., et al. (2005). Brain injury and neuropsychological outcome after coronary artery surgery are affected by complement activation. *Annals of Thoracic Surgery*, 79(5), 1597-1605.
- Bedford, P. D. (1955). Adverse cerebral effects of anaesthesia on old people. *Lancet*, 269(6884), 259-263.
- Bekker, A. Y., & Weeks, E. J. (2003). Cognitive function after anaesthesia in the elderly. *Best Practice and Research*, 17(2), 259-272.
- Boodhwani, M., Rubens, F. D., Wozny, D., Rodriguez, R., Alsefaou, A., Hendry, P. J., et al., (2006). Predictors of early neurocognitive deficits in low-risk patients undergoing on-pump coronary artery bypass surgery. *Circulation* 114(I Supple), 1461-1466.
- Bucerius, J., Gummert, J. F., Borger, M. A., Walther, T., Doll, N., Falk, V., et al. (2004). Predictors of delirium after cardiac surgery: Effect of beating-heart (off pump) surgery. *Journal of Thoracic and Cardiovascular Surgery*, 127, 57-64.
- Burke, S. N., & Barnes, C. A. (2006). Neural plasticity in the ageing brain. *Nature Reviews Neuroscience*, 7, 30-40.
- Canet, J., Raeder, J., Rasmussen L. S., Enlund, M., Kuipers, H. M., Hanning, C. D., et al. (2003). Cognitive dysfunction after minor surgery in the elderly. *ACTA Anaesthesiologica Scandinavica*, 47, 1204-1210.
- Collie, A., Darby, D. G., Falleti, M. G., Silbert, F. S., & Maruff, P. (2002). Determining the extent of cognitive change after coronary surgery: A review of statistical procedures. *The Annals of Thoracic Surgery*, 73, 2005-2011.

# References

---

- Crosby, G. & Culley, D. J. (2003). Anesthesia, the aging brain, and the surgical patient. *Canadian Journal of Anesthesia*, 50(6), R1-R5.
- Culley, D. J., Xie, Z., & Crosby, G. (2007). General anesthetic-induced neurotoxicity: an emerging problem for the young and old? *Current Opinion in Anaesthesiology*, 20, 408-413.
- Dijkstra, J. B., Houx, P. J., & Jolles, J. (1999). Cognition after major surgery in the elderly: Test performance and complaints. *British Journal of Anaesthesia*, 82(6), 867-874.
- Dodds, C., & Allison, J. (1998). Postoperative cognitive deficit in the elderly surgical patient. *British Journal of Anaesthesia*, 81, 449-462.
- Farag, E., Chelune, G. J., Schubert, A., & Mascha, E. J. (2006). Is depth of anesthesia, as assessed by the Bispectral Index, related to postoperative cognitive dysfunction and recovery. *Anesthesia & Analgesia*, 103(3), 633-640.
- Gau, L., Taha, R., Gauvin, D., Othmen, L. B., Wang, Y., & Blaise, G. (2005). Postoperative cognitive dysfunction after cardiac surgery. *Chest*, 128(5), 3664-3670.
- Grimm, M., Zimpfer, D., Czerny, M., Kilo, J., Kasimire, M. T., Kramer, L. et al. (2003). Neurocognitive deficit following mitral valve surgery. *European Journal of Cardio-thoracic Surgery*, 23, 265-271.
- Ho, P. M., Arciniegas, D.B., Grigsby, J., McCarthy, M., McDonald, G. O., Moritz, T. E., et al. (2004). Predictors of cognitive decline following coronary artery bypass graft surgery. *Annals of Thoracic Surgery*, 77, 597-603.
- Hudetz, J. A., Iqbal, Z., Gandhi, S. D., Patterson, K. M., Hyde, T. F., Reddy, D. M., et al. (2007). Postoperative cognitive dysfunction in older patients with a history of alcohol abuse. *Anesthesiology*, 106(3), 423-430.
- Kadoi, Y. & Goto, F. (2006). Factors associated with postoperative cognitive dysfunction in patients undergoing cardiac surgery. *Surgery Today*, 36(12), 1053-1057.
- Keith, J. R., Puente, A. E., Malcolmson, K. L., Tartt, S., Coleman, A. E., & Marks, H. F. (2002). Assessing postoperative cognitive change after cardiopulmonary bypass surgery. *Neuropsychology*, 16, 411-421.
- Kojima, Y., & Narita, M. (2005). Postoperative outcome among elderly patients after general anesthesia. *Acta Anaesthesiologica Scandinavica* 50(1), 19-25.
-



# References

---

- Likosky, D.S., Caplan, L.R., Weintraub, R.M., Hartman, G.S., Malenka, D.J., Ross, C. S. et al. (2004a). Intraoperative and postoperative variables associated with strokes following cardiac surgery. *Heart Surgery Forum*, 7(4), E271-276.
- Likosky, D. S., Leavitt, B. J., Marrin, A.S., Malenka, D. J., Reeves, A. G., Weintraum, R. M., et al. (2003). Intra- and postoperative predictors of stroke after coronary artery bypass grafting. *Annals of Thoracic Surgery*, 76, 428-435.
- Likosky, D. S., Roth, R. M., Saykin, A.J., Eskey, C. J., Ross, C. S., & O'Connor, G. T. (2004b). Neurologic injury associated with CABG surgery: Outcomes, mechanisms, and opportunities for improvement. *Heart Surgery Forum*, 7(6), E650-662.
- Linstedt, U., Meyer, O., Kropp, P., Berkau, A., Tapp, E., & Zenz, M. (2002). Serum concentration of S-100 protein in assessment of cognitive dysfunction after general anesthesia in different types of surgery. *Acta Anaesthesiologica Scandinavica*, 46, 384-389.
- Moller, J. T. (1997). Cerebral dysfunction after anaesthesia. *Acta Anaesthesiologica Scandinavica*, 110, 13-16.
- Moller, J. T., Cluitmans, P., Rasmussen, L. S., Houx, P., Rasmussen, H., Canet, J., et al. (1998). Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study. *Lancet*, 351, 857-861.
- Moller, J. T., Svehnilid, I., Johannessen, N. W., Jensen, P. F., Espersen, K., Gravenstein, M. D., et al. (1993). Perioperative monitoring with pulse oximetry and late postoperative cognitive dysfunction. *British Journal of Anaesthesia*, 71, 340-347.
- Monk, T. G., Saini, B., Weldon, B. C., & Sigl, J. C. (2005). Anesthetic management and one-year mortality after noncardiac surgery. *Anesthesia and Analgesia* 100, 4-10.
- Monk, T. G., Weldon, B. C., Garvan, C. W., Dede, D. E., van der As, M. T., Heilman, K. M., et al. (2008). Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology* 108(1), 18-30.
- Murkin, J. M., Newman, S. P., Stump, D. A., & Blumenthal, J. A. (1995). Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. *Annals of Thoracic Surgery*, 59, 1289-1295.
- Newman, M. F., Kirchner, J. L., Phillips-Bute, B., Gaver, B., Grocott, H., Jones, R. H., et al. (2001). Longitudinal assessment of neurocognitive function after coronary artery bypass surgery. *NEJM*, 344(6), 395-402.
- Newman, S., Stygall, J., Hirani, S., Shaewfi, S., & Maze, M. (2007). Postoperative cognitive dysfunction after noncardiac surgery: A systematic review. *Anesthesiology*, 106(3), 572-590.
- Quattara, A., Amour, J., & Bouzguenda, H. (2009). Cognitive impairment after cardiac surgery. *Presse Med*, 38(11), 1607-1612.
-

# References

---

- Rasmussen, L. S., Christiansen, M., Eliassen, K., Sander-Jensen, K., & Moller, J. T. (2002a). Biochemical markers for brain damage after cardiac surgery – Time profile and correlation with cognitive dysfunction. *Acta Anaesthesiologica Scandinavica*, *46*, 547-551.
- Rasmussen, L. S., Larsen, K., Houx, P., Skovgaard, L. T., Hanning, C. D., & Moller, J.T. (2001). The assessment of postoperative cognitive function. *ACTA Anaesthesiologica Scandinavica*, *45*, 275-289.
- Rasmussen, L. S. & Moller, J. T. (2000). Central nervous system dysfunction after anesthesia in the geriatric patient. *Anesthesiology Clinics of North America*, *18*, 59-70.
- Rasmussen, L. S., O'Brien, J. T., Silverstein, J. H., Johnson, T.W., & Siersma, V. D. (2005). Is perioperative cortisol secretion related to postoperative cognitive dysfunction. *Acta Anaesthesiologica Scandinavica*, *49*, 1225-1231.
- Rasmussen, L. S., Steentoft, A., Rasmussen, H., Dristensen, P. A., & Moller, J. T. (1999). Benzodiazepines and postoperative cognitive dysfunction in the elderly. *British Journal of Anaesthesia*, *83*(4), 585-589.
- Rosen, H., Rosengren, L., Herlitz, J., & Blomstrand, C. (1998). Increased serum levels of the S-100 protein are associated with hypoxic brain damage after cardiac arrest. *Stroke*, *29*(2), 473-477.
- Rosenburg, J., & Kehlet, H. (1993). Postoperative mental confusion: Association with postoperative hypoxemia. *Surgery*, *114*, 76-81.
- Selnes, O. A., Grega, M. A., Borowicz, L. M., Barry, S., Zeger, S., Baumgartner, W. A., et al. (2005). Cognitive outcomes three years after coronary artery bypass surgery: A comparison of on-pump coronary artery bypass graft surgery and nonsurgical controls. *Annals of Thoracic Surgery*, *79*, 1201-1209.
- Selnes, O. A., Grega, M. A., Borowicz, L. M., Royall, R. M., McKhann, G. M., & Baumgartner, W. A. (2003). Cognitive changes with coronary artery disease: A prospective study of coronary artery bypass graft patients and nonsurgical controls. *Annals of Thoracic Surgery*, *75*, 1377-1386.
- Shann, K. G., Likosky, D. S., Murkin, J. M., Baker, R. A., Baribeau, Y. R., DeFoe, G., et al. (2006). An evidence-based review of cardiopulmonary bypass in adults: A focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *Journal of Thoracic and Cardiovascular Surgery*, *132*, 283-290.
- Silverstein, J. H., Steinmetz, J., Reichenberg, A., Harvey, P. D., & Rasmussen, L. S. (2007). Postoperative cognitive dysfunction in patients with preoperative cognitive decline. *Anesthesiology*, *106*(3), 431-435.
- Stroobant, N., Van Nooten, G., Van Belleghem, Y., & Vingerhoets, G. (2005). Relation between neurocognitive impairment, embolic load, and cerebrovascular reactivity following on- and off-pump coronary artery bypass grafting. *Chest*, *127*(6), 1967-1976.
- 



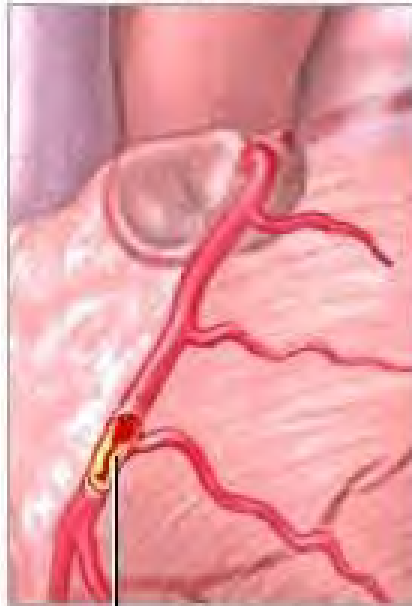
# References

---

- Stump, D., Rogers, A., Hammon, J., & Newman, S. (1996). Cerebral emboli and cognitive outcome after cardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia*, *10*(1), 113-119.
- Symes, E., Marruf, P., & Ajani, A. (2000). Issues associated with the identification of cognitive change following coronary artery bypass grafting. *Australian and New Zealand Journal of Psychiatry*, *34*, 770-784.
- Thornton, E. W., Groom, C., Fabri, B. M., Fox, M. A., Hallas, C., & Jackson, M. (2005). Quality of life outcomes after coronary artery bypass graft surgery: Relationship to neuropsychologic deficit. *Journal of Thoracic and Cardiovascular Surgery*, *130*(4), 1022-1027.
- Van Dijk, D., Spoor, M., Hijman, R., Nathoe, H. M., Borst, C., Jansen, E. W., et al. (2007). Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. *JAMA*, *297*(7), 701-708.
- Wang, V., Sands, L. P., Vaurio, L., Mullen, E. A., & Leung, J. M. (2007). The effects of postoperative pain and its management on postoperative cognitive dysfunction. *The American Journal of Geriatric Psychology*, *15*(1), 50-59.
- Westaby, S., Saatvedt, K., White, S., Katsumata, T., van Oeveren, W., & Halligan, P. W. (2001). Is there a relationship between cognitive dysfunction and systemic inflammatory response after cardiopulmonary bypass? *Annals of Thoracic Surgery*, *71*, 667-672.
- Wu, C. L., Hsu, W., Richman, J. M., & Raja, S. N. (2004). Postoperative cognitive function as an outcome of regional anesthesia and analgesia. *Regional Anesthesia and Pain Medicine*, *29*(3), 257-268.
- Yin, Y., Luo, A., Guo, X., Li, L., & Huang, Y. (2007). Postoperative neuropsychological change and its underlying mechanism in patients undergoing coronary artery bypass grafting. *Chinese Medical Journal*, *120*(22), 1951-1957.
- Zimpfer, D., Czerny, M., Kilo, J., Kasimir, M. T., & Madl, C. (2002). Cognitive deficit after aortic valve replacement. *Annals of Thoracic Surgery*, *74*, 407-412.
- Zimpfer, D., Czerny, M., Schuch, P., Fakin, R., & Madl, C. (2006). Long-term neurocognitive function after mechanical aortic valve replacement. *Annals of Thoracic Surgery*, *81*, 29-33.
- Zimpfer, D., Czerny, M., Vogt, F., Schuch, P., Kramer, L., Wolner, E., et al. (2004). Neurocognitive deficit following coronary artery bypass grafting: A prospective study of surgical patients and nonsurgical controls. *Annals of Thoracic Surgery*, *78*, 513-519.
- 

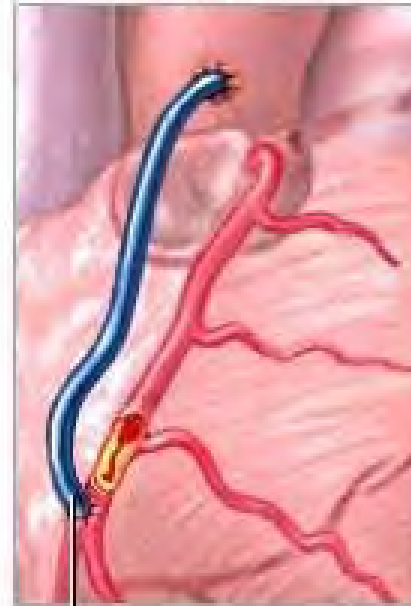


Before

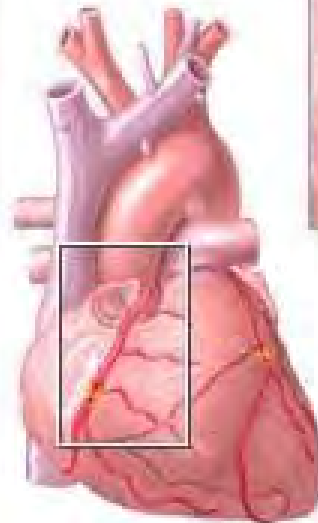


Blocked coronary artery

After



Vein graft sewn in to bypass blockage



Biological valve  
(human or porcine)

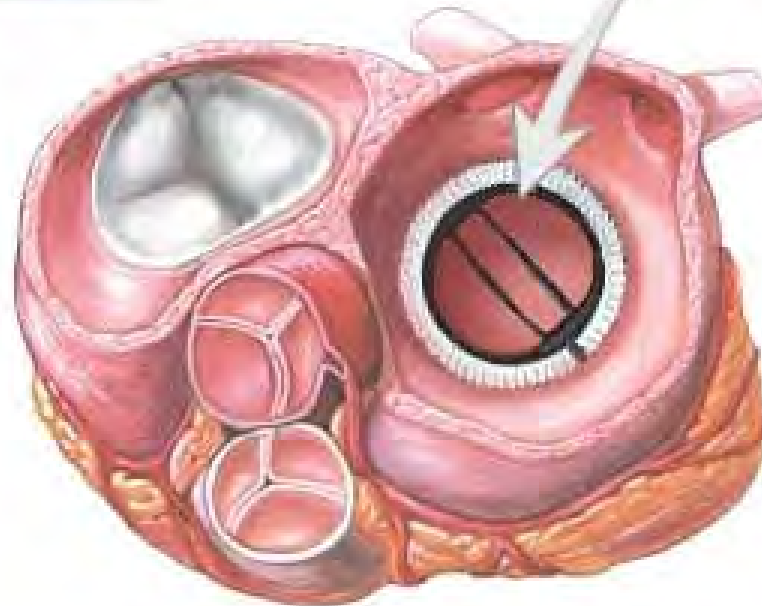


Mechanical valve





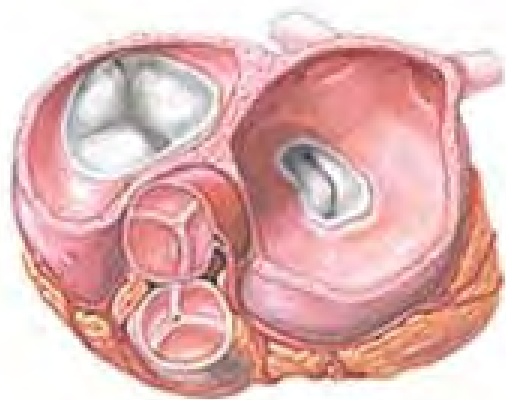
Mechanical  
valve



ADAM.



Before



After

