# Syndrome inflammatoire en chirurgie cardiaque

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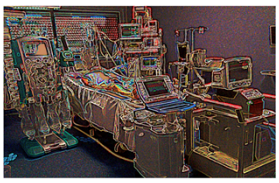

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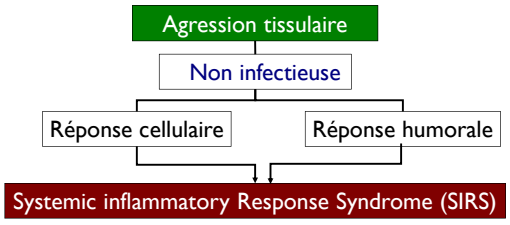
## Hemodialysis Leukopenia

PULMONARY VASCULAR LEUKOSTASIS RESULTING FROM COMPLEMENT ACTIVATION BY DIALYZER CELLOPHANE MEMBRANES

PHILIP R. CRADDOCK, JORG FEHR, AGUSTIN P. DALMASSO, KENNETH L. BRIGHAM, and HARRY S. JACOB

ABSTRACT Acute leukopenia occurs in all patients during the first hour of hemodialysis with cellophane-membrane equipment. This transient cytopenia specifically involves granulocytes and monocytes, cells which share plasma membrane reactivity towards activated complement components. The present studies document that complement is activated during exposure of plasma to dialyzer cellophane, and that upon reinfusion of this plasma into the venous circulation, granulocyte and monocyte entrapment in the pulmonary vasculature is induced. During early dialysis, conversion of both C3 and factor B can be demonstrated in plasma as it leaves the dialyzer. Moreover, simple incubation of human plasma with dialyzer cellophane causes conversion of C3 and factor B, accompanied by depletion of total hemolytic complement and C3 but sparing of hemolytic C1. Reinfusion of autologous, cellophane-incubated plasma into rabbits produces selective granulocyto-penia and monocytopenia identical to that seen in dialyzed patients. Lungs from such animals reveal striking pulmonary vessel engorgement with granulocytes. The activated complement component(s) responsible for leukostasis has an approximate molecular weight of 7,000–20,000 daltons. Since it is generated in C2-deficient plasma and is associated with factor B conversion, it is suggested that activation of complement by dialysis is predominantly through the alternative pathway.

*The Journal of Clinical Investigation Volume 59 May 1977·879–888*

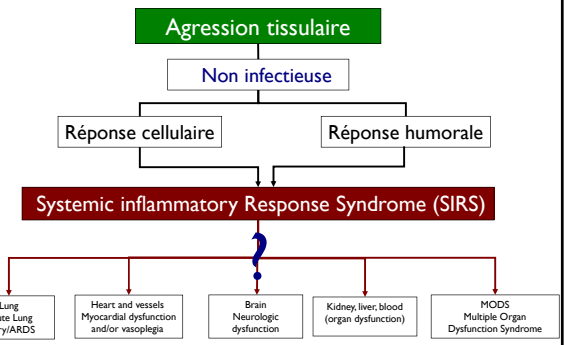


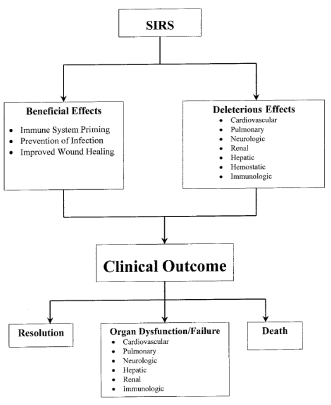

**SIRS (Systemic Inflammatory Response Syndrome)**

Two or more of:

- Temperature >38°C or <36°C
- Heart rate >90/min
- Respiratory rate >20/min or $PaCO_2$ <32 mm Hg (4.3 kPa)
- White blood cell count >12 000/$mm^3$ or <4000/$mm^3$ or >10% immature bands

Bone RC et al. JAMA 1992; 268:3452-5




*Laffey JG et al. Anesthesiology 2002;97:215-52*

## Réaction inflammatoire systémique et chirurgie cardiaque

# Constante!

Expression biologique et clinique variables…
(CRP, hyperleucocytose, hyperfibrinogénémie, vasoplégie, SDMV…)
(Incidence 5-60% selon la définition retenue)

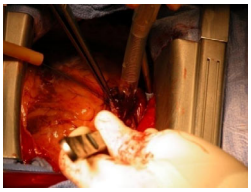
# Réponses individuelles variables

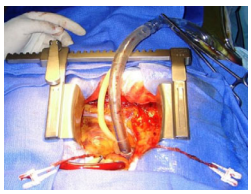
- Contexte chirurgical (urgence, hémorragique, CEC longue…)
- Phénomènes hypoperfusion d'organes (conduite optimale+++)
- Prédisposition génétique (polymorphisme génétique)

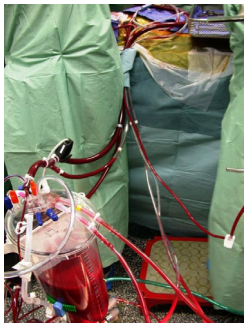
## Facteurs initiateurs de la réponse inflammatoire

- Agression tissulaire (chirurgicale mais pas uniquement…)
- Exposition du sang à surface non-épithéliale (activation phase contact)
- Interface air/sang (réservoir de cardiotomie, médiastin, cavité pleurale…)
- Hypoperfusion organes (poumon, tube digestif,…+++)
  - Translocation bactérienne
  - Libération endotoxines (lipopolysaccharides bactériens…)
- Phénomènes d'ischémie-reperfusion d'organes (cardiaque, cérébrale, rénale, pulmonaire, digestive, hépatique…)
- Héparinisation (complexe héparine/protamine)

*Davies SW et al. J Thorac Cardiovasc Surg 1993; 105:979-87*
*Sawa Y et al. J Thorac Cardiovasc Surg 1996;111:29-35*

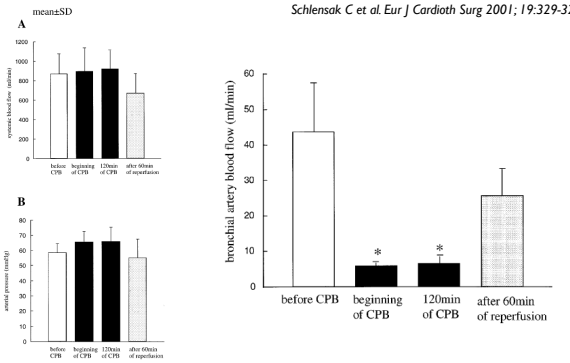


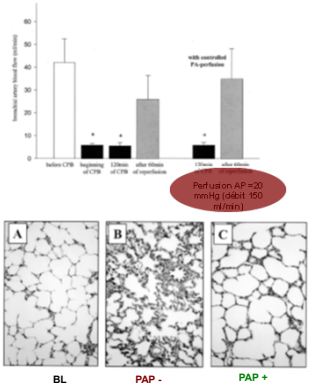




Bronchial artery perfusion during cardiopulmonary bypass does not prevent ischemia of the lung in piglets: assessment of bronchial artery blood flow with fluorescent microspheres☆

*Schlensak C et al. Eur J Cardioth Surg 2001; 19:329-32*




*Schlensak C et al. J Thorac Vasc Surg 2002;123:1199-205*

## Cardiac surgery/ Cardiopulmonary Bypass

Initiating Factors
- Contact Activation
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

↓

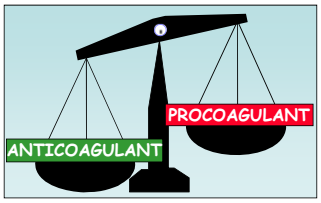
Immune System Activation
- Coagulation/fibrinolysis
- Complement
- Cytokines
- Endothelium
- Cellular Immune System
- Oxidative stress

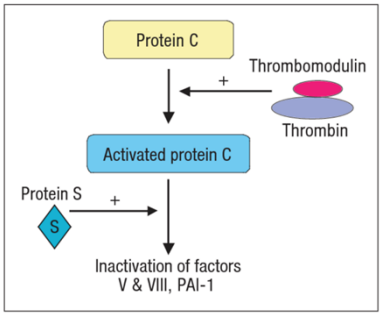
↓

**SIRS**

## Conditions physiologiques : Surface endovasculaire endothéliale anti-thrombogénique

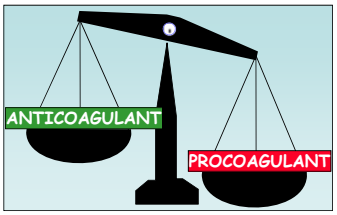
- Synthèse de facteurs antiplaquettaires: $PGI_2$, NO
- Expression à la surface des cellules endothéliales de la thrombomoduline (anti-coagulante)
- Libération de protéines fibrinolytiques (t-PA)

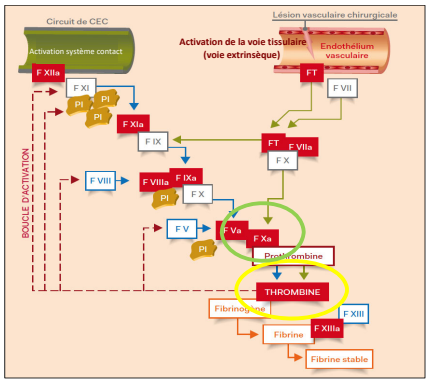


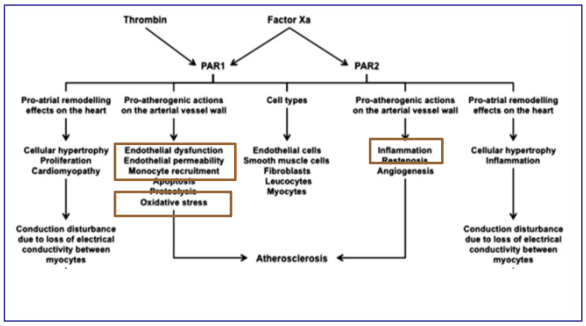

## Au cours de l'inflammation…état procoagulant

Surexpression du Facteur tissulaire (FT), Plaminogen activator inhibitor (PAI)-1 et von Willebrand Factor (vWF)



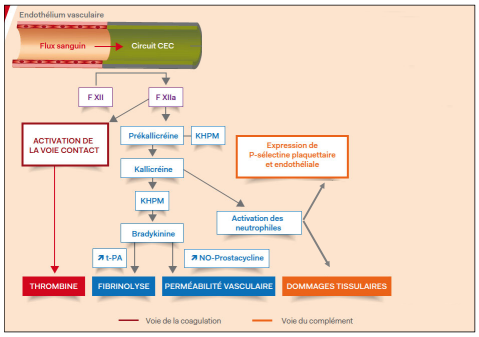




## Pleiotropic effects of thrombin and Factor Xa




*PAR = protease-activated receptor*

## Interaction coagulation et syndrome inflammatoire




KHPM=kininogène de haut poids moléculaire (sérine protéase)

## Cardiac surgery/ Cardiopulmonary Bypass

Initiating Factors
- Tissular injury
- Contact Activation
- Blood-air interface
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

Immune System Activation
- Coagulation/fibrinolysis
- Complement
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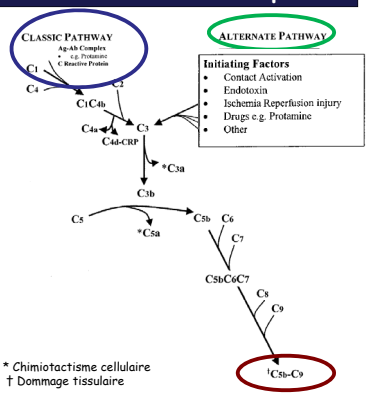
- Oxidative stress

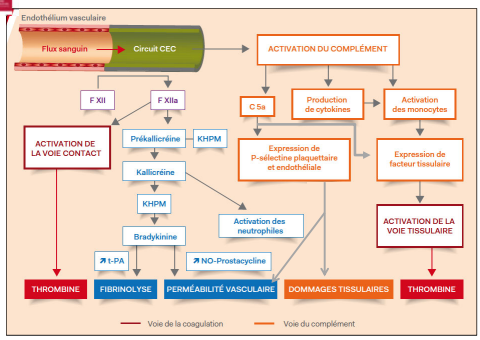
**SIRS**

## Activation de la voie du complément




* Chimiotactisme cellulaire
† Dommage tissulaire

## Interaction activation coagulation et syndrome inflammatoire




Interaction forte hémostase/inflammation+++

KHPM=kininogène de haut poids moléculaire

Rinder CS, Rinder HM, Johnson K, et al. Role of C3 cleavage in monocyte activation during extracorporeal circulation. Circulation 1999; 100: 553-8

Park KW, Tofukuji M, Metais C, et al. Attenuation of endothelium-dependent d… of pig pulmonary arterioles after cardiopulmonary bypass is prevented by monoclonal … C5a. Anesth Analg 1999; 89: 42-8

Tofukuji M, Stahl GL, Agah A, et al. Anti-C5a monoclo… reduces cardiopulmonary bypass and cardioplegia-induced coronary endothelial dysf… orac Cardiovasc Surg 1998; 116: 1060-8

Tofukuji M, Stahl GL, Metais C, et… dysfunction after cardiopulmonary bypass: Role of complement C5a. Ann Thor… 69: 799-807

Gupta-Bansal R, P… nden KR. Inhibition of complement alternative pathway function with anti-properdi… nal antibodies. Mol Immunol 2000; 37: 191-201

Larsson R, Elgue G, Larsson A, et al. Inhibition of complement activation by soluble recombinant CR1 under conditions resembling those in a cardiopulmonary bypass circuit: Reduced upregulation of CD11b and complete abrogation of binding of PMNs to the biomaterial surface. Immunopharmacology 1997; 38: 119-27

Negative trials.

## Cardiac surgery/ Cardiopulmonary Bypass

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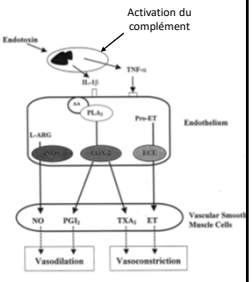
**SIRS**

## Cytokines en chirurgie cardiaque

- Polypeptides solubles
- Messagers paracrines du système immunitaire
- Monocytes activés, macrophages tissulaires, lymphocytes, cellules endothéliales…
- Effet pro-inflammatoire (TNFα, IL-1B, IL-6) et anti-inflammatoire (IL-10)
- Rôle majeur dans homéostasie immunologique
- Produite en réponse à des stimuli physiopathologiques (signaux de danger, endotoxines, activation complément…)
- Association statistique: taux élevé de cytokines et morbidité postopératoire (IL-6 et mortalité en chirurgie cardiaque congénitale)
- Relation de causalité (???)

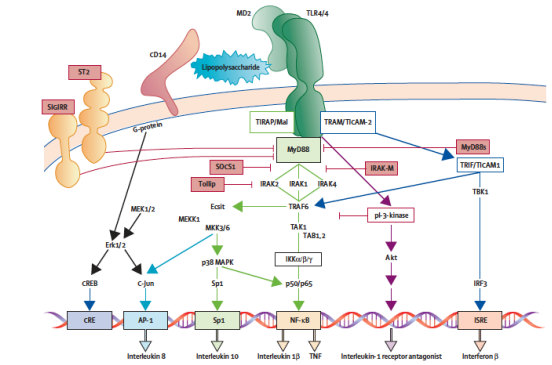


# INFLAMMATORY SIGNALING

- Danger signals
- Interaction between exogenous molecules as Microbial- or Damage-Associated Molecular Patterns (MAMPs or DAMPs) and Pattern Recognition receptors (PRR) on surface or in the cytosol of immune cells (macrophages, monocytes, granulocytes, Natural Killer Cell, dendritic cells...)
- Transcription, maturation and secretion of pro and anti-inflammatory cytokines

| MAMPs (surfaces molecules) | DAMPs (internal motifs, alarmins) | PRR (internal motifs) |
|---|---|---|
| • Endotoxin (LPS)<br>• Lipoproteins<br>• Flagellin, Fimbrae<br>• Peptidoglycan,<br>• Beta-D-glucan… | • Heat shock proteins<br>• Mitochondrial DNA<br>• ATP<br>• High Mobility Group Box (HMGB) 1<br>• S100 protein | Surface<br>• Toll-like receptors (+++)<br>• C-type lectin receptors<br>Cytosol<br>• Nod1 and 2 receptors<br>• RIG-I-Like receptors |

*Annane D et al. Lancet 2005;365:63-78*




AP= activator protein
ISRE Interferon sensitive response element

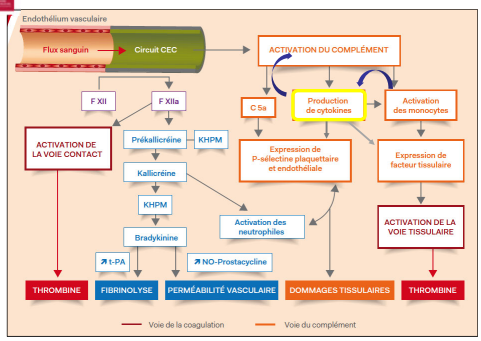
Lancet 2005;365:63-78

# Proinflammatory cytokines

- Auto-amplification phenomenon by increasing numbers, lifespan, and activation state of innate immune cells
- Activation of endothelial cells by increasing the expression of adhesion molecule and chemokine
- Cause the release of microparticles (by activated platelets, endothelial cells, and leukocytes) that contain inflammatory, pro-oxidant, and pro-coagulant lipids and proteins (platelet-activating factor, thromboxan, tissue factor, plasminogen activator inhibitor-1, von Willebrand factor multimers...)
- Upregulate intravascular Tissue Factor expression by blood monocytes
- Induce hepatic production of acute phase proteins such as complement, fibrinogen or C-reactive protein (stimulation of chemotaxis, coagulation, vascular permeability) and thus exacerbate inflammatory response

*Gotts JE et al. BMJ 2016;353:i1585*

## Interaction activation coagulation et syndrome inflammatoire




Interaction forte hémostase/inflammation+++

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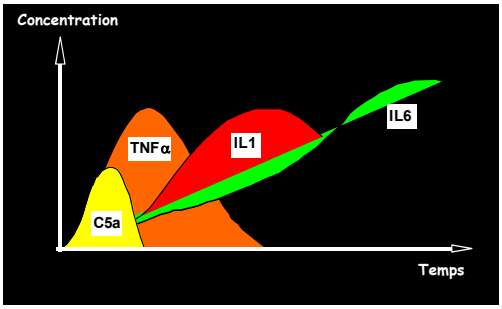
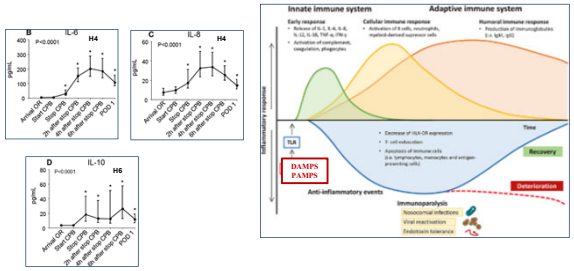
## Libération de cytokines après chirurgie cardiaque cardiaque

| Pro-inflammatoire | | Anti-inflammatoire |
|---|---|---|
| TNFα<br>IL-1β<br>IL6<br>IL8 | Précoce<br>Tardive | IL-10<br>TGF b<br>IL-1ra<br>TNFsr 1 et 2 |



**Understand the temporal pathway of inflammation**




Nature Reviews Immunology 2013(12), 862-74

**« Effets anti-inflammatoires indirects »**

- IL-10 est un puissant inhibiteur de la production de cytokines pro-inflammatoires (TNF-α, IL-1β, IL-6 et IL-8)

Auto-limitation du syndrome inflammatoire

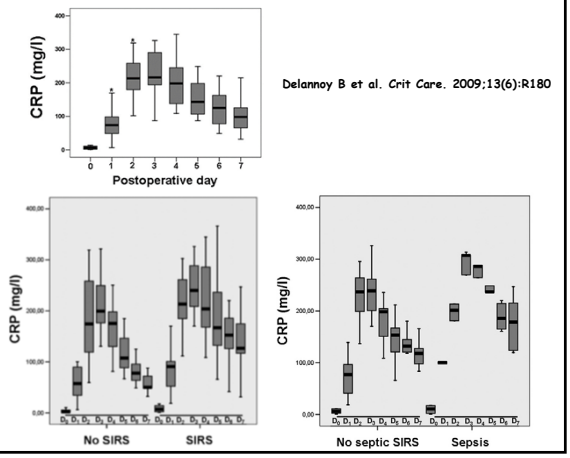
## Resolution pathways

**Auto-limitation of inflammatory process**

- IL-10 produced by leucocytes suppress IL-6 production
- IL-10 activates production of soluble TNF receptor (ligand function for TNF alpha) and IL-1 receptor antagonist
- Autophagy process to eliminate MAMPs (lysosomal degradation)

**Resolution of inflammation**

- Damaged cells and infiltrating leucocytes undergo apoptosis and engulfed by macrophages
- Role of bioactive lipids to reduce ROS production, endothelial permeability and leucocyte recruitment
- Regulatory T cells (Tregs) and myeloid derived suppressor cells play a role in elimination of cytotoxic cells and productions of anti-inflammatory cytokines
- Cholinergic stimulation (inhibition of inflammatory cytokines production)

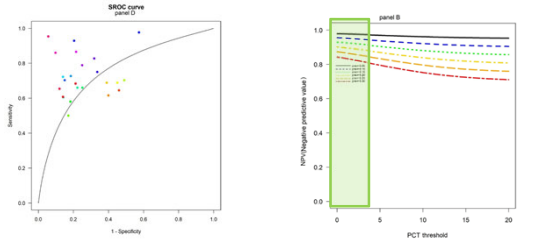



Delannoy B et al. Crit Care. 2009;13(6):R180

RESEARCH Open Access

Procalcitonin for the diagnosis of postoperative bacterial infection after adult cardiac surgery: a systematic review and meta-analysis

Critical Care 2024; 28:44



Pour une valeur seuil de 3 ng/ml, $Se_m$ 67% et $Sp_m$ 73%

Une valeur < 3 ng/ml à J2 = VPN > 90%

**Cardiac surgery/ Cardiopulmonary Bypass**

Initiating Factors
- Contact Activation
- Blood-air interface
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

↓

Immune System Activation
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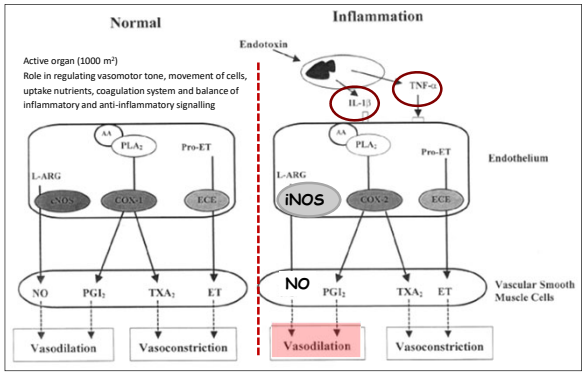
- Oxidative stress

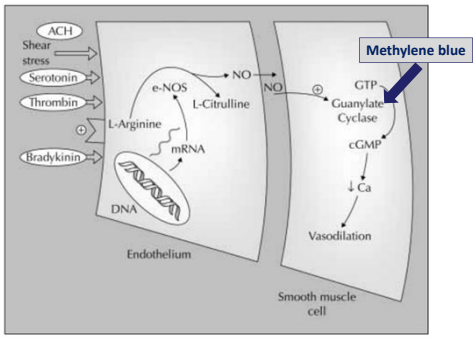
↓

**SIRS**

## Endothélium et syndrome inflammatoire




## Mode d'action du monoxyde d'azote

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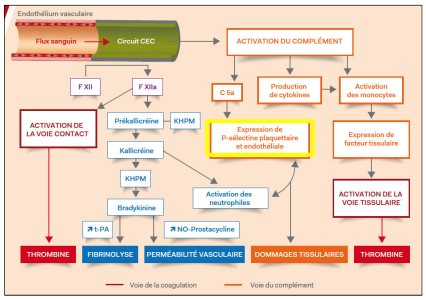
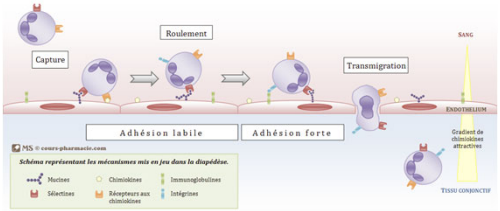
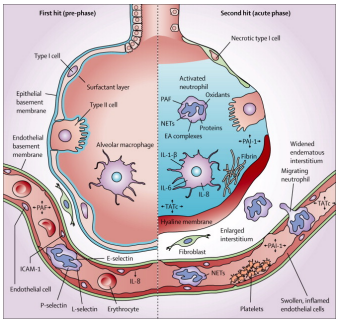


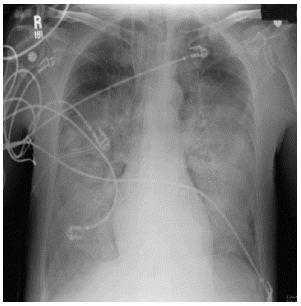

## Réponse immunitaire cellulaire
### *Interaction Leucocytes / endothélium*




- Sur-expression de P-selectine endothéliale
- Séquestration pulmonaire +++




*Alexander P J Vlaar APJ et al. Lancet* 2013; 382: 984–94



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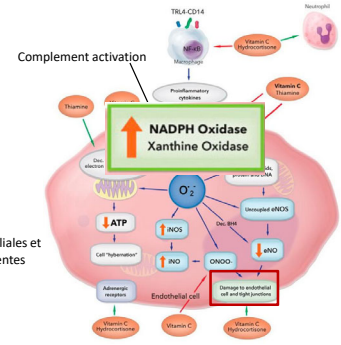
**SIRS**

## Stress oxydatif
### Production de radicaux libre de l'oxygène




$O2^-$ anion superoxyde
$ONOO^-$ peroxyntrite
$OH^-$ radical hydroxyle

Cellules endothéliales et immunocompétentes (monocytes…)

*Wang W et al. Am J Resp Crit Care Med 1994;150:1449-52*

## Oxidative stress during extracorporeal circulation

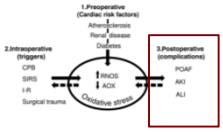
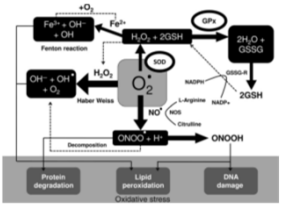
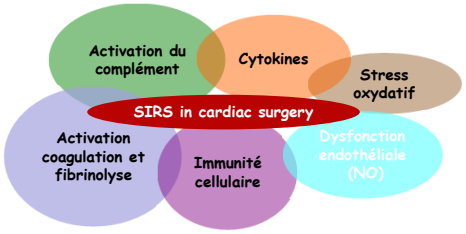



**Table 1:** Potential triggers for increased RNOS generation during ECMO

| Potential triggers for increased RNOS generation during ECMO |
|---|
| Exposure to ECC (ECMO circuits [42], dialysis [5]) |
| SIRS syndrome [43] |
| Acute respiratory distress syndrome [16] |
| Hyperoxia [26] |
| Mechanical ventilation [44] |
| Sepsis [45] |
| Ischaemia-reperfusion [46] |
| Transfusion [27, 28] |
| Sequestration of antioxidant trace elements by the ECMO circuit [19] |




*Mc Donald CI et al. Eur J Cardiothorac Surg 2014;46:937-43*




## Réaction inflammatoire systémique et chirurgie cardiaque

### Constante!

Expression biologique et clinique variables…
(CRP, hyperleucocytose, hyperfibrinogénémie, vasoplégie, SDMV…)

### Réponses individuelles variables

- Contexte de la chirurgie (urgence, hémorragique, CEC longue…)
- Episodes d'hypoperfusion d'organes (conduite optimale+++)
- Prédisposition génétique (???)

## Polymorphisme génétique et CEC
*Balance Pro- & Anti-inflammatoire*

**Polymorphisme du gène pour fraction du complément**

1. **Chirurgie des cardiopathies congénitales**
2. **Syndrome de fuite capillaire post-CEC accentué chez enfants homozygotes C4A00**

*Zhang S, Anesthesiology 2004; 100: 944-9*

## Polymorphisme génétique et CEC
*Balance Pro-& Anti-inflammatoire*

**Polymorphisme du gène du TNFα**

**1.1. Génotypes :**

- **Forme commune : TNF1**
- **Forme plus rare : TNF2 (surproduction+++)**

**1.2. Majoration production TNF**

- **Augmentation de lactatémie**

*Ryan T, Ann Thorac Surg 2002; 73: 1905-9*

- **Fréquence accrue des dysfonctions VG**
- **Fréquence des défaillances pulmonaires postopératoires**

*Tomasdottir H, Anesth Analg 2003; 97: 944-9*

**Polymorphisme des gènes de la famille des interleukines (IL)**

1. **Libération accrue IL10 en post-CEC**

***Galley HF, Br J Anaesth 2003; 91 :424-6***

2. **ACFA après chirurgie cardiaque sous CEC**

***Gaudino M, Circulation 2003; 108 Suppl 1: II 195-9***

Quelle(s) mesure(s) pour limiter le syndrome inflammatoire au cours de la chirurgie cardiaque?

## Facteurs influençant la réponse inflammatoire

- Altération de la fonction ventriculaire gauche
- Patient diabétique
- Instabilité hémodynamique (via hypoperfusion mésentérique)
- Relation entre hypoperfusion splanchnique et SDRA postopératoire
- pH gastrique intra-muqueux prédictif de complication postopératoire
- Effet bénéfique péridurale
- Stratégie ventilatoire perioperatoire

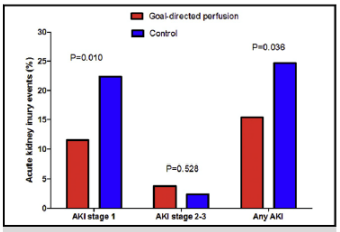
*Loick HM et al. Anesth Analg 1999;88:701-9*

*Fiddian-Green RG et al. Crit Care Med 1987;15:153-6*

**Goal-directed perfusion to reduce acute kidney injury: A randomized trial**

*Ranucci M et al. J Thorac Cardiovasc Surg 2018; 156:1918-27*

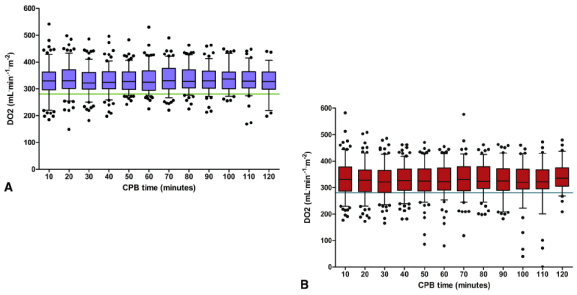
**Goal-directed Perfusion was defined as $DO_2$ > 280 ml.min-1.m-2**




Acute kidney injury in the goal-directed perfusion and control groups.

## Goal-directed perfusion to reduce acute kidney injury: A randomized trial

*Ranucci M et al. J Thorac Cardiovasc Surg 2018; 156:1918-27*




## Goal-directed perfusion to reduce acute kidney injury: A randomized trial

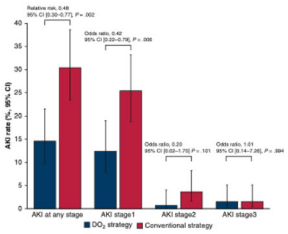
*Mukaida H et al. J Thorac Cardiovasc Surg 2023; 165:750-60*

Multicenter randomized controlled trial (n=275, 2018-2020)

A fixed rate of 2.6 L/min/m2 versus GDP defined as $DO_2$ > 300 $ml.min^{-1}.m^{-2}$

Body temperature 35 C

Primary outcome : postoperative rate of AKI.

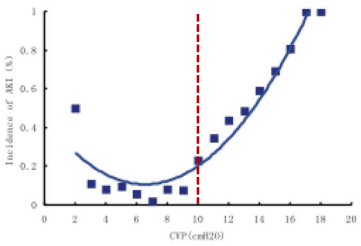



Journal of Critical Care

### High central venous pressure is associated with acute kidney injury and mortality in patients underwent cardiopulmonary bypass surgery

Yanli Yang *, Jun Ma, Liyun Zhao

Center of Anesthesiology, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Rd, Chaoyang District, Beijing 100029, China




*Yang Y et al. J Crit Care 2018; 48:211-5*

Acute Kidney Injury in different CVP groups.

| Variables | Low CVP Group (n %) (CVP < 10 $cmH_2O$) | | High CVP Group (n %) (CVP ≥ 10$cmH_2O$) | | p Value |
|---|---|---|---|---|---|
| n | 1140 | | 801 | | |
| Acute Kidney Injury level | | | | | |
| KDIGO stage 1 | 63 | 5.526 | 275 | 34.332 | <0.0001 |
| KDIGO stage 2 | 11 | 0.964 | 46 | 5.742 | <0.0001 |
| KDIGO stage3 | 12 | 1.052 | 26 | 0.312 | <0.0001 |
| Total AKI | 86 | 7.543 | 347 | 43.32 | <0.0001 |
| CRRT | 5 | 0.438 | 18 | 2.247 | <0.0001 |

AKI = Acute Kidney Injury; CRRT = continuous renal replacement therapy; KDIGO = Kidney Disease Improving Global Outcomes; sCR = serum creatinine.

Factors Associated With Mortality in Multivariate Analysis.

| Variables | Hazard Ratio (95% CI) | Wald Statistic | P Value |
|---|---|---|---|
| Age | 1.016 (1.001–1.035) | 2.724 | 0.009 |
| CVP | 1.196 (1.114–1.285) | 24.209 | <0.0001 |
| CAD | 1.050 (1.275–2.325) | 8.712 | 0.003 |
| CPB | 1.003 (1.001–1.005) | 10.441 | 0.001 |
| Blood plasma | 1.001(1.000–1.003) | 56.441 | <0.0001 |

CI = confidence interval; CVP = central venous pressure; CAD = Coronary artery disease; CPB = cardiopulmonary bypass.

*Yang Y et al. J Crit Care 2018; 48:211-5*

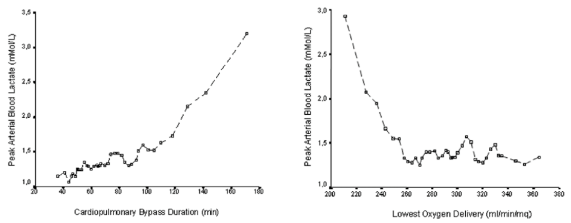
Research

Open Access

### Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome

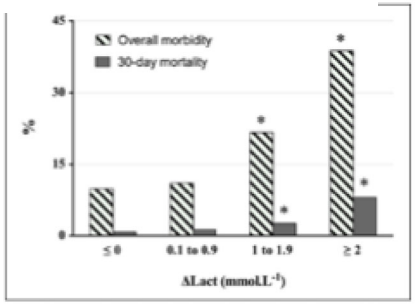
Marco Ranucci, Barbara De Toffol, Giuseppe Isgrò, Federica Romitti, Daniela Conti and Maira Vicentini

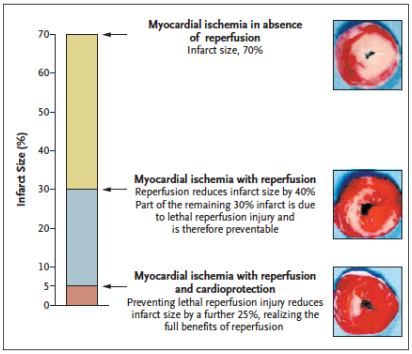
*Critical Care* 2006, **10**:R167 (doi:10.1186/cc5113)



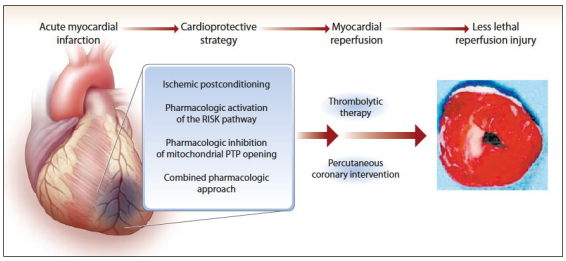

### Intraoperative changes in blood lactate levels are associated with worse short-term outcomes after

**Benoit Duval,[1,2] Thibaud Besnard,[1,2] Stefano Mion,[1,2] Sébastien Louillet,[3] Olivier Jecker,[4] Louis Labrousse,[5] Alain Rémy,[1] Cedrick Zaouter[1] and Alexandre Ouattara[1,2]**






*Yellon DM et al. N Engl J Med 2007;357:1121-35*




*Yellon DM et al. N Engl J Med 2007;357:1121-35*

## Agents médicamenteux et syndrome inflammatoire

- Propofol ↗ IL-10, IL-1ra, ↘ IL-8 (+scavenger des RL)
- Fentanyl ↗ IL-1ra
- Midazolam ↘ accumulation IL-8 extracellulaire
- Kétamine ↗ IL6
- Halogénés ↘ IL-1b, TNF a
- Transfusion homologue ↗
- Xénon (organo-protection)
- Héparine – Protamine : complexe non covalent (C4a, CRP)
- Aprotinine (effet anti-protéase) ↘ cytokines pro-inflammatoires

## Circulation extra-corporelle…

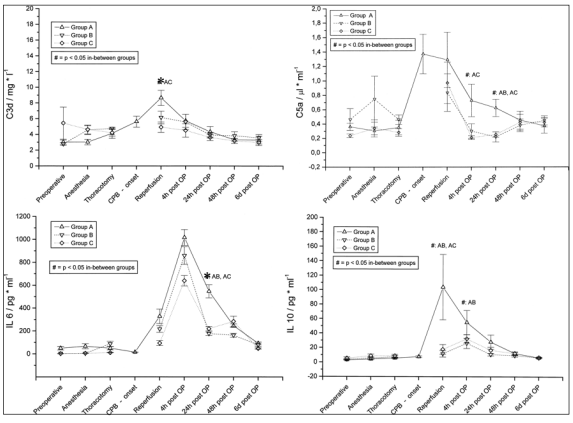
- Sans CEC…(traumatisme chirurgical…)
- Limiter hémodilution
- limiter hypoperfusion d'organes (???)
- Circulation extra-corporelle biocompatible
  - Réservoir souple (interface air/sang)
  - Circuit pré-traités (héparine, phosphorylcholine…)
  - Gestion des aspirations
- Pulsatilité?
- Température de perfusion

**Humoral Immune Response During Coronary Artery Bypass Grafting. A Comparison of Limited Approach, « Off-Pump » Technique, and Conventional CPB**

## Pontage aorto-coronaire

- Groupe A: sternotomie + CEC (n = 10)
- Groupe B: sternotomie sans CEC (n = 10)
- Groupe C: mini-thoracotomie sans CEC (n = 10)

*Anno Diegeler et al, Circulation 2000; 102:III-95*




*Anno Diegeler et al, Circulation 2000; 102: III-95*

**Pulsatile Versus Nonpulsatile Cardiopulonary Bypass Flow: An Evidence-Based Approach**

*Abdullah A. Alghamdi, M.D, and David A. Latter, M.D*
*Division of Cardiac Surgery, Department of Surgery, Universitu of Toronto, Toronto, Ontario, Canada (J Cardio Surg 2006; 21:347-54)*

"*Conclusion:* The evidence is conflicting and therefore does not support making recommendation for or against routinely providing the PP to reduce the incidence of mortality or MI. The evidence is insufficient to recommend for or against routinely providing the pulsatile profusion to reduce the incidence of stroke or renal failure."

**An Evaluation of the Benefits of Pulsatile versus Nonpulsatile Perfusion during Cardiopulmonary Bypass Procedures in Pediatric and Adult Cardiac Patients**

Bingyang Ji and Akif Undar (*ASAIO Journal 2006; 52:357-361*)

**«These results clearly suggest that pulsatile flow is superior to no pulsatile flow during and after open-heart surgery in paediatric and adult patients »**

## QUANTIFICATION OF PULSATILITY : ENERGY EQUIVALENT PRESSURE

- Flow is mainly generated by gradient of energy more than pressure gradient
- Pulsatile flow generates hemodynamic energy into vascular system based on flow and pressure at each cycle
- Equivalent Energy Pressure (EEP) expressed in mmHg
- Total hemodynamic energy (THE) transmitted by pump to periphery is the ratio of total work (pressure X flow) in the vascular bed distal in time to volume of blood which passed in the same time (flow)
- In steady blood flow, EEP = MAP
- The difference in EEP and MAP represents the energy in flow secondary to pulsatile property = Surplus Hemodynamic Energy.

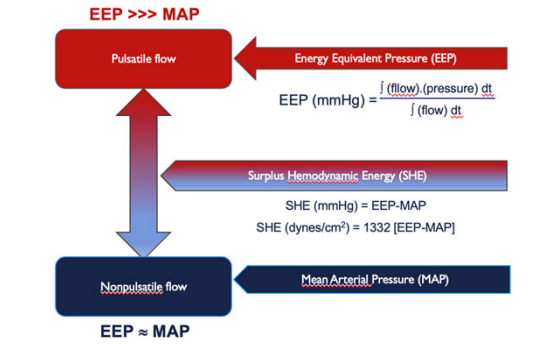
$$EEP\ (mmHg) = \frac{\int (flow).(pressure)\ dt^*}{\int (flow)\ dt^{**}}$$

* Area under hemodynamic power curve

**Area under pump flow curve

SHE (ergs/cm3) = **1332** X(EEP-MAP)

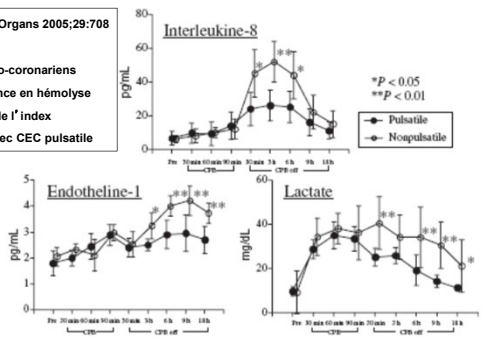
*Shepard RB et al.Arch Surg 1966;93:730-40*
*Wang S et al.JECT 2009;41:P20-P25*



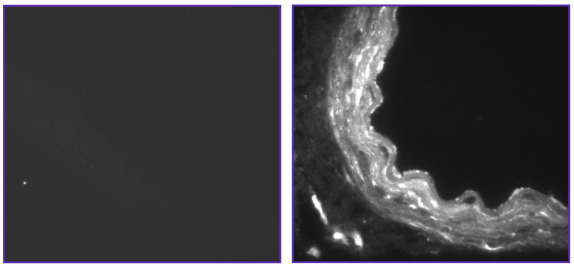

## Aspects microcirculatoires Inflammation et dommage endothélial

**Sezai *et al* Artif Organs 2005;29:708**

- **Pontages aorto-coronariens**
- **Pas de différence en hémolyse**
- **Amélioration de l'index respiratoire avec CEC pulsatile**

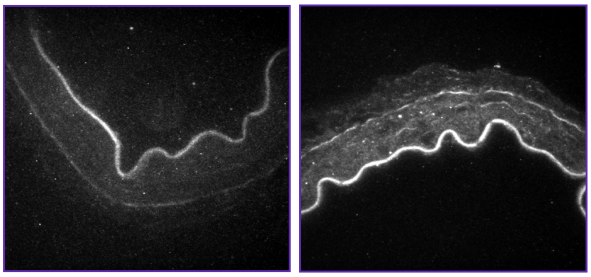



## Molécules d'adhésion (MCP-1)



Pulsé Non Pulsé

## iNOS

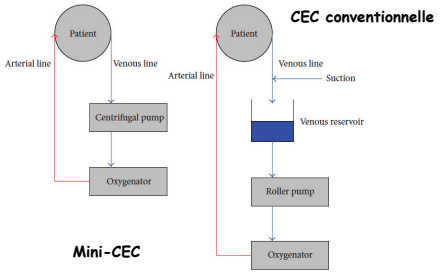


Pulsé Non Pulsé

*Review Article*

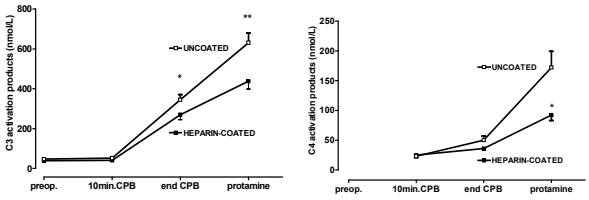
**The Inflammatory Response to Miniaturised Extracorporeal Circulation: A Review of the Literature**

Hunaid A. Vohra, Robert Whistance, Amit Modi, and Sunil K. Ohri




# Heparin-coated circuits
## preliminary results

**Complement activation is reduced by 30 to 50%**




**Alternative pathway**

**Classical pathway**

*Baufreton et al. Ann Thorac Surg 1997;63:50-6.*

## The Cardiotomy Trial

**A Randomized, Double-Blind Study to Assess the Effect of Processing of Shed Blood During Cardiopulmonary Bypass on Transfusion and Neurocognitive Function**

*Rubens FD et al. Circulation 2007;116 [suppl I]:I-89-97*

- Etude prospective randomisée
- Patients bénéficiant d'une chirurgie coronaire isolée non urgente
- CEC à galets (volume d'amorçage 1300 ml) en hypothermie
- Aspirations médiastinales par cell-saver avec retransfusion au travers un filtre à déleucocytation
- Utilisation postopératoire systématique d'un cell-saver jusqu'à H4 (Brat, COBE Cardiovascular Inc)
- Critère de jugement : transfusion de concentrés érythrocytaires et déficit neurocognitive à J5

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

**Table 2:** Cytokines in cardiotomy suction blood and in the systemic circulation at the same time point ($n = 25$)

| | Cardiotomy suction blood | Systemic circulation | *P*-value |
|---|---|---|---|
| IL-1Ra (pg/ml) | 312 (88–1534) | 82 (32–309) | <0.001 |
| IL-4 (pg/ml) | <2 (<2–7.2) | <2 (<2) | 0.43 |
| IL-10 (pg/ml) | 19.7 (<2–113) | 31 (<2–122) | 0.21 |
| IL-6 (pg/ml) | 210 (13–2678) | 45 (3–1119) | <0.001 |
| TNF-α (pg/ml) | 4.3 (<2–40) | 2.5 (<2–62) | 0.033 |
| IL-6-to-IL-10 ratio | 10.2 (1.1–75) | 1.7 (0.2–24) | <0.001 |

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

**Table 3:** Cytokines in cardiotomy suction blood before and after cell-saver processing ($n = 13$)

| | Before cell salvage | After cell salvage | *P*-value |
|---|---|---|---|
| IL-1Ra (pg/ml) | 260 (88–526) | 73 (28–359) | 0.002 |
| IL-4 (pg/ml) | <2 (<2) | <2 (<2–3.0) | 0.18 |
| IL-10 (pg/ml) | 17 (8.4–62) | 7 (<2–27) | 0.011 |
| IL-6 (pg/ml) | 140 (13–2678) | 57 (<1–760) | 0.10 |
| TNF-α (pg/ml) | 4.3 (<2–39) | <2 (<2–15) | 0.008 |

The values represent the median and range.
IL: interleukin; TNF: tumour necrosis factor.

Ann Thorac Surg 2010; 89:1511-7

**Cell Saver for On-pump Coronary Operations Reduces Systemic Inflammatory Markers: A Randomized Trial**

Sune Damgaard, MD, PhD, Claus H. Nielsen, MD, PhD, Lars W. Andersen, MD, DMSc, Klaus Bendtzen, MD, DMSc, Michael Tvede, MD, and Daniel A. Steinbrüchel, MD, DMSc

Departments of Cardiothoracic Surgery, Anesthesiology, Clinical Microbiology and the Institute for Inflammation Research, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

*Table 2. Concentrations of Inflammatory Markers*

| Marker | Group | Induction | Cross-clamp Before | Cross-clamp After | After Cardiopulmonary Bypass 5 Minutes | 6 Hours* | 24 Hours | 72 Hours | Interactive |
|---|---|---|---|---|---|---|---|---|---|
| Median (IQR) pg/mL | | | | | | | | | |
| IL-6 | Cell saver | 0 (0–5) | 0 (0–6) | 13 (4–31) | 38 (13–67) | 112 (66–168) | 89 (45–153) | 38 (17–84) | 0.021 |
| | Control | 0 (0–0) | 3 (0–8) | 17 (7–59) | 51 (29–116) | 228 (142–331) | 90 (44–190) | 44 (29–64) | |
| IL-8 | Cell saver | 6 (5–8) | 6 (4–11) | 15 (7–34) | 17 (10–40) | 23 (17–36) | 17 (11–31) | 11 (7–42) | 0.058 |
| | Control | 7 (3–9) | 8 (6–11) | 23 (15–38) | 28 (24–46) | 42 (25–68) | 18 (13–31) | 18 (10–26) | |
| IL-10 | Cell saver | 0 (0–1) | 0 (0–2) | 6 (0–9) | 9 (4–19) | 2 (0–2) | 0 (0–3) | 0 (0–3) | 0.530 |
| | Control | 0 (0–2) | 1 (0–3) | 7 (4–12) | 10 (8–22) | 3 (2–8) | 3 (1–5) | 2 (1–3) | |
| Median (IQR) ng/mL | | | | | | | | | |
| sTNF-RI | Cell saver | 0.9 (0.8–1.8) | 0.7 (0.5–1.1) | 1.8 (1.5–2.4) | 2.1 (1.5–2.8) | 1.9 (1.1–2.7) | 1.7 (1.2–2.7) | 1.8 (1.5–4.4) | 0.158 |
| | Control | 1.0 (0.8–1.6) | 0.9 (0.5–1.2) | 1.9 (1.7–2.5) | 2.4 (1.8–2.9) | 2.6 (1.2–3.8) | 2.0 (1.1–2.9) | 2.4 (1.8–4.1) | |
| sTNF-RII | Cell saver | 2.5 (1.5–2.9) | 1.6 (1.0–2.0) | 3.0 (1.6–3.4) | 3.0 (2.1–3.8) | 3.4 (2.6–4.7) | 2.8 (1.6–3.9) | 3.1 (2.7–5.8) | 0.40 |
| | Control | 2.4 (1.6–2.9) | 1.5 (1.1–1.9) | 2.8 (2.3–3.4) | 3.5 (2.7–3.9) | 4.4 (2.8–4.9) | 3.3 (2.0–4.6) | 3.6 (2.7–5.0) | |
| PCT | Cell saver | 0.1 (0.1–0.2) | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.1 (0.1–0.2) | 0.2 (0.2–0.6) | 0.4 (0.3–1.1) | 0.4 (0.2–2.3) | 0.472 |
| | Control | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.1 (0.1–0.2) | 0.5 (0.3–1.0) | 0.7 (0.3–1.4) | 0.4 (0.3–0.8) | |

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

## IL-6/IL-10

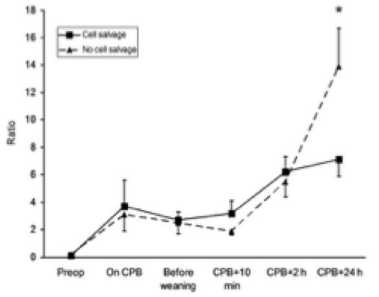



Figure 1: The mean IL-6-to-IL-10 ratio in patients where cardiotomy suction blood was either cell salvaged or not before retransfusion. *P < 0.05. The vertical lines represent the standard deviations.

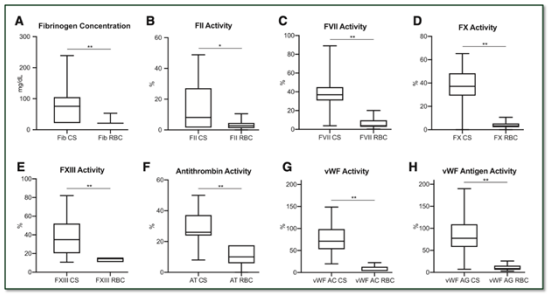
Munoz M et al. Blood Transfus 2011;9:248-61

## PERFORMANCES COMPARÉE DES SYSTÈMES

| Parameter | Sequestra* (Medtronic) | BRAT 2* (Cobe) | CATS* (Fresenius) | Cell Saver* (Haemonetics) | AUTOLOG* (Medtronic) | OrthoPAT* (Haemonetics) | Colloid ** sedimentation |
|---|---|---|---|---|---|---|---|
| RBC recovery, % | 65 - 76 | 71 - 93 | 51 - 87 | 64 - 94 | 79 | 80 | 90 |
| WBC removal; % | 31 - 78 | 30 | 45 - 80 | 22 - 55 | 78 | 72 | 60 |
| PLT removal; % | 87 - 93 | 68 | 92 - 96 | 86 - 87 | 99 | 88 | 48 |
| PFHB removal; % | 89 | 63 | 65 - 95 | 85 - 93 | 92 | 96 | 53 |
| TP or ALB removal; % | 97 - 98 | 91 - 93 | 93 - 99 | NA | NA | 97 | 76 |
| $K^+$ removal; % | 92 | 90 | 90 - 98 | 91 | 89 | 97 | NA |
| Cytokine removal; % | 95 | 95 | 95 | 91 - 95 | NA | 90 | 70 - 77 |

Values are minimum – maximum interval. CATS: continuous autotra nsfusion system; RBC: red blood cells; WBC: leucocytes; PLT: platelets; PFHB: plasma free haemoglobin; TP: total protein; ALB: albumin. NA: not assessed. References: * (68-77), ** (51).

Adam EH et al. Anesth Analg 2020; 130:1389-95

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journal homepage: www.elsevier.com/locate/bean

### Perioperative ventilatory strategies in cardiac surgery

François Lellouche, M.D., Ph.D., Professeur Agrégé [a, *],
Mathieu Delorme, PT, MSc [a, b],
Jean Bussières, MD, FRCPC, DABA, PTEBC, Professeur Agrégé [a],
Alexandre Ouattara, M.D., Ph.D., Professeur Agrégé [b]

## IMMUNE DYSFUNCTION AFTER CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS: BENEFICIAL EFFECTS OF MAINTAINING MECHANICAL VENTILATION

*Gaudriot B et al. Shock 2015; 44:228-33*

Patients de plus de 18 ans
Chirurgie coronaire et/ou valvulaire
Anesthésie (Propofol/sufentanil/atracurium)
Ventilation mécanique pré et post-CEC
(VAC 8 ml.kg$^{-1}$ PIT, FR 10-15 rpm, PEEP 5 cm$H_2O$, $FiO_2$ 50%)
Ventilation perCEC:
✓Pas de ventilation. Déconnexion du respirateur
✓VAC 2,5 ml.kg$^{-1}$ PIT PEEP 5 cm$H_2O$ FR 8-10 rpm

Critères de jugement
✓PaO2/FiO2 avant et 3 heures après CEC
✓Expression HLA-DR et monocytes CD14+ HLA-DRlo/j
✓TNF alpha et IL-10

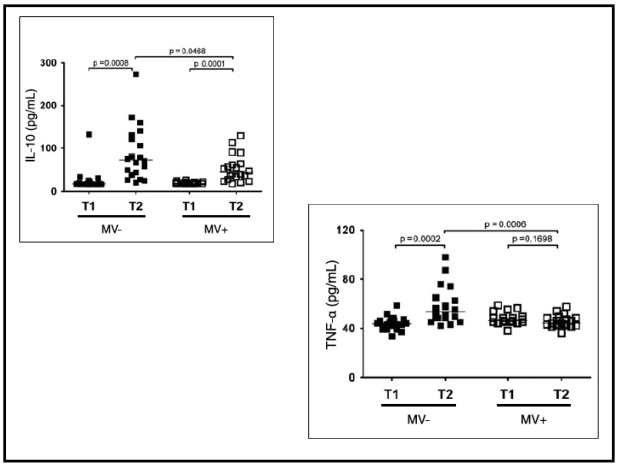
} **Avant et dans l'heure qui suit l'intervention**

Table 1. **Baseline characteristics of patients before CBP**

| | MV⁻ (n = 25) | MV⁺ (n = 25) | P |
|---|---|---|---|
| Age, y | 75 (65–79) | 73 (69–80) | 0.79 |
| Surgery | | | |
| Valvular replacement | 17 | 8 | |
| CABG | 5 | 9 | |
| Mixed (valvular and CABG) | 3 | 8 | |
| BMI, kg/m$^2$ | 26 (23–28) | 30 (27–33) | 0.007 |
| Euroscore II | 2.2 (1.4–2.9) | 2.3 (1.4–3.3) | 0.6 |
| CVP before CPB, mmHg | 7 (6–10) | 10 (7–12) | 0.15 |
| mPAP before CPB, mmHg | 23 (20–24) | 19 (11–25) | 0.28 |
| $Pa_{O_2}/Fi_{O_2}$ ratio before CPB | 326 (225–381) | 240 (173–320) | 0.07 |

Table 2. **Effects of MV on outcome and clinical parameters**

| | MV⁻ (n = 25) | MV⁺ (n = 25) | P |
|---|---|---|---|
| CVP after CPB, mmHg | 8 (6–11) | 11 (8–12) | 0.16 |
| mPAP after CPB, mmHg | 19 (18–27) | 21 (16–24) | 0.74 |
| $Pa_{O_2}/Fi_{O_2}$ ratio after CPB | 276 (199–360) | 242 (211–310) | 0.34 |
| CPB duration, min | 61 (52–76) | 54 (48–68) | 0.32 |
| Surgery duration, min | 170 (148–210) | 150 (139–182) | 0.3 |
| ICU stay, d | 3 (3–6) | 3 (3–5) | 0.59 |
| Hospital stay, d | 10 (4–16) | 10 (4–13) | 0.52 |
| Postoperative infections | 5 (20%) | 2 (8%) | 0.5 |




Reactive oxygen species modulate coronary wall shear stress and endothelial function during hyperglycemia

Stress oxydatif

Eric B. Gross,[1,2,3] John F. LaDisa, Jr.,[1,3] Dorothee Weihrauch,[1] Lars E. Olson,[1] Tobias T. Kress,[1] Douglas A. Hettrick,[1,3] Paul S. Pagel,[1,3] David C. Warltier,[1,2,3,4] and Judy R. Kersten[1,3]

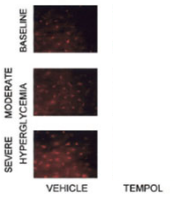
Am J Physiol Heart Circ Physiol 284: H1552–H1559, 2003.

**Modèle *in vivo* canin**

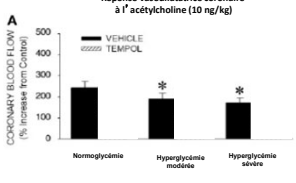
**Effets hyperglycémie 350 et 600 mg/dL (Glucose IV) sur production de RL et fonction endothéliale**

**Antagonisation par le tempol = analogue de la SOD (scavenger des radicaux libres)**

Détection par fluorescence des RL dans les biopsies myocardiques




Réponse vasodilatatrice coronaire à l'acétylcholine (10 ng/kg)




86

Anaesth Crit Care Pain Med 36 (2017) 97–102

SFAR
Société Française d'Anesthésie et de Réanimation

Special article

A special article following the relicence of aprotinin injection in Europe

David Royston[a,*], Stefan De Hert[b], Jan van der Linden[c], Alexandre Ouattara[d,e], Kai Zacharowski[f]

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[b] Department of anesthesiology, Ghent University, Ghent university hospital, De Pintelaan 185, 9000 Ghent, Belgium
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[d] Department of anaesthesia and critical care B, CHU de Bordeaux, 33600 Pessac, France
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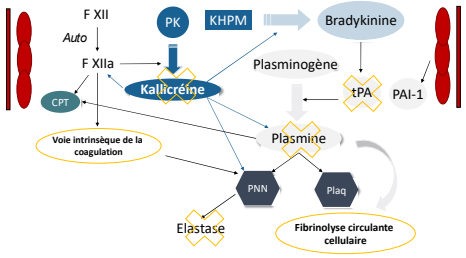
[f] Klinik für Anästhesiologie, Intensivmedizin und Schmerztherapie, Universitätsklinikum Frankfurt, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany

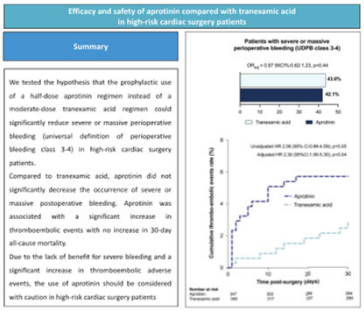
**Mode d'action de l'aprotinine**
(inhibiteur des sérine protéases)




**Use of Aprotinin versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE) trial: a multicentre retrospective comparative non-randomized historical study**

Eloise Gallo[a], Philippe Gaudard[b], Sophie Provenchère[c], Fouzia Souab[d], Anaïs Schwab[e], Damien Bedague[f], Hugues de La Barre[g], Christian de Tymowski[c], Laysa Saadi[h], Bertrand Rozec[d], Bernard Cholley[g], Bruno Scherrer[h], Jean-Luc Fellahi[a] and Alexandre Ouattara[b,*], for APACHE investigators

European Journal of Cardio-Thoracic Surgery 2024, 65(2), ezae001




# Intraoperative High-Dose Dexamethasone for Cardiac Surgery

## A Randomized Controlled Trial

JAMA. 2012;308(17):1761-1767

Jan M. Dieleman, MD
Arno P. Nierich, MD
Peter M. Rosseel, MD
Joost M. van der Maaten, MD
Jan Hofland, MD
Jan C. Diephuis, MD
Ronald M. Schepp, MD
Christa Boer, PhD
Karel G. Moons, PhD
Lex A. van Herwerden, MD
Jan G. Tijssen, MD
Sandra C. Numan, MSc
Cor J. Kalkman, MD
Diederik van Dijk, MD
for the Dexamethasone for Cardiac Surgery (DECS) Study Group

Etude randomisée multicentrique (n=4494)

DXM (1 mg/Kg à l'induction) versus placebo

Critère de jugement composite

**Table 2.** Primary Study End Point and Components of the Primary Study End Point in the Dexamethasone and Placebo Groups

| | No. (%) of Patients | | |
|---|---|---|---|
| | Dexamethasone (n = 2235) | Placebo (n = 2247) | Relative Risk (95% CI) |
| Primary study end point[a] | 157 (7.0) | 191 (8.5) | 0.83 (0.67-1.01) |
| Components of the primary study end point | | | |
| Death | 31 (1.4) | 34 (1.5) | 0.92 (0.57-1.49) |
| Myocardial infarction | 35 (1.6) | 39 (1.7) | 0.90 (0.57-1.42) |
| Stroke | 29 (1.3) | 32 (1.4) | 0.91 (0.55-1.50) |
| Renal failure | 28 (1.3) | 40 (1.8) | 0.70 (0.44-1.14) |
| Respiratory failure | 67 (3.0) | 97 (4.3) | 0.69 (0.51-0.94) |

[a] Primary study end point was a composite of death, myocardial infarction, stroke, renal failure, or respiratory failure, within 30 days after surgery.

**Table 3.** Secondary End Points in the Dexamethasone and Placebo Groups

| Secondary End Points | Dexamethasone (n = 2235) | Placebo (n = 2247) | Relative Risk (95% CI) | *P* Value[a] |
|---|---|---|---|---|
| | Median (IQR) | | | |
| Duration of postoperative mechanical ventilation, h | 7.0 (4.7-10.0) | 7.0 (5.0-11.0) | NA | <.001 |
| Length of stay in the ICU, h | 22.0 (19.0-24.0) | 22.0 (19.0-25.0) | NA | <.001 |
| Length of hospital stay, d | 8 (7-13) | 9 (7-13) | NA | .009 |
| | Mean (SD) | | | |
| Highest serum glucose concentration in the ICU, mg/dL | 195 (50) | 177 (59) | NA | <.001 |

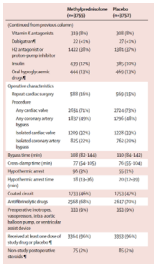
## Methylprednisolone in patients undergoing cardiopulmonary bypass (SIRS): a randomised, double-blind, placebo-controlled trial

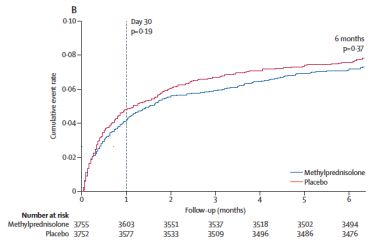
*Lancet* 2015; 386: 1243-53

Richard P Whitlock, P J Devereaux, Kevin H Teoh, Andre Lamy, Jessica Vincent, Janice Pogue, Domenico Paparella, Daniel I Sessler, Ganesan Karthikeyan, Juan Carlos Villar, Yuruoia Zuo, Álvaro Avezum, Mackenzie Quantz, Georgios I Tagarakis, Pallav J Shah, Seyed Hesameddin Abbasi, Hong Zheng, Shirley Pettit, Susan Chrolavicius, Salim Yusuf, for the SIRS Investigators*

Etude multicentrique (80 hôpitaux au sein de 18 pays) incluant patients avec EuroSCORE ≥ 6

Traitement prophylactique 250 mg prednisolone à l'induction et au départ de la CEC






## Prophylactic corticosteroids for cardiopulmonary bypass in adults (Review)

*Dieleman JM et al. Cochrane Database Syst Rev 2011:CD005566*

| Comparison outcome | Number of studies | Participants | Peto OR (Fixed) [95 % CI] | Heterogeneity ($I^2$-%) | Mantel-Haenszel OR (random) [95% CI] |
|---|---|---|---|---|---|
| **Primary endpoints** | | | | | |
| Mortality | 49 | 3213 | 1.06 [0.58, 1.95] | 1 | 1.00 [0.55, 1.82] |
| Myocardial complications | 26 | 2103 | 0.95 [0.57, 1.60] | 4 | 0.95 [ 0.55, 1.64] |
| Pulmonary complications | 21 | 1340 | 0.83 [0.49, 1.40] | 5 | 0.90 [0.51, 1.58] |
| Atrial fibrillation | 17 | 1399 | 0.60 [0.46, 0.78] | 11 | 0.61 [0.45, 0.82] |
| Infections | 16 | 1517 | 0.86 [0.56, 1.31] | 0 | 0.88[0.57, 1.36] |
| Time to extubation (min) | 23 | 1351 | -1.81 [-11.46, 7.83] | 93 | -46.87 [-100.25, 6.25] |
| ICU stay (hours) | 25 | 1215 | -2.32 [-2.84, -1.81] | 87 | -5.47 [-8.13, -2.82] |
| Hospital stay (days) | 15 | 635 | -0.59 [-0.84, -0.34] | 96 | -0.97 [-2.42, 0.47] |

## Cardiovascular Surgery

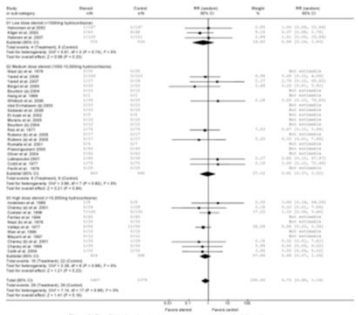
### Benefits and Risks of Corticosteroid Prophylaxis in Adult Cardiac Surgery

### A Dose-Response Meta-Analysis

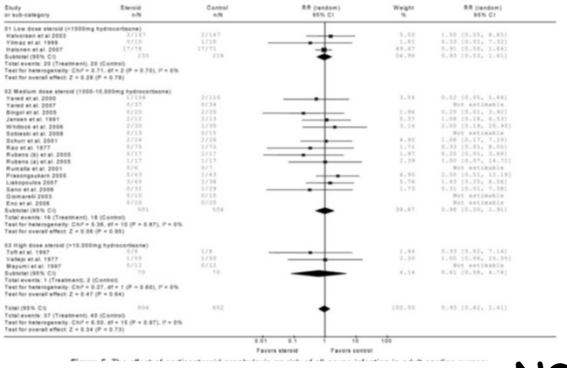
Kwok M. [illegible], PhD, [illegible] FRCP, FHCM; Jen Aik Tan, MBBS

Circulation 2009;119:1853-66

**Mortality**

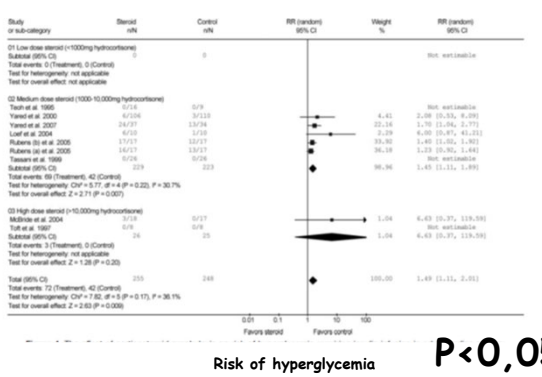


**NS**



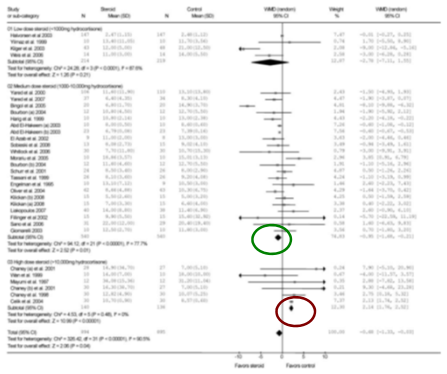
**Risk of infection**

**NS**



**Risk of hyperglycemia**

**P<0,05**



**Risk of atrial fibrillation**

Stress doses of hydrocortisone in high-risk patients undergoing cardiac surgery: Effects on interleukin-6 to interleukin-10 ratio and early outcome*

*Weiss F et al. Crit Care Med 2009; 37:1685-90*

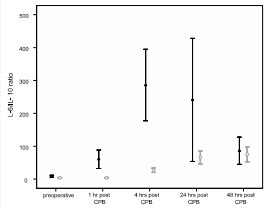
High risk cardiac surgical patients (EF> 40%, combined procedure, CABGX3 or +)

Stress doses of hydrocortisone (IV): Bolus 100 mg before induction and 10 mg.h$^{-1}$ $POD_1$, 5 mg.h$^{-1}$ $POD_2$, 30 mg X 3/j IV $POD_3$, 10 mg X 3/j $POD_4$

Outcomes: cytokines and early clinical outcomes

Table 1. Comparison of demographic data between the study groups

| | Placebo (n = 17) | Hydrocortisone (n = 19) | p |
|---|---|---|---|
| Age (yrs) | 69 (63/72) | 67 (61/78) | n.s. |
| Sex (f/m) | 7/10 | 8/11 | n.s. |
| EF (%) | 31 (21/49) | 29 (26/38) | n.s. |
| BSA (m$^2$) | 1.76 (1.68/1.92) | 1.9 (1.75/2.0) | n.s. |
| ACE inhibitors (n) | 13 | 15 | n.s. |
| COPD (n) | 5 | 7 | n.s. |
| Preop. bilirubine (mg/L) | 0.7 (0.5/1.0) | 0.7 (0.6/0.9) | n.s. |
| Preop. creatinine (mg/dL) | 1.1 (1/1.4) | 1.0 (0.9/1.2) | n.s. |
| Higgins Score (points) | 6 (4/7.5) | 6 (4/8) | n.s. |
| Parsonnet Score (points) | 14 (10/20) | 15 (12/21) | n.s. |
| CPB (min) | 107 (62/135) | 98 (71/154) | n.s. |
| Clamping (min) | 77 (41/112) | 58 (45/79) | n.s. |



| | Placebo (n = 17) | Hydrocortisone (n = 19) | p |
|---|---|---|---|
| $PaO_2/FiO_2$ 4 hrs post-CPB | 373 (287/349) | 443 (326/468) | 0.06 |
| $PaO_2/FiO_2$ on POD 1 | 285 (232/349) | 350 (408) | 0.09 |
| $PaO_2/FiO_2$ on POD 2 | 243 (199/309) | 330 (263/343) | 0.06 |
| Mechanical ventilation (hrs) | 14 (7/17.5) | 11 (8/14) | n.s |
| Noninvasive ventilation (n) | 7 | 3 | n.s. |
| Max. dose of norepinephrine (mg/h) | 0.6 (0.3/1.6) | 0.5 (0.3/1.6) | n.s. |
| Duration of catecholamine support (d) | 4 (2/4.5) | 1 (1/2) | <0.01 |
| Intraoperative urine output (mL) | 1500 (1150/2100) | 1500 (1100/1900) | n.s. |
| Fluid balance POD 1 (mL) | 810 (357/1015) | 668 (44/1520) | n.s. |
| Fluid balance POD 2 (mL) | 332 (−162/482) | 565 (−91/1267) | n.s. |
| SOFA-score POD 1 (points) | 3 (3/10) | 4 (2/9) | n.s. |
| SOFA score POD 2 (points) | 6 (3/9) | 4 (2/7.5) | n.s. |
| Perioperative blood transfusion (n) | 3 (1/5) | 1 (0/3) | n.s. |
| Max. level of bilirubine (mg/dL) | 0.8 (0.5/1.2) | 0.7 (0.5/1.0) | n.s. |
| Max. level of lactic acid (mg/dL) | 2.6 (2.0/4.5) | 2.3 (2.0/3.4) | n.s. |
| Minimal level of cholesterine (mg/dL) | 73 (29/84) | 69 (57/88) | n.s. |
| Delirium (%/n) | 35/6 | 16/3 | n.s. |
| SAPS II (points) | 36 (31/45) | 34 (30/38) | n.s. |
| IABP support (n) | 0 | 1 | n.s. |
| Mortality within 28 days (%) | 0 | 0 | n.s. |
| Hemofiltration (n) | 3 | 1 | n.s. |
| Postoperative atrial fibrillation (n) | 10 | 5 | 0.04 |
| Length of stay in the ICU (d) | 6 (4/8) | 2 (2/3) | <0.01 |
| Length of stay in hospital (d) | 11 (8.5/14.5) | 13 (11/14) | n.s. |

Potential side effects of hydrocortisone (sepsis, sternal wound infection ...) were not significantly different between groups

Research

**Open Access**

**Statin prophylaxis and inflammatory mediators following cardiopulmonary bypass: a systematic review**

Catherine Morgan[1], Michael Zappitelli[2] and Peter Gill[3]

Critical Care 2009;13:R165

# Inflammation, CEC et statines

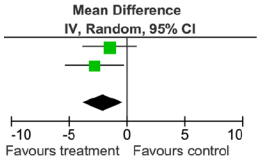
- Méta-analyse
- 8 randomized controlled trials
- CPB open heart surgery adults and children
- Prophylactic statins treatment of inflammation
- Marqueurs de l'inflammation : TNFα, CRP, IL6

**Benefit with the use of statin to reduce the post-operative level of TNF-α (WMD -2.10 pg/ml, 95% CI -3.8 to -0.4)**

| | Statin | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Chello 2006 | 10.4 | 3.8 | 20 | 11.9 | 3.8 | 20 | 54.0% | -1.50 [-3.86, 0.86] |
| Chello 2007 | 8.8 | 3.2 | 15 | 11.6 | 3.9 | 15 | 46.0% | -2.80 [-5.35, -0.25] |
| Total (95% CI) | | | 35 | | | 35 | 100.0% | -2.10 [-3.83, -0.37] |

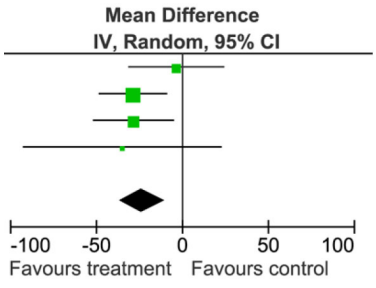
Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 1 (P = 0.46); I² = 0%

Test for overall effect: Z = 2.38 (P = 0.02)



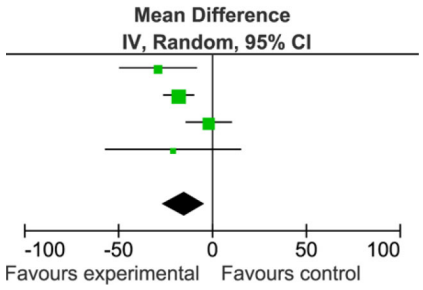

*Morgan C. et al. Critical Care 2009, 13: R165*

**Benefit with the use of statin to reduce the post-operative peak level of IL-6 (WMD -23.5 pg/ml, 95% CI -36.6 to -10.5) measured at four to six hours post-CPB.**




*Morgan C. et al. Critical Care 2009, 13: R165*

**Benefit with the use of statin to reduce the post-operative peak level of hsCRP (WMD -15.3 mg/L, 95% CI -26.9 to -3.7).**




*Morgan C. et al. Critical Care 2009, 13: R165*

**Randomized Trial of Atorvastatin for Reduction of Postoperative Atrial Fibrillation in Patients Undergoing Cardiac Surgery**

**Results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) Study**

Giuseppe Patti, MD; Massimo Chello, MD; Dario Candura, MD; Vincenzo Pasceri, MD; Andrea D'Ambrosio, MD; Elvio Covino, MD; Germano Di Sciascio, MD

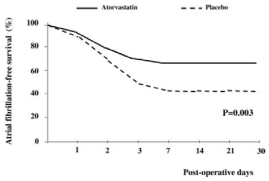
*Circulation*. 2006;114:1455-1461

**Etude prospective, randomisée , double aveugle et placebo control**
**Chirurgie cardiaque sous CEC (n=200)**
**Impact Atorvastatine sur ACFA postop (40 mg/j 7j avt intervention)**

**Incidence ACFA postopératoire**
**35% vs 57% (P=0,003)**

**Durée de l'ACFA**
**24 ±4h vs 24±5 h (NS)**

**Délai de survenue**
**51±15h vs 50 ±17 h (NS)**




## Agents vasopresseurs de recours

Rescue Agents and Relevant Dosing Derived From the Current Literature

| Drug | Dose |
|---|---|
| Vasopressin | 0.02-0.1 U/min |
| Terlipressin* | 1-2 µg/kg/h |
| Methylene blue* | 2-3 mg/kg over 10 minutes, followed by 0.5 mg/kg/h for 6 h |
| Hydroxocobalamin* | 5 g infused over 15 min; may repeat once |
| Angiotensin II (Giapreza) | 10-40 ng/kg/min |
| Vitamin C* | 1.5 g intravenously every 6 h |
| Flurbiprofen (Ropion)* | 50-100 mg |
| Hydrocortisone | 50-100 mg once, then 50 mg every 6 h |

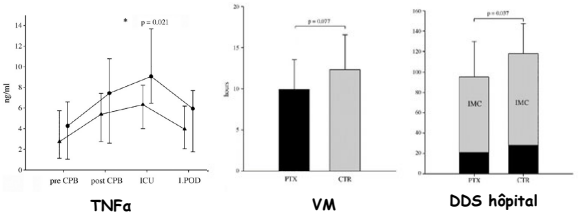
* Off-label use.

*Ortoleva J et al. J Cardiothoracic Vasc Anesth 2020;34:2766-75*

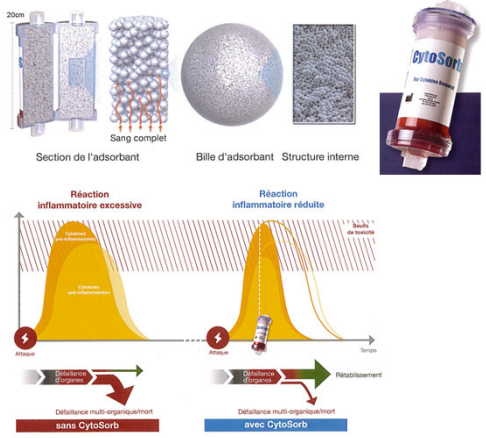
ELSEVIER
European Journal of Cardio-thoracic Surgery 32 (2007) 83–89
EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY
www.elsevier.com/locate/ejcts

A single prophylactic dose of pentoxifylline reduces high dependency unit time in cardiac surgery – a prospective randomized and controlled study*

Etude prospective, randomisée, placebo control
PTX (n=20) 5 mg.kg$^{-1}$ après induction anesthésique versus CTRL (n=20) groupe placebo
Anesthésie générale (etomidate/propofol/sufentanil/pancuronium)
CEC conventionelle non pulsée en hypothermie




**TNFα** **VM** **DDS hôpital**




Hemadsorption during cardiopulmonary bypass reduces interleukin 8 and tumor necrosis factor α serum levels in cardiac surgery: a randomized controlled trial

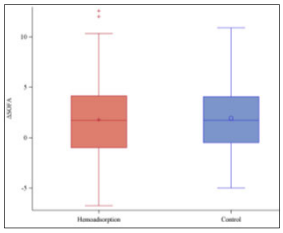
Garau I et al. Minerva Anestesiologica 2019;85:715-23

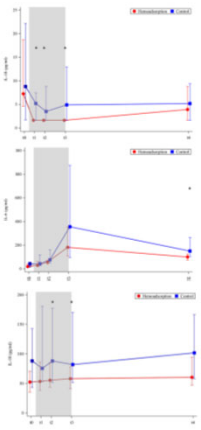
*Clinical Study*

**Extracorporeal Hemadsorption *versus* Glucocorticoids during Cardiopulmonary Bypass: A Prospective, Randomized, Controlled Trial**

Stupica GT et al. Cardioavsc Therapeutics 2020

## Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial

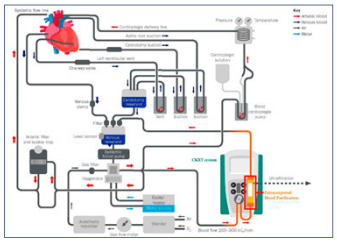


Diab M et al. Circulation 2022; 145:959-68

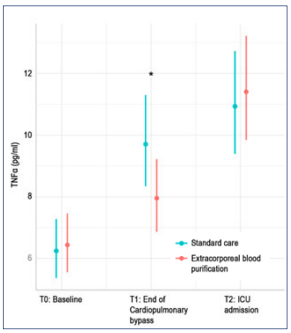
## Extracorporeal Blood Purification and Acute Kidney Injury in Cardiac Surgery
### The SIRAKIO2 Randomized Clinical Trial

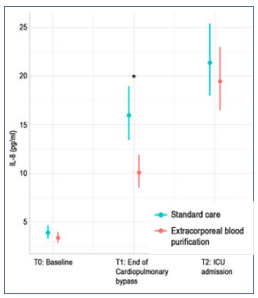
Multicentric institutionally and commercially sponsored
RCT 343 cardiac surgical patients with expected
CPB time >90 min
Oxiris 450 ml/min



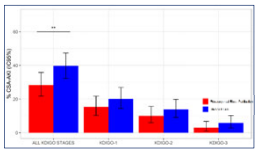
| | Extracorporeal blood purification (n = 169) | Standard care (n = 174) |
|---|---|---|
| Age, mean (SD), y | 68.8 (9) | 68.8 (10) |
| Sex, No. (%) | | |
| Female | 56 (33) | 63 (36) |
| Male | 113 (67) | 111 (64) |
| Weight, mean (SD), kg | 75.1 (15) | 75.3 (13) |
| Body mass index, mean (SD) | 27.5 (4) | 27.5 (4) |
| Medical history, No. (%)* | | |
| High blood pressure | 118 (70) | 132 (76) |
| Dyslipidemia | 86 (51) | 80 (46) |
| Diabetes | 56 (33) | 48 (28) |
| Chronic heart failure | 51 (30) | 50 (29) |
| Chronic atrial fibrillation | 44 (26) | 43 (25) |
| Chronic obstructive pulmonary disease | 27 (16) | 42 (24) |
| Chronic kidney disease stage 1-3† | 34 (20) | 29 (17) |
| Currently smokes | 24 (14) | 37 (21) |
| Alcohol misuse | 5 (3) | 6 (3) |
| Chronic liver failure | 2 (1) | 4 (2) |

*JAMA. 2024;332(17):1446-1454*




## Extracorporeal Blood Purification and Acute Kidney Injury in Cardiac Surgery
### The SIRAKIO2 Randomized Clinical Trial



| Outcome | Mean (SD) Extracorporeal blood purification (n = 169) | Mean (SD) Standard care (n = 174) | Unadjusted Difference (95% CI)[a,b] | Unadjusted P value* | Adjusted Difference (95% CI)[a,b] | Adjusted P value* |
|---|---|---|---|---|---|---|
| Primary outcome | | | | | | |
| Occurrence of CSA-AKI by day 7, No./total No. of patients (%) | 48/169 (28.4) | 69/174 (39.7) | 11.25 (1.30 to 21.21) | .03 | 10.42 (2.34 to 18.49) | .01 |
| Elements of primary outcome | | | | | | |
| Peak serum creatinine, mg/dL‡ | 1.26 (0.61) | 1.39 (0.89) | 0.13 (−0.03 to 0.30) | .11 | | |
| Oliguria <6 h* | 22 (13) | 35 (20) | 7.14 (−0.83 to 15.10) | .08 | | |
| CSA-AKI | | | | | | |
| I | 26 (15) | 35 (20) | 4.73 (−3.34 to 12.80) | | | |
| II | 17 (10) | 24 (14) | 3.73 (−3.11 to 10.58) | | | |
| III | 5 (3) | 1 (6) | 2.79 (−1.31 to 7.09) | | | |
| 3/RR | 22 (13) | 34 (20) | 6.52 (−1.25 to 14.30) | .08 | | |
| Post hoc exploratory analysis related to primary outcome | | | | | | |
| Kidney replacement therapy, No./total No. of patients (%) | 3/169 (1.8) | 6/174 (3.5) | 1.67 (−1.69 to 5.04) | .50 | | |
| Early CSA-AKI (first 48 h) | 39 (23) | 57 (33) | 9.88 (0.25 to 19.51) | .05 | | |

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### Inflammatory response and extracorporeal circulation

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## Conclusion

- Réaction inflammatoire constante
- Effets bénéfiques probables
- Effets délétères évidents
- Syndrome de défaillance multiviscérale
- Prédisposition génétique
- Facteurs déclenchant modulables (chirurgie, anesthésie, type de CEC…)
- Appréhender par une prise en charge multimodale périopératoire optimale
- Place des corticoïdes très discutable…


Questions ou commentaires…..?