

Avec le soutien de Fondation A. de Rothschild De l'oeil au cerveau

université PARIS DIDEROT PARIS 7

Hôpital Robert Debré

PROTECT
Promoting Research Oriented Toward Early CNS Therapies

L'ancien prématuré : nouveautés dans la prise en charge pour chirurgie mineure

Pr Souhayl DAHMANI

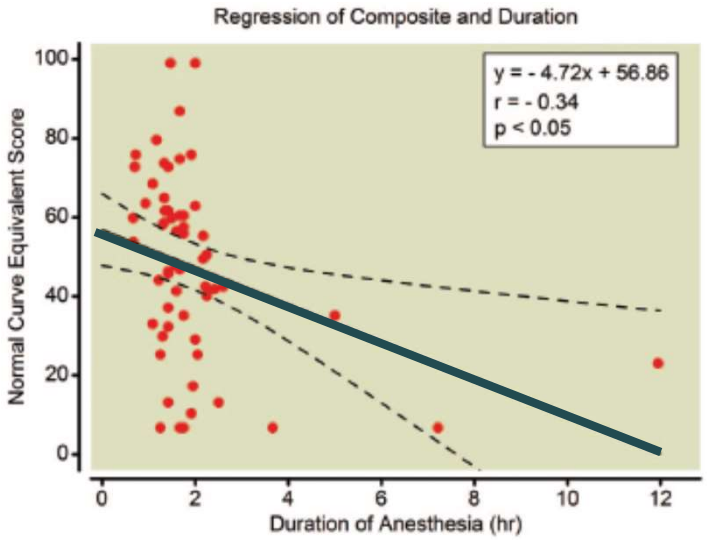
DAR Robert Debré & DHU PROTECT. Paris

Il y a des nouveautés…

- Nouvelles données
- Anciennes données qu'on redécouvre
- … ce qui deviendra peut-être une nouveauté

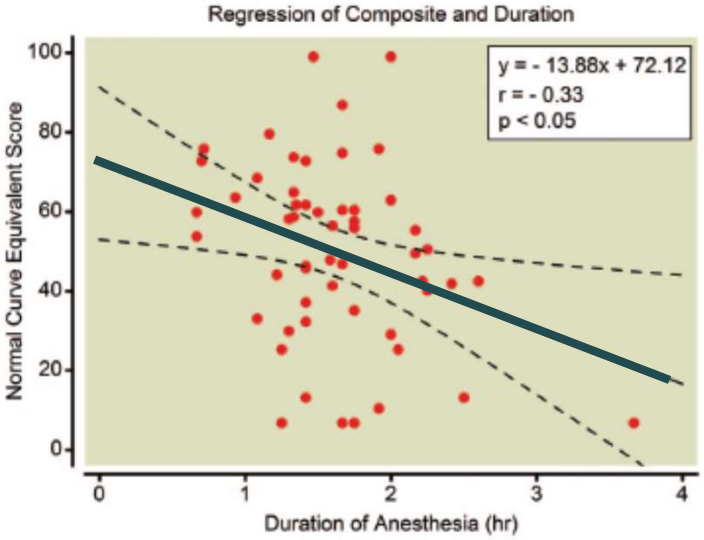
Anesthésiques et neurotoxicité

- **Expérimentalement : mort neuronale consécutive à l'administration d'agents anesthésiques.**
- **Mort cellulaire associée à l'altération durable des fonctions cognitives à l'âge adulte.**
- **Toutefois:**
  - Administration prolongée : 3 heures pour les halogénés.
  - **Concentrations Thérapeutiques.**



Patients sans atteinte SNC

(N=58)



Patients sans atteinte SNC
Une seule intervention
(N=54)

623 Patients:
opérés avant l'âge de 3 ans
Sous AG
Chirurgies simples

336 éliminés
Refus de participer
Data non retrouvées

287 patients avec test
Score < 5émé P: 12 %

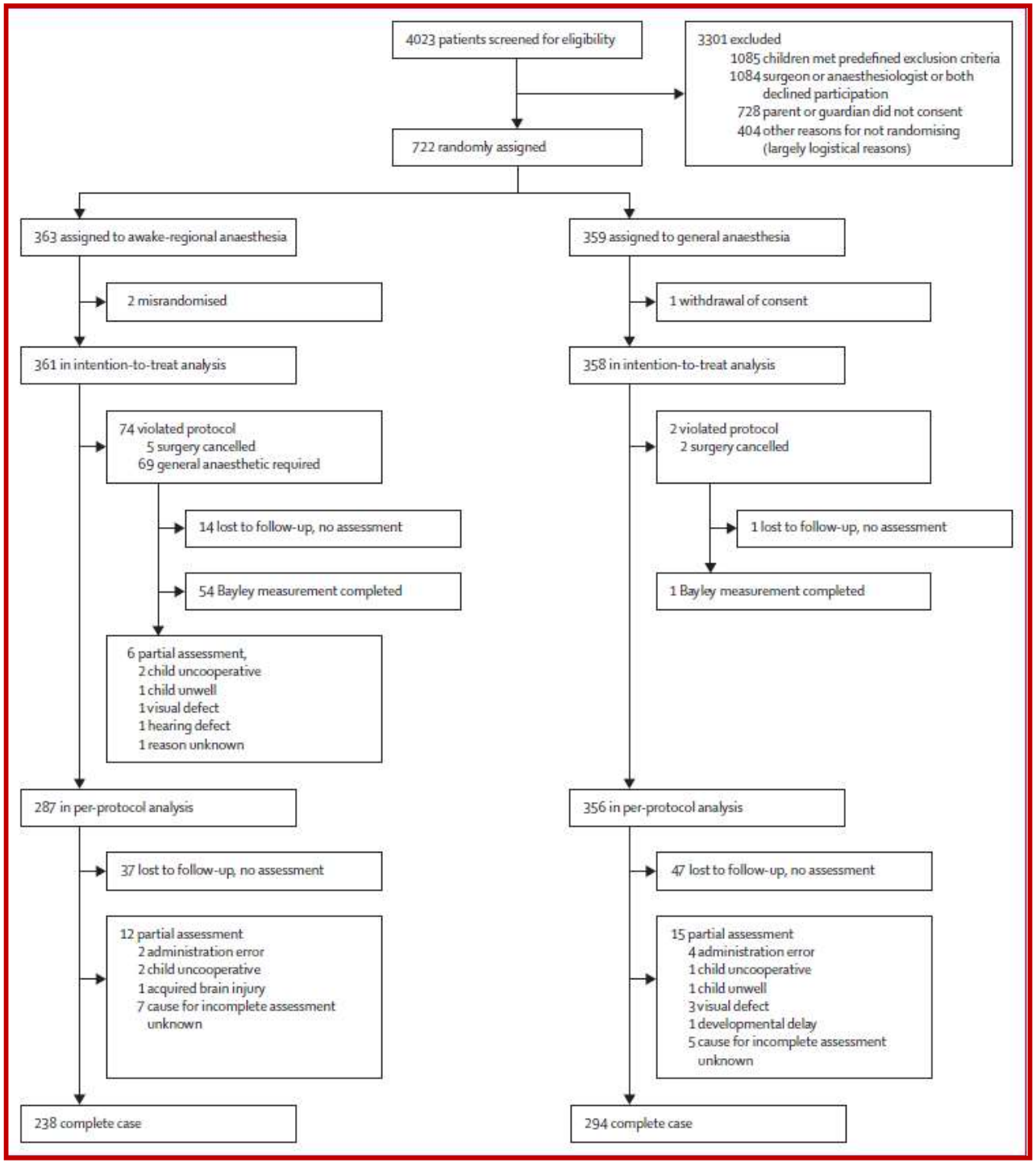
133 patients
Ayant accepté de participer
Score < 5émé P: 11 %

58
sans FDR atteinte SNC
Score < 5émé P: 14 %

75
FDR atteinte SNC
Score < 5émé P: 9 %

L'anesthésie pendant l'enfance est possiblement un FDR de troubles cognitifs à l'âge adulte

Block RI et al. Anesthesiology 2012.



GAS Trial
< 60 S APC

Davidson A et al. Lancet 2016.

	Difference in RA–GA*	Difference in SE	95% CI for difference in RA–GA
Cognitive composite score			
APP multiple imputation	0·169	1·26	−2·30 to 2·64
APP complete case	0·458	1·26	−2·02 to 2·94
ITT multiple imputation	0·256	1·18	−2·06 to 2·57
ITT complete case	0·430	1·19	−1·90 to 2·76
Language composite score			
APP multiple imputation	1·146	1·39	−1·59 to 3·88
APP complete case	0·628	1·37	−2·07 to 3·32
ITT multiple imputation	1·454	1·32	−1·14 to 4·05
ITT complete case	0·942	1·30	−1·61 to 3·49
Motor composite score			
APP multiple imputation	0·598	1·20	−1·77 to 2·97
APP complete case	0·410	1·19	−1·92 to 2·74
ITT multiple imputation	0·143	1·13	−1·08 to 3·37
ITT complete case	1·031	1·14	−1·20 to 3·26
Social-emotional composite score			
APP multiple imputation	1·005	2·09	−3·12 to 5·13
APP complete case	2·012	1·70	−1·32 to 5·35
ITT multiple imputation	1·183	2·03	−2·82 to 5·19
ITT complete case	2·015	1·62	−1·17 to 5·20
Adaptive behaviour composite score			
APP multiple imputation	−0·893	1·34	−3·52 to 1·73
APP complete case	−1·223	1·33	−3·83 to 1·38
ITT multiple imputation	−0·502	1·28	−3·03 to 2·02
ITT complete case	−0·830	1·28	−3·34 to 1·68
MacArthur-Bates percentile score			
APP multiple imputation	−1·811	3·06	−7·85 to 4·23
APP complete case	−2·359	2·71	−7·69 to 2·98
ITT multiple imputation	−0·544	2·87	−6·20 to 5·11
ITT complete case	−1·113	2·57	−6·17 to 3·94

RA=awake-regional anaesthesia. GA=general anaesthesia. APP=as per protocol. ITT=intention to treat. *Adjusted for gestational age at birth.

Table 4: **Between-group comparisons in Bayley-III and MacArthur-Bates scores**

	RA group as per protocol (N=287)	GA group as per protocol (N=356)	RA group intention to treat (N=361)	GA group intention to treat (N=358)
Child has a hearing defect				
Conductive	9 (3%)	6 (2%)	9 (2%)	6 (2%)
Sensorineural	0	3 (1%)	1 (<1%)	3 (1%)
Hearing aid	1 (<1%)	3 (1%)	2 (1%)	3 (1%)
Legally blind (<6/60 in both eyes)	1 (<1%)	0	1 (<1%)	0
Cerebral palsy	1 (<1%)	4 (1%)	1 (0%)	4 (1%)
Autism spectrum disorder	2 (1%)	0	2 (1%)	0

Data are n (% of non-missing data). RA=awake-regional anaesthesia. GA=general anaesthesia.

Table 5: **2-year non-psychometric outcome data**

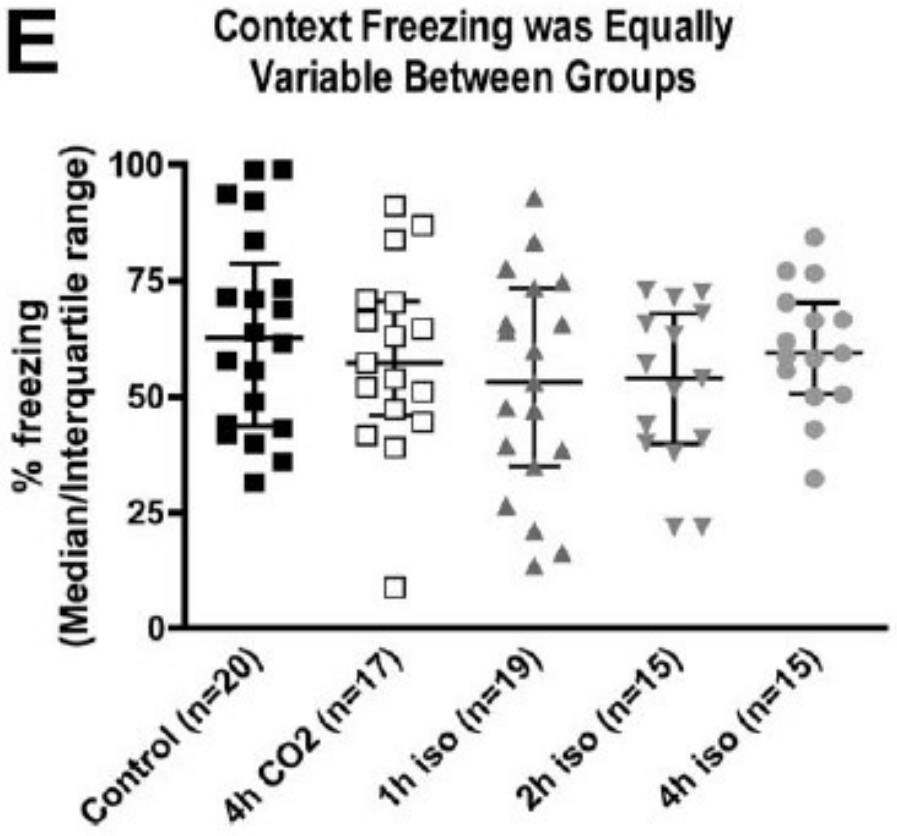
- Puissance
- Intervention < 60 mn
- Une seule exposition
- Sexe masculin

Davidson A et al. Lancet 2016.

Les anesthésiques comme seuls fautifs ??

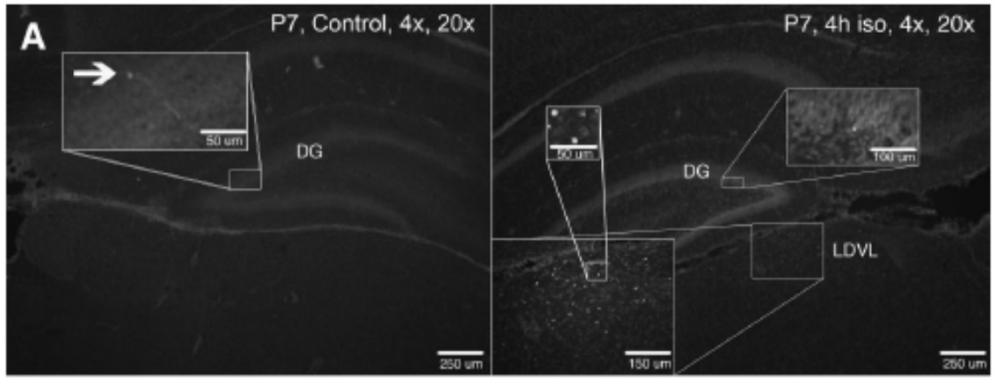
- Hypercapnie ?
- Hyponatrémie ?
- Douleur ?
- Hypotensions périopératoires ?

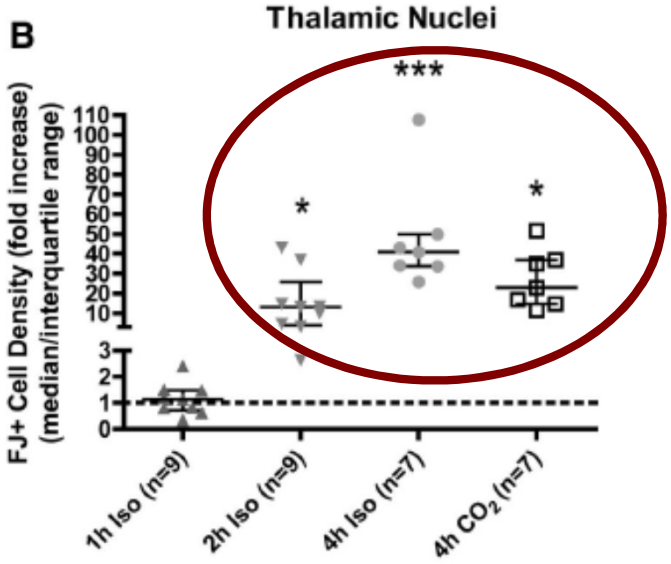
Rats, 7 JPN :
Isoflurane 1 MAC ou hypercapnie



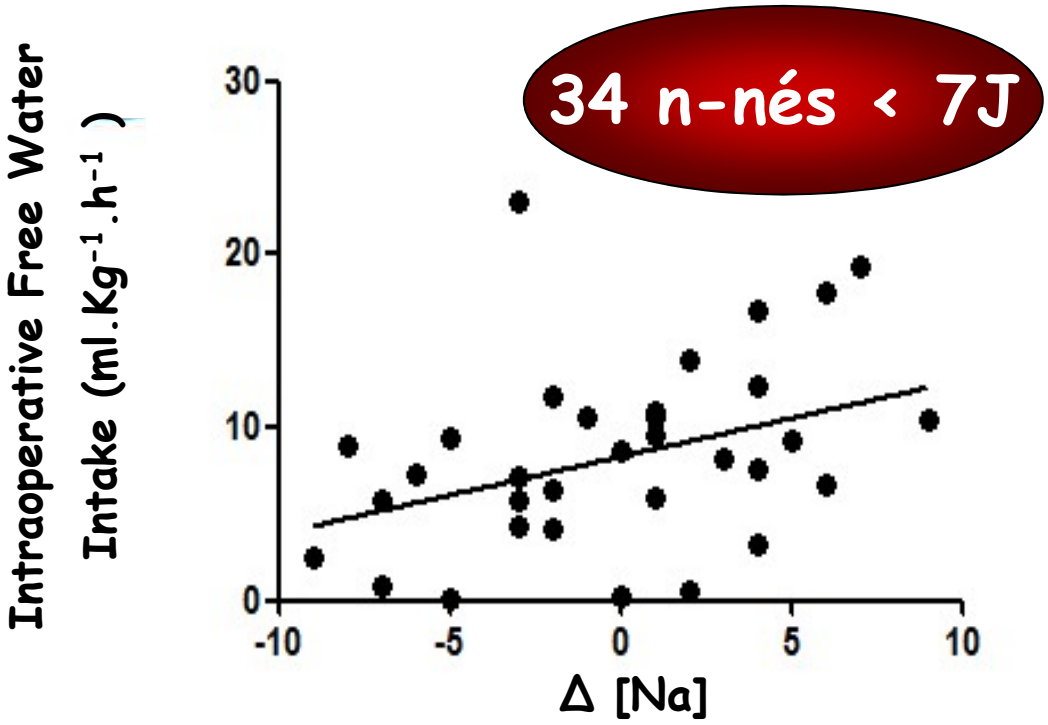
Fonctions Cognitives à 8 Semaines

Mort Cellulaire





Stratmann G et al. Anesthesiology 2009; 111: 1365.



Hyponatrémie néonatale = Anomalies du développement Objectivés à 2 ans !!

	Soluté	Débit (ml/kg/h) pour chute natrémie ≥ 4 mmol/l
A Eviter	G 5 %, G 10 %	6,5
	B27, B45	10
	B46	12
Utilisables ≥ 4 g Na/L	B26	18
	B66	44
	RL	87
	Sérum ρ	Infini

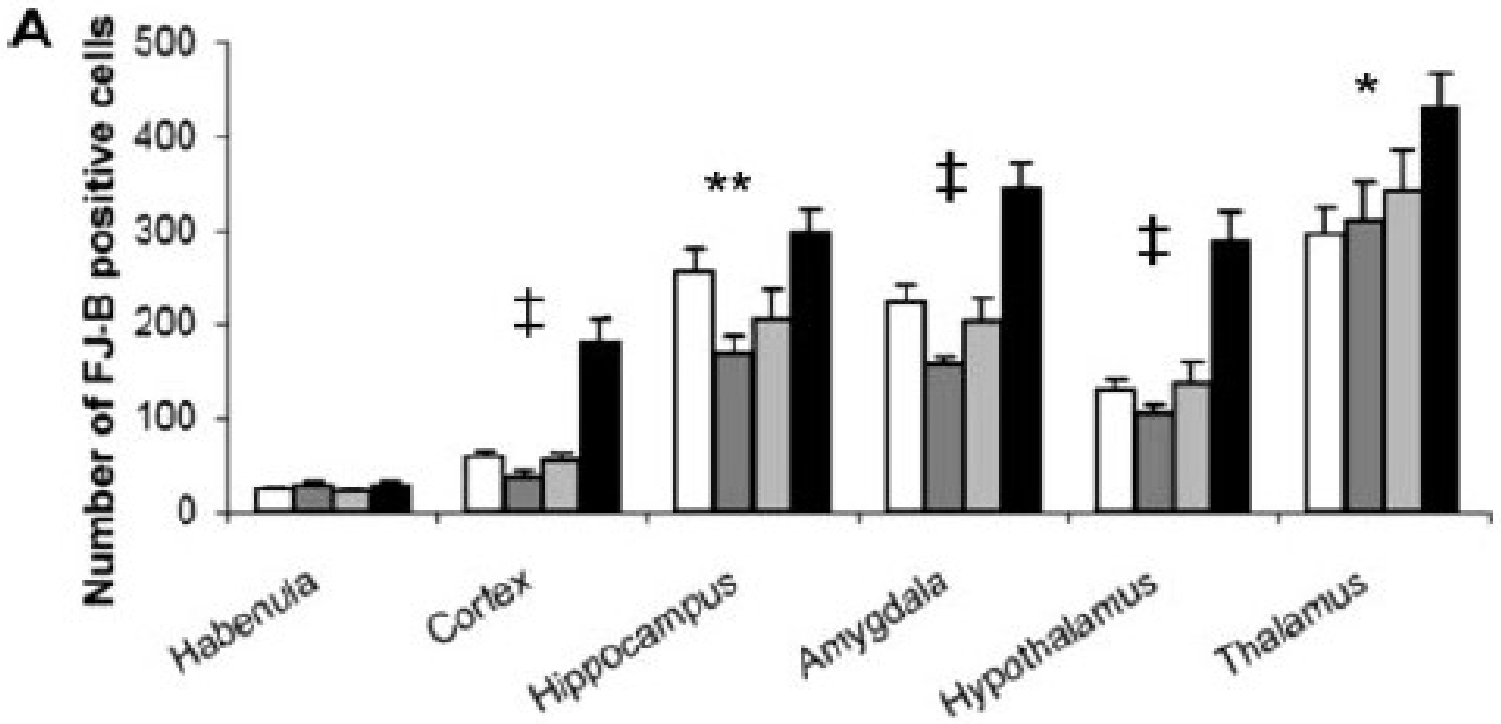
Edjo Nkilly G et al. Brit J Ananesth 2014.

Contrôle

Kétamine (K)

F+K

Formalline (F)



Rat P1-P14 : test formalline pendant 4 heures, 5 mg/Kg kétamine

Anand KJ et al. Ped Res: 2007.

	AUC	Cut off (mmHg)	Sensitivity (%)	95% CI	Specificity (%)	95% CI
MAP under anesthesia						
All the population	0.904	39	78	71–84	90	69–98
Children <6 months	0.808	33	71	58–81	83	58–96
Children >6 months	0.944	43	83	75–90	100	30–100
	AUC	Cut off (%)	Sensitivity (%)	95% CI	Specificity (%)	95% CI
MAP variation						
All the population	0.8	−37	75	68–82	76	52–91

SBP	AUC	J point	Se J	Sp J	Gray zone
All patients	0.79 [0.74 - 0.84]	28.5 %	0.7 [0.6 - 0.8]	0.75 [0.72 - 0.77]	20.5 % - 37.5 %
Preterm	0.84 [0.77-0.88]	31.5 %	0.74 [0.6 - 0.8]	0.74 [0.7 - 0.78]	32.5 % - 39.5 %
Term	0.76 [0.7 - 0.83]	28.5 %	0.63 [0.57 - 0.80]	0.7 [0.77 - 0.8]	20.5 % - 36.5 %

MBP	AUC	J point	Se J	Sp J	Gray zone
All patients	0.67 [0.6 - 0.75]	40.5 %	0.4 [0.33 - 0.59]	0.83 [0.81 - 0.86]	15.5 % - 44.5 %
Preterm	0.72 [0.6-0.83]	40.5 %	0.5 [0.3 - 0.7]	0.8 [0.74 - 0.85]	30.5 % - 47.5 %
Term	0.65 [0.55 -0.75]	42.5 %	0.4 [0.3 - 0.6]	0.87 [0.85 - 0.9]	13.5 % - 42.5 %

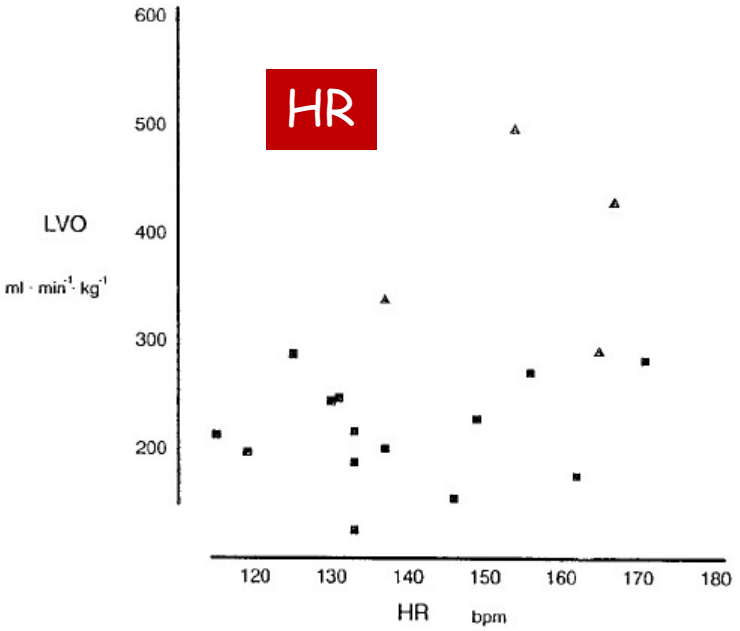
Rhondali O et al. Pediat Anesth 2014.
Michelet D et al. Pediat Anesth 2016.

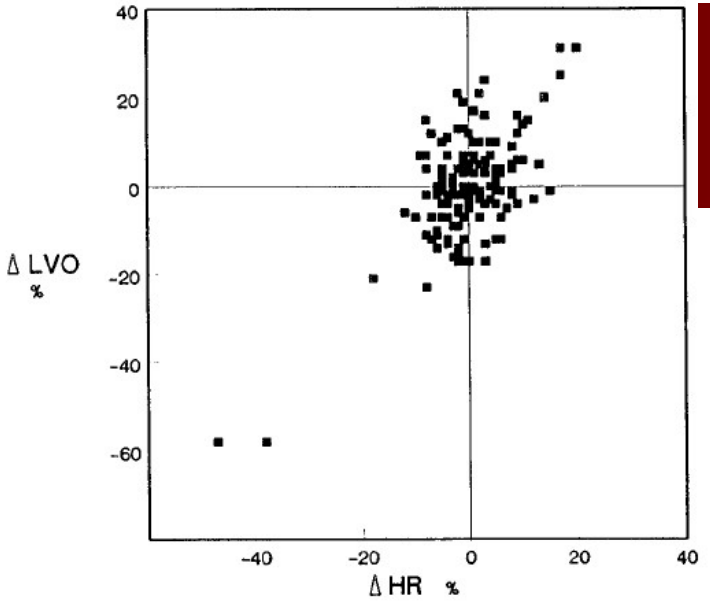


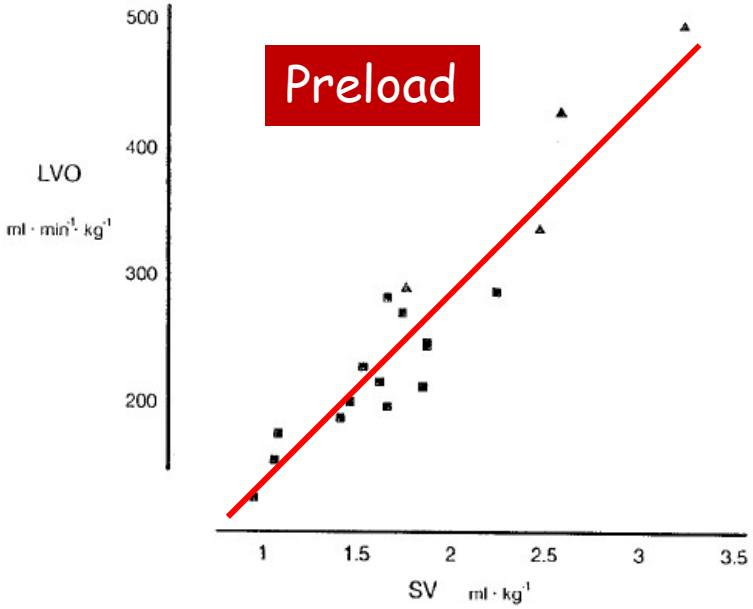
1990

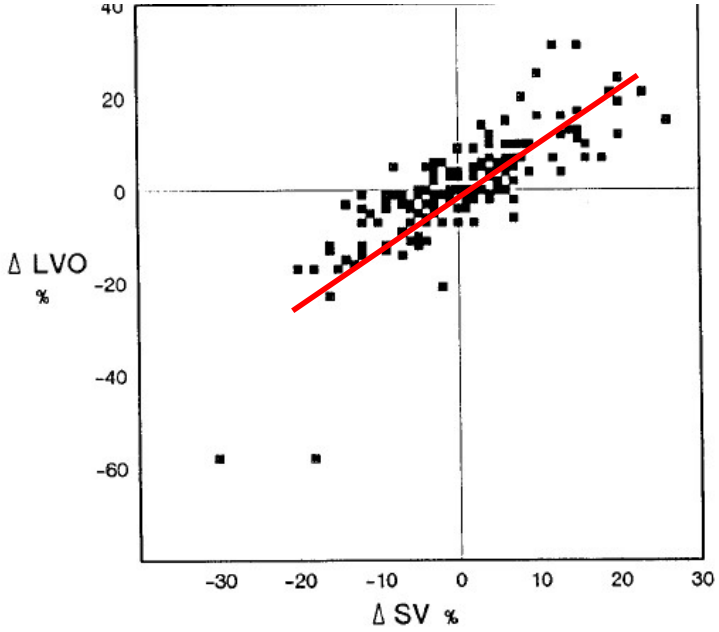


Dépendance du DC à la FC ?





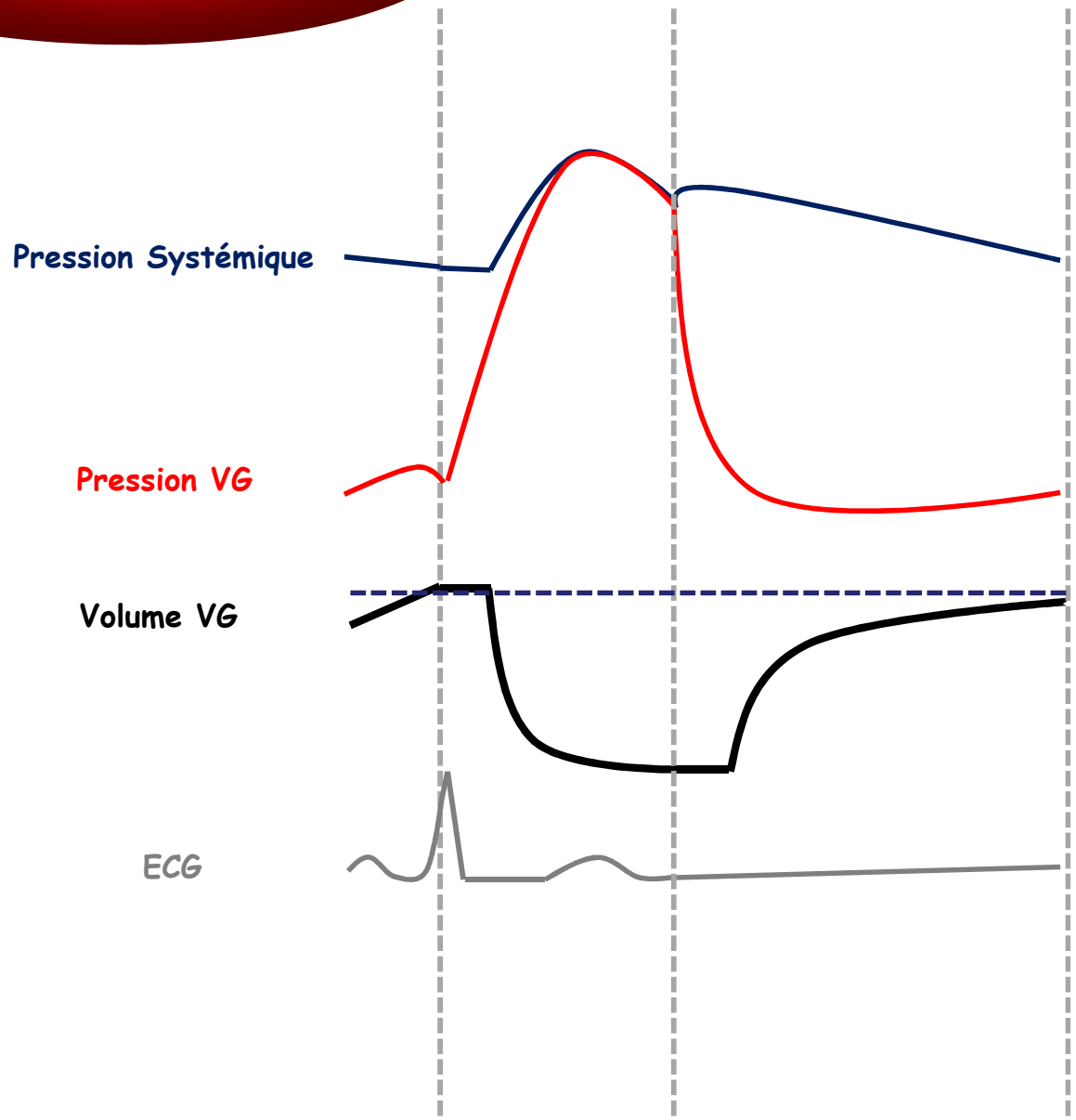




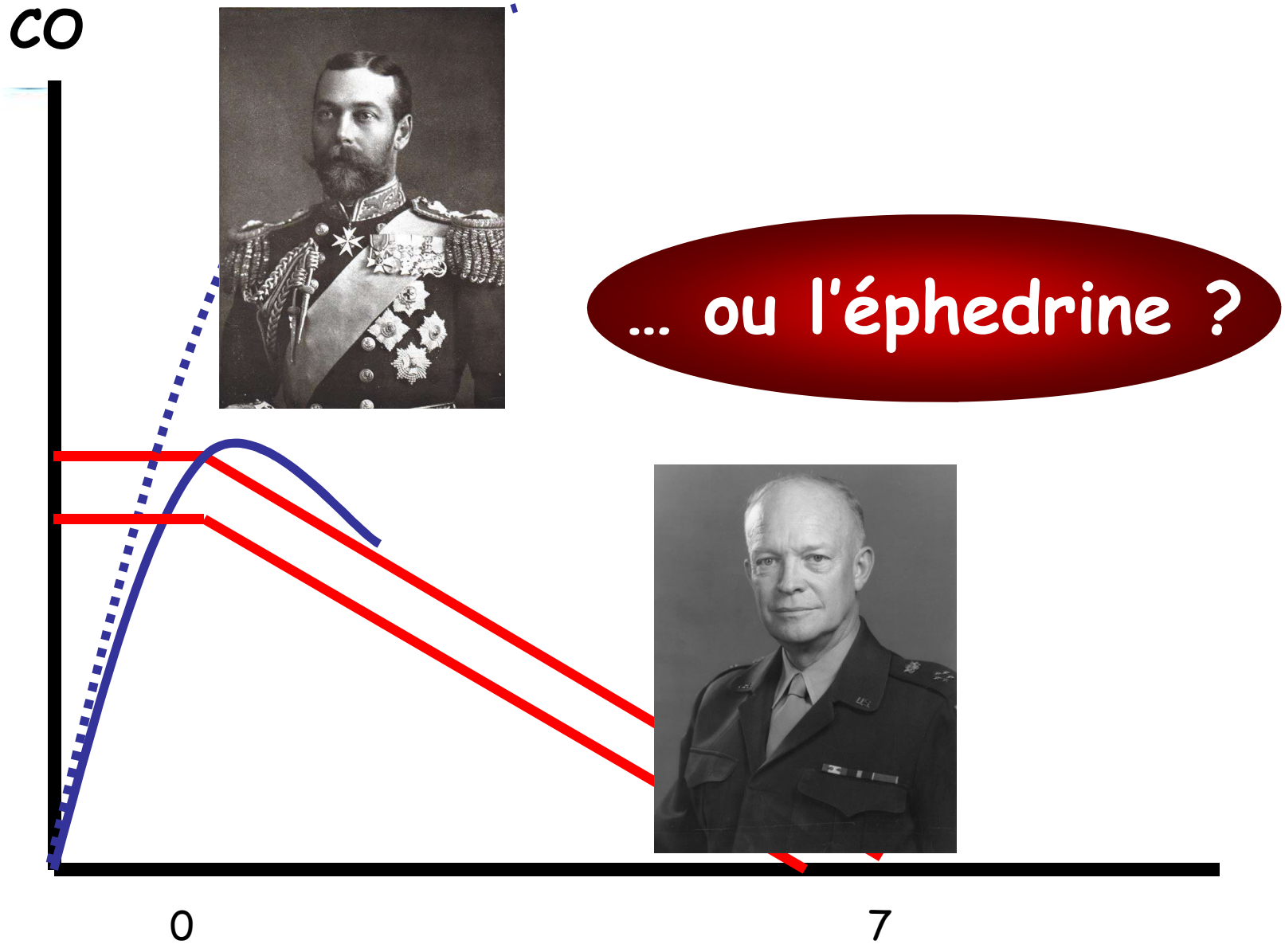
Nourrissons de 29 SA
Age 10 JPN

Winberg P et al. Pediat Resear 1992.

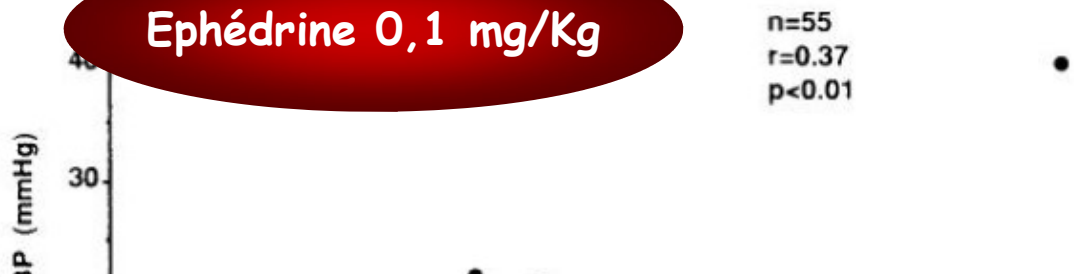
… l'atropine ?



Q ↗ =
FC ↗↗ x VES ↘


CO
… ou l'éphedrine ?
0
7
Pression Auriculaire droite

Ephédrine 0,1 mg/Kg



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Try our beta test site

Determination of the Optimal Dose of Ephedrine in Intraoperative Arterial Hypotension of Newborns and Infants up to 6 Months of Age. (EPHEDRINE)

This study is currently recruiting participants. (see Contacts and Locations)

Verified March 2016 by Hospices Civils de Lyon

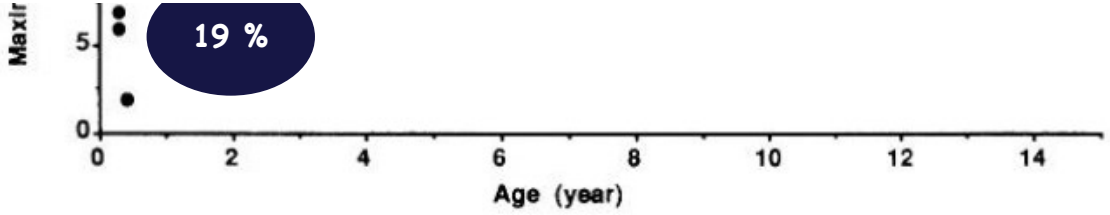
Sponsor:
Hospices Civils de Lyon

Information provided by (Responsible Party):
Hospices Civils de Lyon

ClinicalTrials.gov Identifier:
NCT02384876

First received: February 27, 2015
Last updated: March 15, 2016
Last verified: March 2016
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record



Tagushi N et al. Anesth & Analg 1996.

37e CONGRÈS ANNUEL DE L'ADARPEF

24 et 25 MARS 2017 PARIS



2017

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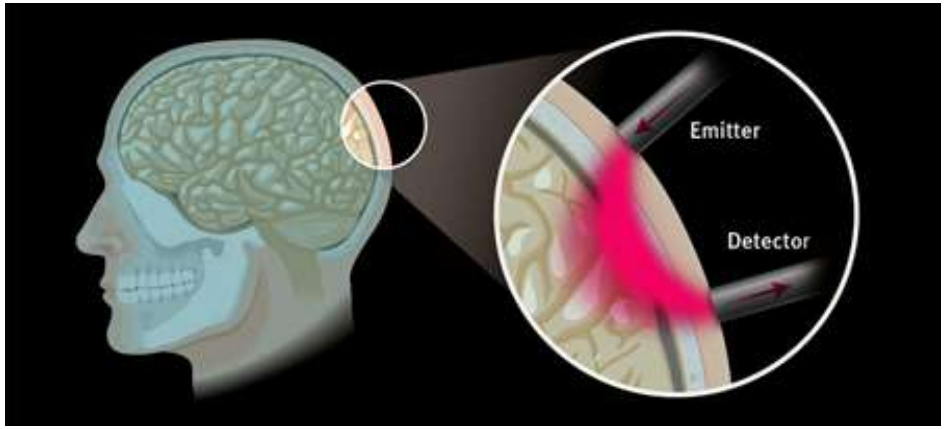


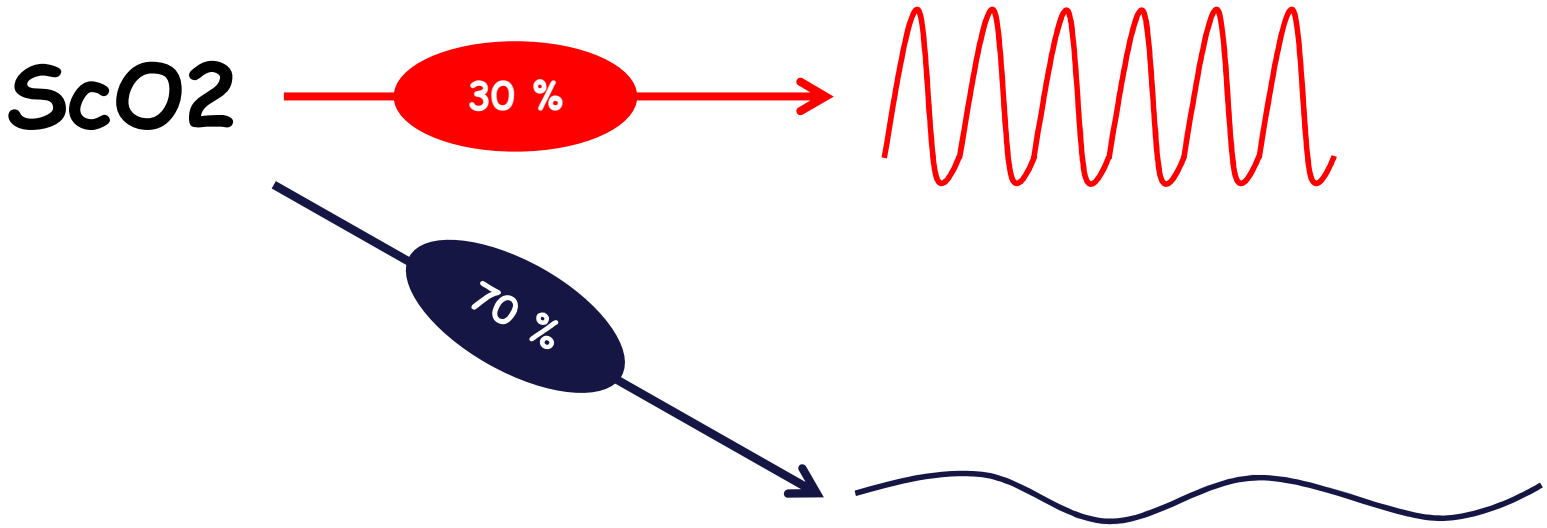
ECG

PA

SpO2

Spectroscopie Proche de l'infra-rouge (NIRS)





$$SvO2 = SaO2 - \left[\frac{VO2}{Q \times Hb \times 1,34} \right]$$

Table 1 Major characteristics of the 25 CDH infants studied

Gender (male/female)	15/10
Gestational age, wk (mean ± SD)	37.8 ± 1.8
Birth weight, g (mean ± SD)	3057 ± 354
Prenatal diagnosis (n)	21
Side of hernia (left/right)	19/6
Age at surgery, d (mean [median] ± SD)	3.5 [2.7] ± 2.5

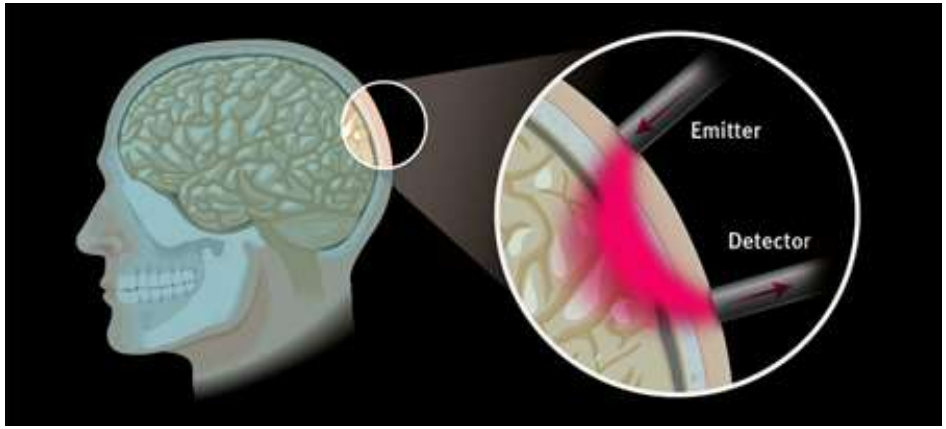


Table 2 Cardiorespiratory variables at the beginning (T_1) and at the end (T_2) of surgical repair

	T_1	T_2	ΔT_2-T_1	95% CI
HR (beats/min)	149.5 ± 9.1	165.2 ± 14.2	15.7[a]	10.3-21.1
SaO_2 (%)	94.1. ± 4.6	93.4 ± 4.4	−0.7	−3.1 to 1.6
FIO_2	0.25 ± 0.05	0.37 ± 0.14	0.12[a]	0.07-0.17
MABP (mm Hg)	54.7 ± 7.7	55.6 ± 8.1	0.9	−2.7 to 4.6

Values are expressed as means ± SD or 95% CI.
[a] Significance of difference: $P < .001$.

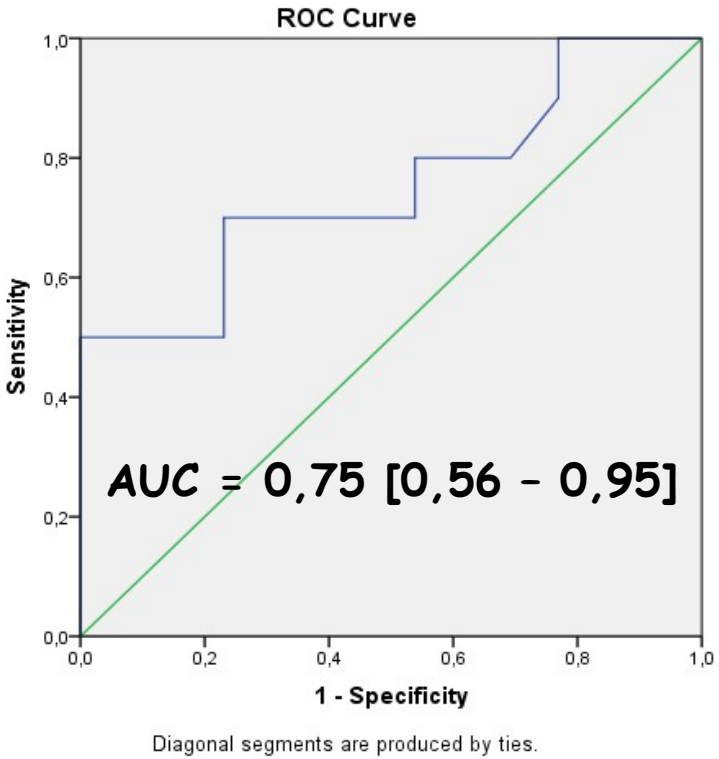
Table 3 Changes in cerebral hemodynamics and oxygenation measured by NIRS before (T_1) and after (T_2) surgical repair

	ΔT_2-T_1	95% CI	P
TOI(%)	−6.05 ± 10.6	−10.9 to −1.2	<.05
O_2Hb (μmol/L)	−10.90 ± 9.7	−14.0 to −6.9	<.001
tHb (μmol/L)	−7.53 ± 11.7	−12.4 to −2.7	<.005
HHb (μmol/L)	3.50. ± 6.8	0.7-6.3	<.05

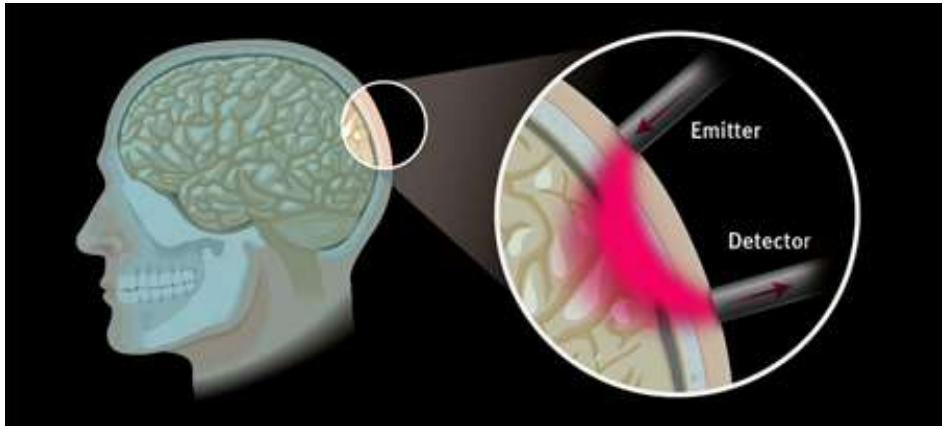
Values are expressed as mean differences between T_2 and T_1 with SD and 95% CI.

O_2Hb: oxygenated Hb
tHb : total Hb
HHb: deoxygenated Hb and total
TOI = O2Hb/(O2Hb++ HHb)

Dotta A et al. J Pediatr Surg 2005.



Courbe ROC $StcO_2$ Avant remplissage.



29 patients < 1 an
Monitorage par NIRS
Remplissage efficace si PAM ≥ 15 %

	$StcO_2$ après remplissage
Sensibilité 90 %	78
Spécificité 90 %	59
Valeur optimale	66 Se = 0,7 [0,6 – 0,79] Sp = 0,77 [0,7 – 0,83]

Hilly J et al. ACCPM 2016.

Pediatric Anesthesia

REVIEW ARTICLE

Cerebral oximetry for pediatric anesthesia: why do intelligent clinicians disagree?

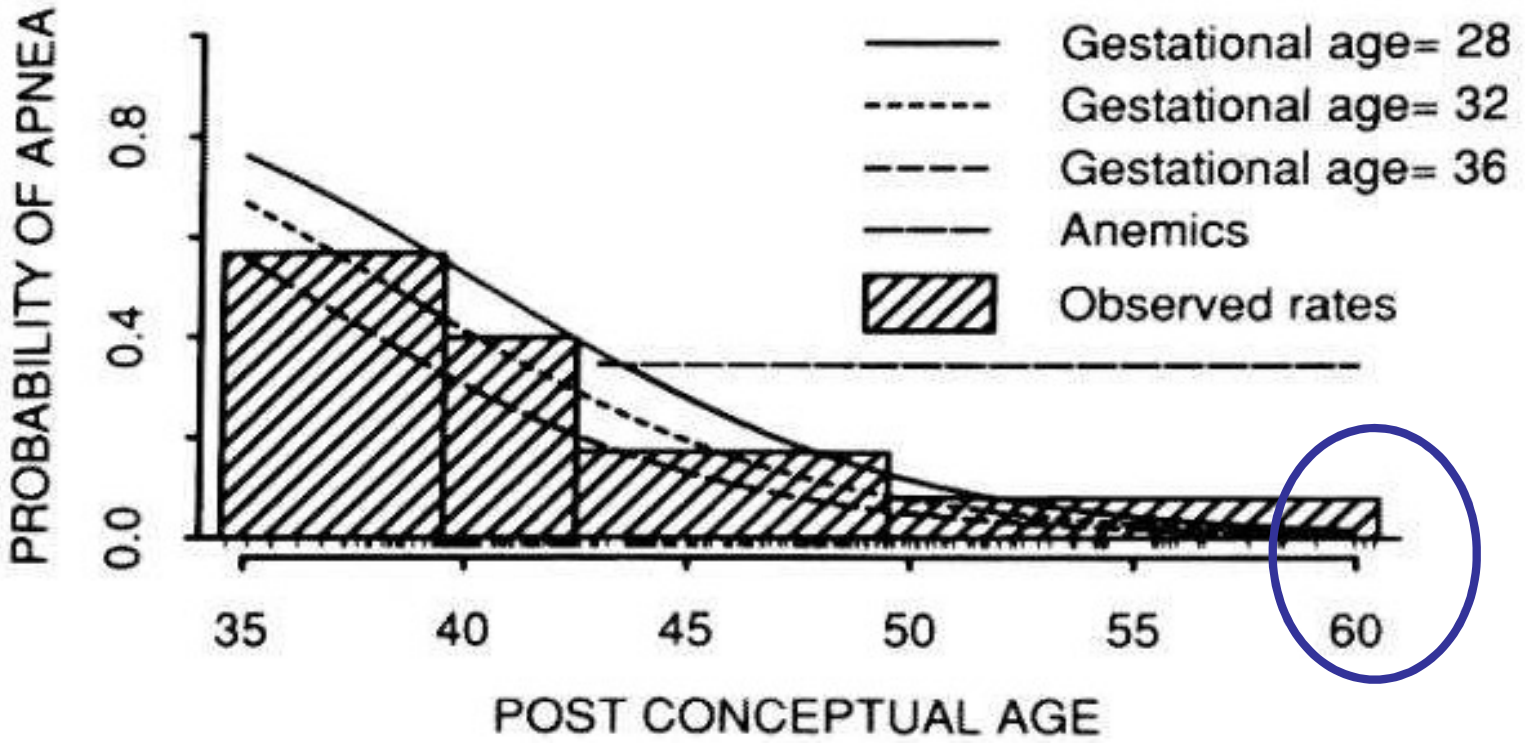
Nicholette Kasman[1] & Ken Brady[2]

Variable	Clinical scenario causing cerebral desaturation	Intervention
O_2 delivery		
CPP	Hypotension, elevated ICP, elevated central venous pressure	Maintain ABP above the lower limit of autoregulation. Check venous drainage cannula
r^A	Hypocarbia, vasospasm, malpositioned arterial cannulae	Decrease minute ventilation, pH-stat management. Check aortic cannula position
[Hb]	Anemia	Transfusion
% Sat	Cyanosis	Lung recruitment maneuvers, increase F_IO_2, manage Q_P/Q_S ratio
η	Polycythemia, sickle-cell disease	Partial exchange transfusion, permissive anemia
O_2 consumption	Fever, seizure, arousal	Cooling, sedation

CPP, cerebral perfusion pressure; ICP, intracranial pressure; ABP, arterial blood pressure; r, resistance vessel radius; [Hb], blood concentration of hemoglobin; % Sat, arterial oxygen saturation; η, blood viscosity.

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Apnée postopératoire



Cote A et al. Anesthesiology 1995.

Regional (spinal, epidural, caudal) versus general anaesthesia for preterm infants having inguinal herniorrhaphy in early infancy

Patient or population: Preterm infants requiring surgery for inguinal hernia in early infancy
Settings: Neonatal/Paediatric intensive care.
Intervention: Spinal anaesthesia
Comparison: General anaesthesia

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk[1]	Corresponding risk				
	General anaesthesia	Spinal anaesthesia				
Neurodevelopmental status at 2 years corrected age	See comment[2]	See comment[2]	Not estimable	0 (0)	See comment[2]	
Apnoea/bradycardia occurring 12-24 hours following completion of operation	477 per 1000	343 per 1000 (229 to 506)	RR 0.72 (0.48 to 1.06)	138 (4 studies)	⊕⊕⊕◯ moderate[3]	
Any oxygen desaturation occurring 12-24 hours following completion of the operation	870 per 1000	713 per 1000 (530 to 965)	RR 0.82 (0.61 to 1.11)	48 (2 studies)	⊕⊕⊕◯ moderate[3]	
Use of post-operative respiratory support	91 per 1000	8 per 1000 (1 to 149)	RR 0.09 (0.01 to 1.64)	98 (3 studies)	⊕⊕◯◯ low[3,4,5]	
Post-operative apnoea with preoperative sedatives excluded	477 per 1000	253 per 1000 (162 to 391)	RR 0.53 (0.34 to 0.82)	129 (4 studies)	⊕⊕⊕◯ moderate[3]	
Anaesthetic agent failure	0 per 1000	0 per 1000 (0 to 0)	RR 7.83 (1.51 to 40.58)	92 (3 studies)	⊕⊕◯◯ low[3,4,5]	
Anaesthetic placement failure	0 per 1000	0 per 1000 (0 to 0)	RR 7.38 (0.98 to 55.52)	90 (3 studies)	⊕⊕◯◯ low[3,4,5]	

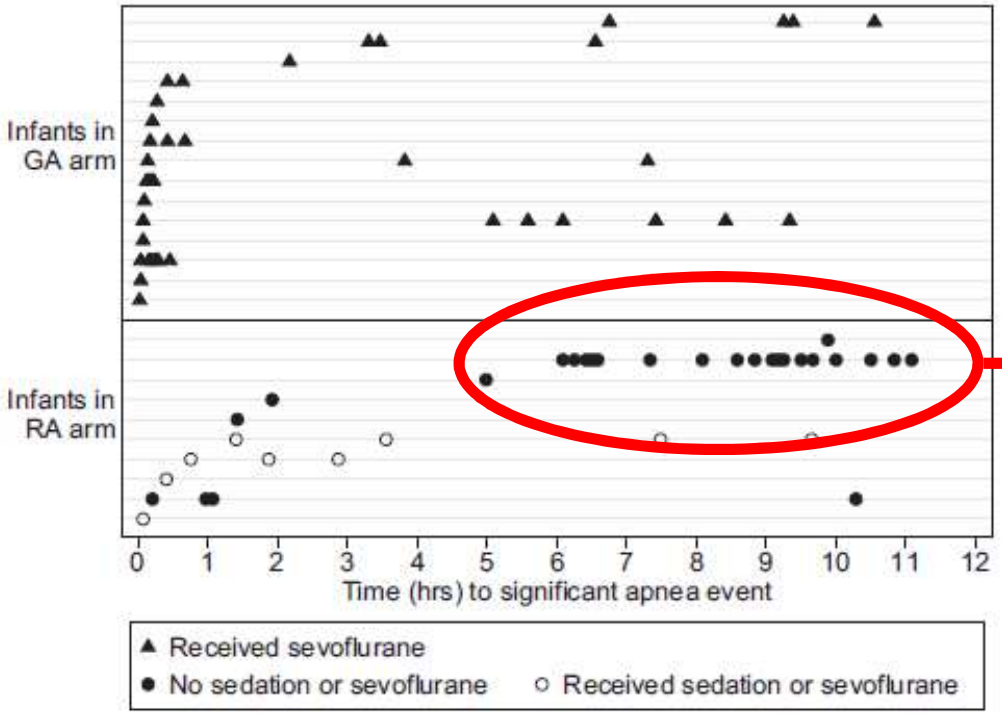
*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

Craven PD. Cochrane Database Syst Rev. 2015:CD003669.

Rachianesthésie

Variables			Failure	No Failure	OR	95% CI	*P* Value
Patient factors	Gestational age (wk)		35.5 (4.1)	35.4 (4.1)	1.01	0.93–1.08	0.86
	Postmenstrual age (wk)		10.7 (5.4)	9.9 (4.4)	1.03	0.95–1.12	0.41
	Current weight (kg)		4.37 (1.11)	4.18 (1.08)	1.16	0.87–1.57	0.31
Technique	CSCA *vs.* spinal	Spinal	29 (13.1%)	193 (86.9%)	1 (Reference)	0.72–11.0	0.14
		CSCA	28 (23.9%)	89 (76.1%)	2.82		
	Bloody tap	No	27 (12.3%)	193 (87.7%)	1 (Reference)	1.24–4.87	0.01
		Yes	30 (25.2%)	89 (74.8%)	2.46		
Experience*	Time of site in study when performing block (per 6 months)	All			0.91	0.81–1.02	0.11
		Exp			0.94	0.80–1.10	0.44
	Number of blocks (per five blocks)	All			0.88	0.77–1.00	0.06
		Exp			0.92	0.80–1.05	0.21
	Seniority of person performing first block	Other	6 (24%)	19 (76%)	1 (Reference)	0.31–1.07	0.08
		Consultant	51 (16.2%)	263 (83.8%)	0.58		
Local anesthetic†	Dose of bupivacaine (mg)	0.5%	3.9 (0.9)	4.1 (1.2)	0.87	0.60–1.27	0.47
	0.75 *vs.* 0.5% bupivacaine	0.75%	11 (6.2%)	167 (93.8%)	1 (Reference)		
			4 (28.6%)	10 (71.4%)	5.66	1.59–20.1	0.007
		Bupivacaine	11 (6.2%)	167 (93.8%)	1 (Reference)		
	0.5% levobupivacaine *vs.* 0.5% bupivacaine	Levobupivacaine	1 (20%)	4 (80%)	3.55	0.81–15.5	0.09

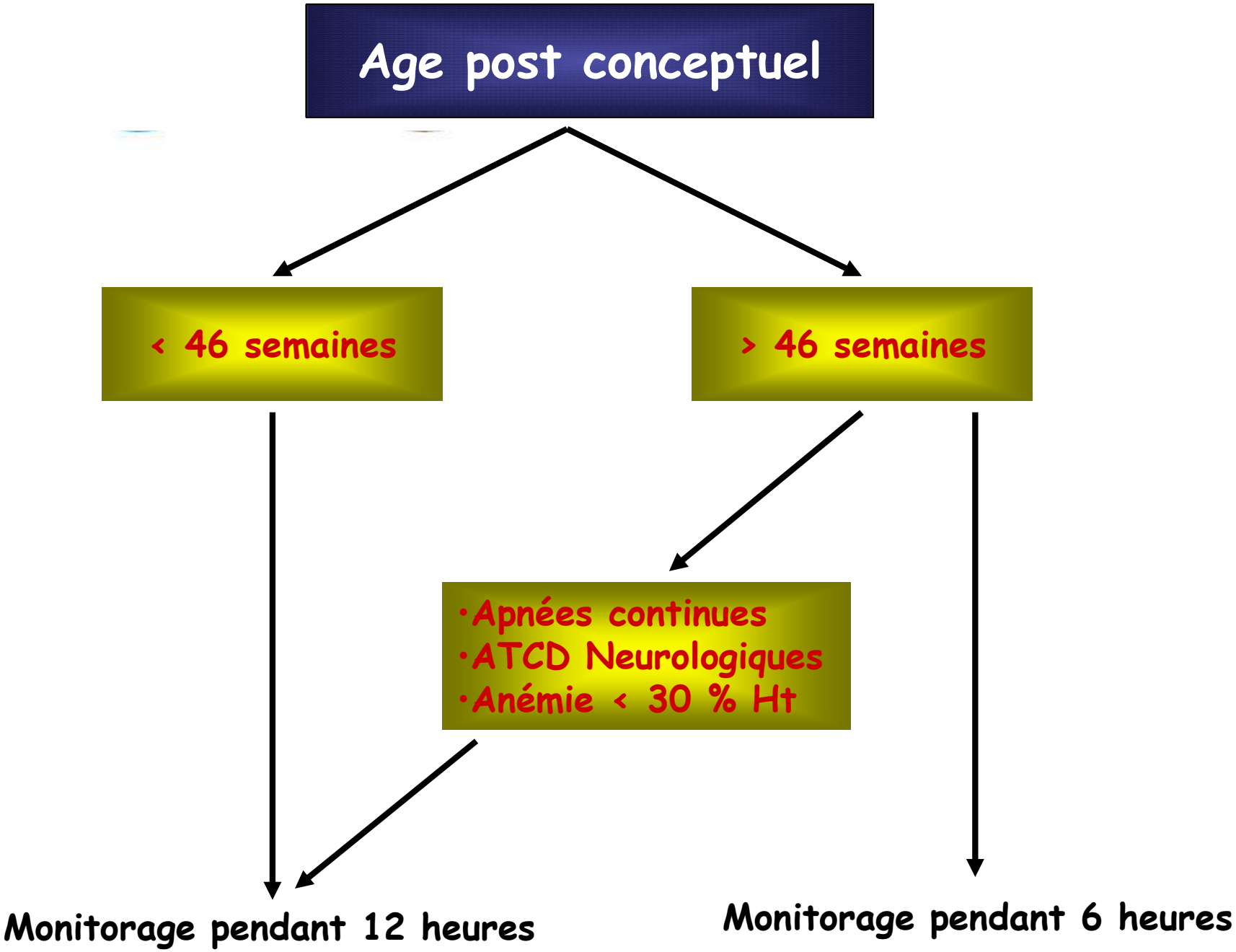
Frawley G et al. Anesthesiology 2015.



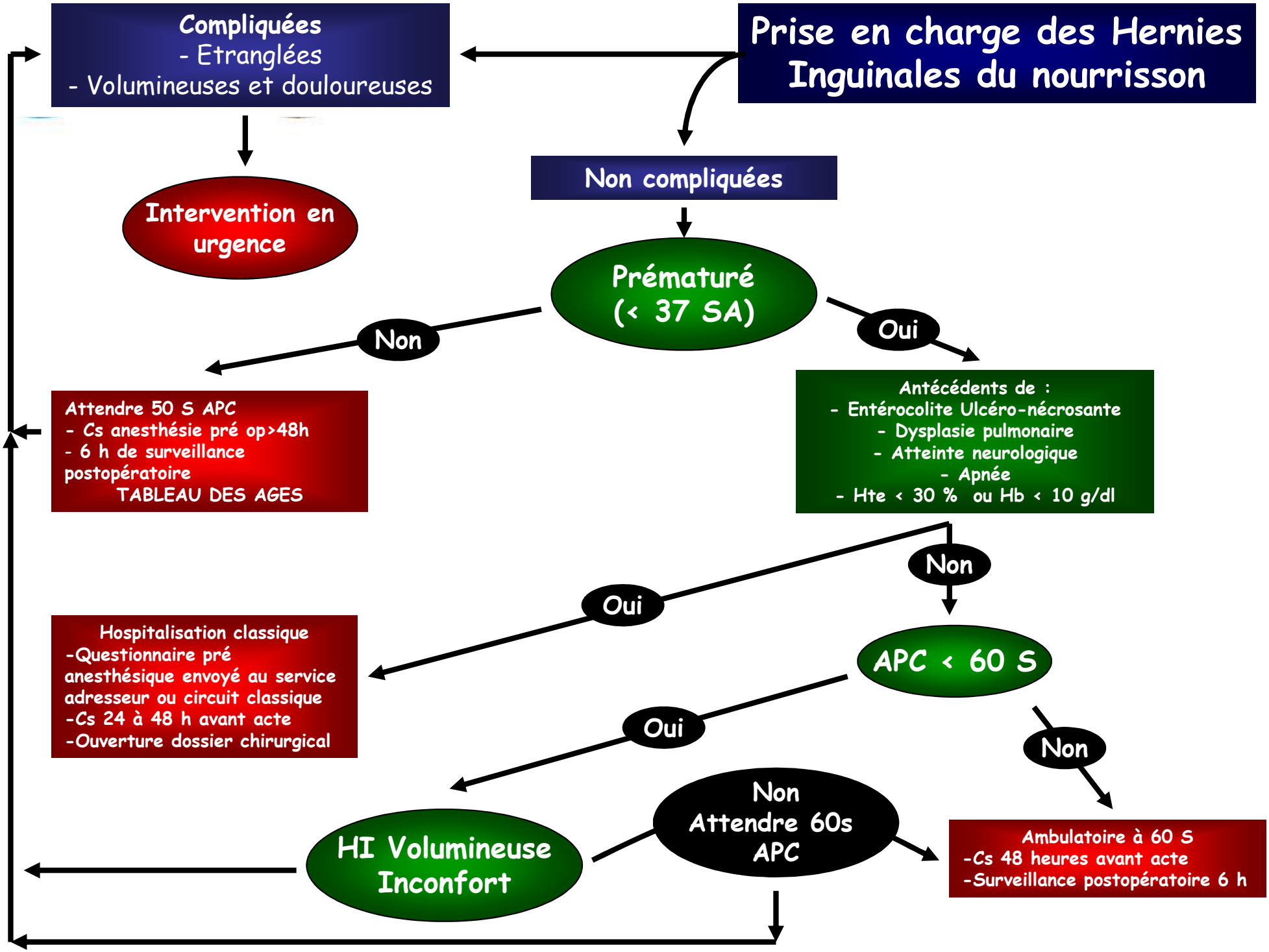
Apnée tardives sous ALR pure

Outcome	Intention to Treat		As per Protocol—RA	RA to Partial GA/Sedation	RA to Full GA
	RA (N = 355)	GA (N = 356)	(N = 286)	(N = 23)	(N = 46)
Any apnea (0–12 h)	10 (3)	15 (4)	6 (2)	0	4 (9)
Any early apnea (0–30 min)	3 (1)	12 (3)	1 (<1)	0	2 (4)
Any late apnea (30 min–12 h)	8 (2)	7 (2)	6 (2)	0	2 (4)
Any late apnea if discharged ≥12 h postoperatively	8 (3)	6 (2)	6 (3)	0	2 (5)
Required significant intervention for apnea (0–5 d)*	7 (2)	18 (5)	4 (1)	0	3 (7)
Required significant intervention for apnea (0–30 min)*	1 (<1)	12 (3)	0	0	1 (2)
Required significant intervention for apnea (30 min–12 h)*	5 (1)	5 (1)	3 (1)	0	2 (4)
Required significant intervention for late apnea if discharged ≥12 h postoperatively	5 (2)	5 (2)	3 (1)	0	2 (5)
Required significant intervention for apnea after 12 h (12 h–5 d)*	2 (1)	4 (1)	2 (1)	0	0
Any caffeine administered postoperatively (0–5 d)	2 (1)	4 (1)	2 (1)	0	0

Davidson A et al. Anesthesiology 2015.



Walther-Larsen S et al. Acta Anaesth Scand 2006; 50: 888.


Prise en charge des Hernies Inguinales du nourrisson
Compliquées
- Etranglées
- Volumineuses et douloureuses
Intervention en urgence
Non compliquées
Prématuré (< 37 SA)
Non
Oui
Attendre 50 S APC
- Cs anesthésie pré op>48h
- 6 h de surveillance postopératoire
TABLEAU DES AGES
Antécédents de :
- Entérocolite Ulcéro-nécrosante
- Dysplasie pulmonaire
- Atteinte neurologique
- Apnée
- Hte < 30 % ou Hb < 10 g/dl
Non
Oui
Hospitalisation classique
-Questionnaire pré anesthésique envoyé au service adresseur ou circuit classique
-Cs 24 à 48 h avant acte
-Ouverture dossier chirurgical
APC < 60 S
Oui
Non
HI Volumineuse Inconfort
Non Attendre 60s APC
Ambulatoire à 60 S
-Cs 48 heures avant acte
-Surveillance postopératoire 6 h



L'a Anesthé

p

Fragilité et vulnérab

monitorage



Garder au chaud

Avec le soutien de
Fondation A. de Rothschild
De l'oeil au cerveau



Conflits d'intérêt

- Baxter, France
- Smith Medical, France
- Editeur associé à ANREA & ACCPM.