



# ASPA 2023

19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

*Equity and Quality in Pediatric Anesthesia*

**16 (Fri) – 18 (Sun) June, 2023**  
**SC Convention Center, Seoul, Korea**



The Korean Society Pediatric Anesthesia



**대한소아마취학회**

# INFORMATION

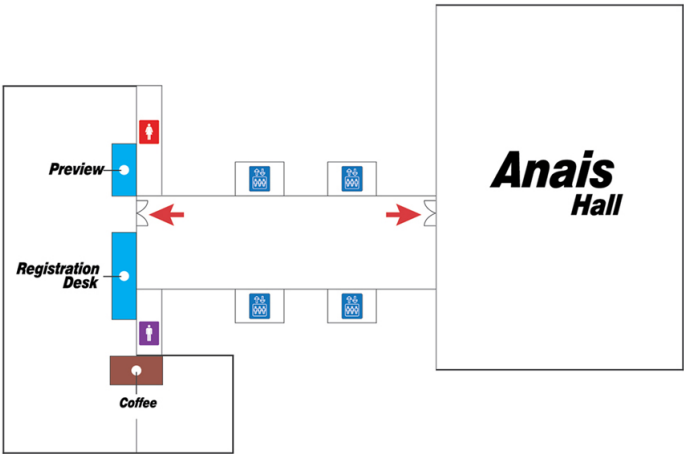


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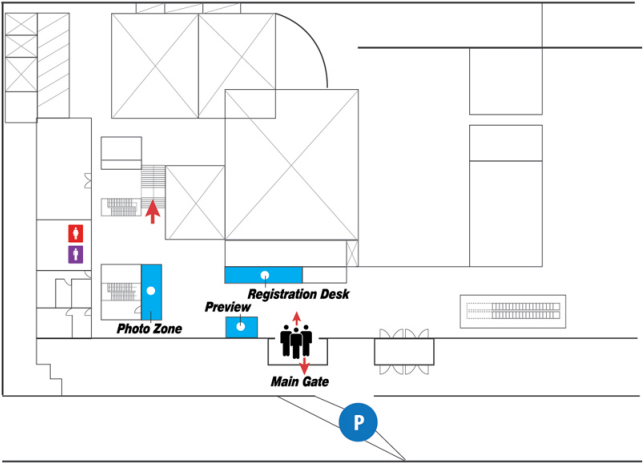
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## Floor Plan

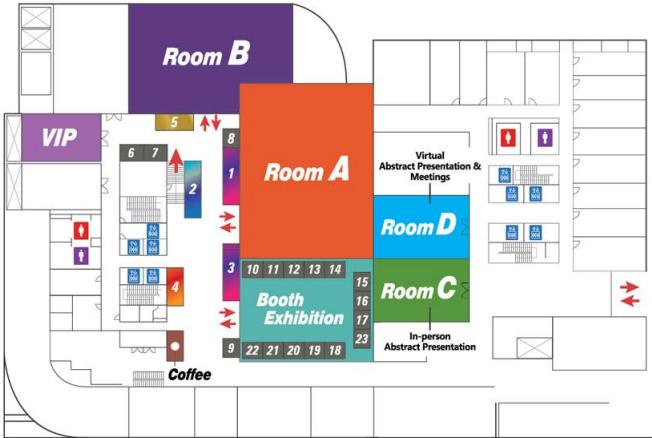
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# WELCOME MESSAGE

The Korean Society of Pediatric Anesthesiologists  
(KSPA)

Dear Colleagues and Friends,

On behalf of the Organizing Committee, I am honored to host the 19th conference of the Asian Society of Paediatric Anaesthesiologists (ASPA 2023) in conjunction with the 31st Korean Society of Pediatric Anesthesiologists annual meeting in Seoul, South Korea on June 16-18, 2023.

Children are our future. Taking care of children's health is keeping "the value of the future." Pediatric anesthesiologists have a mission to ensure the safety and health of pediatric patients during the perioperative period. ASPA 2023 and its scientific program have been prepared with this in mind.

We have an exciting program at ASPA 2023 that will allow all of you to reflect upon and celebrate our past accomplishments, renew friendships and extend our networks, and jointly explore current and future research directions. We hope you will have a productive and fun-filled time at this special conference. The backdrop of the beautiful and historic city of Seoul will add to the pleasure of the meeting and provide lasting memories beyond medicine. You can expect a fascinating, fruitful, and enjoyable time in Seoul.

Looking forward to welcoming you to Seoul, South Korea for ASPA 2023!

President of Korean Society of Pediatric Anesthesiologists

Jin-Tae Kim

A handwritten signature in black ink that reads "Jin-Tae Kim". The signature is written in a cursive, flowing style.



# WELCOME MESSAGE

The Asian Society of Paediatric Anaesthesiologists  
(ASPA)

Dear friends and colleagues

We have now entered a new year, a fresh beginning. With the pandemic mostly under control, I am thankful that we can meet face to face, in Seoul for the 19th ASPA meeting.

People say that "Children's health is our nation's wealth" and health in the early years is important to allow children to thrive and grow into healthy adults.

ASPA is dedicated to fostering safe and high standards of Paediatric Anaesthesia for children in Asia. We hope to achieve this through sharing and supporting each other through research, with development of newer drugs and improved technology enhancing our knowledge of how to monitor our patients in greater detail and depth.

The theme of ASPA 2023 is "Equity and Quality in Paediatric Anaesthesia". We recognize that children are not small adults and Paediatric Anaesthesiologists need to be sharper and have heightened senses when caring for a young child.

I trust that we will be learning plenty from the wonderful programme drawn up by Professor Jin Tae Kim and his team in the organizing committee for ASPA 2023.

I would like to thank everyone for their contributions in making ASPA 2023 a success.

President of Asian Society of Paediatric Anaesthesiologists

**Josephine Tan**

# COMMITTEES

## Committee of KSPA 2023

<b>President</b>	Jin-Tae Kim	Seoul National University
<b>Director of Planning</b>	Byung Gun Lim	Korea University
<b>Director of Academic Affairs</b>	Jeong-Rim Lee	Yonsei University
<b>Director of Publications</b>	Hee Young Kim	Pusan National University
<b>Director of Training</b>	Eugene Kim	Hanyang University
<b>Director of Education</b>	Hyo-Jin Byon	Yonsei University
<b>Director of Medical Insurance</b>	Yong-Hee Park	Chung-ang University
<b>Director of Medical Information</b>	Sooyoung Cho	Ewha Womans University
<b>Director of Treasurer</b>	Seokyoung Song	Daegu Catholic University
<b>Director of Cooperation</b>	In-Kyung Song	University of Ulsan College of Medicine
<b>Director of Research and Development</b>	Won-Jung Shin	University of Ulsan College of Medicine
<b>Director of Public Relation</b>	Woo Suk Chung	Chungnam National University
<b>Executive Secretary</b>	Ji-Hyun Lee	Seoul National University
<b>Steering Members</b>	Hyun-Jung Kim	Jeju National University
	Helen Ki Shinn	Inha University
	Sang Hun Kim	Chosun University
	Jeonghan Lee	Inje University
	Younghee Shin	Samsung Medical Center
<b>Auditor</b>	Hyun Kang	Chung-ang University
<b>Advisor</b>	Il-Ok Lee	Korea University
	Hee-Soo Kim	Seoul National University
	Tae-Hun Ahn	Chosun University
	Sungsik Park	Kyungpook National University
	Ah Young Oh	Seoul National University

## Committee of ASPA 2023

<b>President</b>	Josephine Tan	Singapore
<b>President-Elect</b>	Serpil Ustalar Ozgen	Türkiye
<b>Honorary Secretary</b>	Teddy Fabila	Philippines
<b>Honorary Treasurer</b>	Tracy Tan	Singapore
<b>Committee Member</b>	Vibhavari Naik	India
	Soichiro Obara	Japan
	Fauzia Khan	Pakistan
	Yunita Widyastuti	Indonesia
	Usha Nair	Malaysia
	Lydia Quitarano	Philippines
	Hee-Soo Kim	Republic of Korea
	Duenpen Horatanaruang	Thailand
<b>Internal Auditor</b>	Sokha Tep	Cambodia
	Elsa Verghese	India
	Niki Suneerat	Thailand

## Room A

08:30-09:00	Registration	
09:00-09:20	Welcome and Introduction	
	Opening Remarks	Jin-Tae Kim, President of KSPA
	Congratulatory Message	Jun Heum Yon, President of KSA
		Josephine Tan, President of ASPA

<b>09:20-10:40</b>	<b>Session 1. Society for Pediatric Anesthesia in the World: Past, Present, and Future</b>	Agnes Ng (Singapore) Jin-Tae Kim (Korea)
09:20-09:35	Why Pediatric Anesthesia Society is Special and Needed	Jim Fehr (USA)
09:35-09:50	The Future of Pediatric Anesthesiology around the World; We are Stronger Together	Randall Flick (USA)
09:50-10:05	ASPA: Past, Present, and Future	Josephine Tan (Singapore)
10:05-10:20	ESPA: How to Collaborate Internationally and Intercontinentally	Jurgen de Graaff (Netherlands)
10:20-10:40	Q&A	
10:40-11:00	Coffee Break	

<b>11:00-12:30</b>	<b>Session 2. WFSA Panel Discussion: Universal Coverage of Safe Pediatric Anesthesia All Over Asia</b>	Erlinda Oracion (Philippines) Il-Ok Lee (Korea)
11:00-11:15	Current Status of Pediatric Anesthesia in Cambodia, their Challenges and Opportunities for Improvement	Sokha Tep (Cambodia)
11:15-11:30	Current Status of Pediatric Anesthesia in Bangladesh, their Challenges and Opportunities for Improvement	Debabrata Banik (Bangladesh)
11:30-11:45	Activities of the WFSA Pediatric Anesthesia Committee	Norifumi Kuratani (Japan)
11:45-12:00	Activities and Accomplishments of the WFSA-BARTC Pediatric Fellowship Program	Patcharee Sriswasdi (Thailand)
12:00-12:15	Activities to Improve Patient Safety in WFSA	Erlinda Oracion (Philippines)
12:15-12:30	Q&A	

## DAY 2 17 June 2023 (Sat)

SC Convention International Conference Hall (B1F)

### 12:30-14:00 Luncheon Symposium

EEG Guided Anesthesia in Young Children (Virtual)

Dong Woo Han (Korea)

Ian Yuan (USA)

### 14:00-15:40 Session 3. Preparing for the Future

Choon Looi Bong (Singapore)

Jun Heum Yon (Korea)

Seong-Hyop Kim (Korea)

14:00-14:20 Thoughts on Professional Development and Career Success

Randall Flick (USA)

14:20-14:40 How to Prepare for the Next Pandemic?

Nicola Disma (Italy)

14:40-15:00 Time to Obtain Epidemiologic Data on Pediatric Anesthesia in Asia  
Itself: Introduction of PEACH Study

Soichiro Obara (Japan)

15:00-15:20 Future of Anesthesia-Related Neurotoxicity Issue: Update of TREX  
Study

Dean B Andropoulos (USA)

15:20-15:40 Q&A

15:40-16:00 Coffee Break

### 16:00-17:20 Session 4. Issues We Are Facing & Need to Overcome

Vibhavari Naik (India)

Hee-Soo Kim (Korea)

16:00-16:20 Environmental Impact of Anesthesia (Virtual)

Diane Gordon (USA)

16:20-16:40 Healing the Culture of Medicine

Rebecca Margolis (USA)

16:40-17:00 Challenges Faced in Providing Safe Anaesthesia to Children in Low  
and Middle-Income Countries

Rebecca Jacob (India)

17:00-17:20 Q&A

17:20 Closing Remarks

18:30 **Gala Dinner**

## Room B

09:00-09:20 Welcome and Introduction (Room A)

### 09:20-10:40 Session 1. Optimization of Intraoperative Ventilation in Children

Ekta Rai (India)

Chul-Ho Chang (Korea)

09:20-09:35 Optimal Target of O<sub>2</sub> and CO<sub>2</sub>

Sung-Ae Cho (Korea)

09:35-09:50 PEEP and Recruitment, Mode of Ventilation

Pichaya Waitayawinyu (Thailand)

09:50-10:05 Smart Choice of Ventilation-Related Equipment

Joy Luat-Inciong (Philippines)

10:05-10:20 How to Optimize Our Children's Intraoperative Ventilation Care with POCUS

Ayşe Çiğdem Tutuncu (Türkiye)

10:20-10:40 Q&A

10:40-11:00 Coffee Break

### 11:00-12:30 Session 2. Experts' Advice of Monitoring for Better Anesthesia Care

Joy Luat-Inciong (Philippines)

Hyo-Jin Byon (Korea)

11:00-11:20 Blood Pressure Considerations in Pediatric Anesthesia

Stephen Gleich (USA)

11:20-11:40 The Use of Neuromonitoring in Neonatal Pain Assessment (Virtual)

Ian Yuan (USA)

11:40-12:00 Accurate and Reliable Neuromuscular Monitoring in Children

Serpil Ozgen (Türkiye)

12:00-12:20 How to Assess Fluid Responsiveness in Children

Eun-Hee Kim (Korea)

12:20-12:30 Q&A

### 12:30-14:00 Luncheon Symposium (Room A)

Dong Woo Han (Korea)

EEG Guided Anesthesia in Young Children (Virtual)

Ian Yuan (USA)

## DAY 2 17 June 2023 (Sat)

SC Convention International Conference Hall (B1F)

### 14:00-15:40 Session 3. Sharing the Knowledge of NORA

Vivian Yuen (Hong Kong)

Yong-Hee Park (Korea)

14:00-14:15 Remimazolam and Dexmedetomidine: Clinical Applications and Limitations

Keira Mason (USA)

14:15-14:30 Needle-Free Sedation

Jurgen de Graaff (Netherlands)

14:30-14:45 How to Deal with Challenging Sedation Cases

Eun-Young Joo (Korea)

14:45-15:00 NORA for Children with Special Needs

Ina Ismiarti Binti Shariffuddin (Malaysia)

15:00-15:15 Neonatal Sedation for MRI

Yu Cui (China)

15:15-15:40 Q&A

15:40-16:00 Coffee Break

### 16:00-17:20 Session 4. Perioperative Concerns in Pediatric Anesthesia

Tae-Hun Ahn (Korea)

Woo Suk Chung (Korea)

16:00-16:20 Perioperative Hypothermia in Children: Risk Factor and Preventive Strategy

Djayanti Sari (Indonesia)

16:20-16:40 Emergence Agitation and Long Term Behavioral Consequences

Agnes Ng (Singapore)

16:40-17:00 Anesthesia-Induced Neurotoxicity: Recent Updates and Preclinical Research Trends

Woo Suk Chung (Korea)

17:00-17:20 Q&A

17:20 Closing Remarks (Room A)





**Day 2**

**17 June 2023**



# Room A



## **Session 1.**

# **Society for Pediatric Anesthesia in the World: Past, Present, and Future**

**Chair(s): Agnes Ng (Singapore)  
Jin-Tae Kim (Korea)**

# Why the Society for Pediatric Anesthesia is Special and Needed

Jim Fehr

Stanford's Lucile Packard Children's Hospital, USA

## Disclosures

Nothing to Disclose



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Lucile Packard  
Children's Hospital  
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## Objectives *At the end of this lecture the learner will be able to:*

- Describe the development of the Society for Pediatric Anesthesia (SPA)
- Discuss how the Society for Pediatric Anesthesia is contributing to improving the perioperative care of children
- Access and use the PediCrisis app developed by the SPA

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## History of the SPA

- In the early 1980s there was no organization in the United States of America that represented everyone who practiced pediatric anesthesiology

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## History of the SPA 2

- This prompted Dr. Myron Yaster in 1987 to create the Society for Pediatric Anesthesia (SPA)
- The original goal of the SPA was to hold an annual meeting
- The first SPA meeting was held in October 1987 in Atlanta, Georgia (USA) with 200 attendees



Dr. Myron Yaster  
Founder of the SPA

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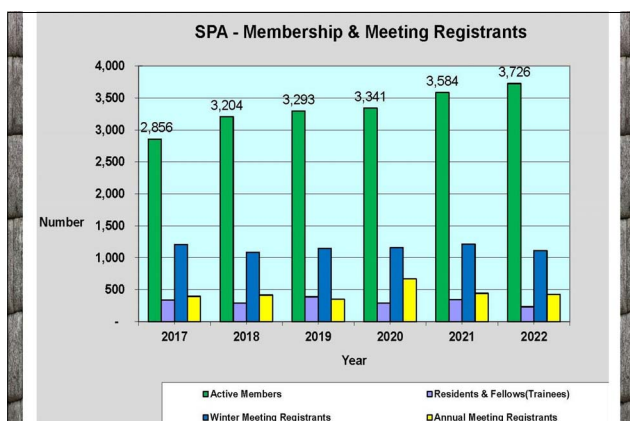
## History of the SPA 3

- The SPA continues to grow and as of March 2023 currently represents over 4,000 pediatric anesthesiologists & trainees
- The SPA now holds 2 meetings annually
- The most recent meeting had over 1,275 attendees, 80% of them attending in person, the remainder attending virtually



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### SPA Mission Statement

The Society for Pediatric Anesthesia advances the safety and quality of anesthesia care, perioperative care, and pain management in children by educating clinicians, supporting research, and fostering collaboration among clinicians, patient families, and professional organizations worldwide.

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### SPA Organizational Structure

- Executive Committee
  - President, Vice-President, Secretary-Treasurer, Past President
  - Each serves two year terms
  - This provides for an 8-year path of leadership continuity
  - Executive Committee members are elected by the SPA membership
- Board of Directors
  - Eight Directors elected by the SPA membership for 2-year terms

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### SPA Component Societies



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### SPA Committees

- Education Committee
- Quality & Safety Committee
- Research Committee
- SPA Global
- SPA Committee on Diversity, Equity and Inclusion (DEI)
- Well Being Committee

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### SPA Special Interest Groups

- Disaster Preparedness
- Mitochondrial Diseases
- Simulation
- Integrative Medicine
- PeDiR-Airway
- Pediatric Neuroanesthesia
- Trainee SIG
- Children with Special Needs SIG
- Liver & Intestinal Transplantation
- Biomedical Informatics
- Blood Management
- Fetal Anesthesia
- Pediatric Ambulatory Anesthesia
- Pediatric Craniofacial
- Pediatric Critical Care
- Sustainability
- Pediatric ERAS
- Ultrasound for Regional & POCUS

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## Dr. Myron Yaster, SPA Founder

- Trained at CHOP under Dr. Jack Downes
- Came to Hopkins under Dr. Mark Rogers
- 1987 Created the Society for Pediatric Anesthesia
- 2014 Received the SPA's Lifetime Achievement Award, subsequently known as the Yaster Award



## "Myron Yaster" Lifetime Achievement Award

- 2015: Bill Greeley, MD, MBA, CHOP
- 2016: Anne Lynn, MD, U Washington
- 2017: Aubrey Maze MD, Valley Anesthesia, Phoenix
- 2018: Chuck Berde, MD, PhD, Children's Boston
- 2019: George Gregory, MD, UCSF
- 2021: Eugenie S. Heitmiller, MD, FAAP, Hopkins/DC Children's
- 2022: Adrian T. Bosenberg, MB, ChB, FFA, U Washington

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## SPA Component Societies



## SPA Component Societies

- CCAS: Congenital Cardiac Anesthesia Society
- SPPM: Society for Pediatric Pain Medicine
- PALC: Pediatric Anesthesia Leadership Council
- PAPDA: Pediatric Anesthesiology Program Directors' Association



## SPA WELI



- Founded by Dr. Jennifer Lee in June 2018, Women's Empowerment Leadership Initiative (WELI) supports the development of female leaders in pediatric anesthesiology
- The mission of WELI is to empower highly productive women pediatric anesthesiologists to achieve equity, promotion, and leadership.
- Mentor-mentee pairings, workshops, and coaching sessions are provided throughout the year

## SPA DEI Committee

- The SPA Committee on Diversity, Equity and Inclusion (DEI) was founded in Spring 2018 and advocates for members of the SPA who have traditionally been underrepresented
- The SPA DEI Committee also speaks for marginalized patients and families whose care may be below standard and seeks to assure that all patients get the best of care regardless of their background

## SPA Investment in Research

- SPA Research, Education & Safety Fund (RE&SF) was established in 2014
- The SPA RE&SF provides \$100,000 annually for research grants to one or two young investigators
- The SPA RE&SF also supports SPA's global outreach

## SPA Global

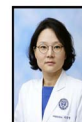
- Created to focus efforts to enhance pediatric perioperative care world wide
- SPA Global has supported a fellow in Kenya for the last 10 years
- SPA Global has added support for a pediatric anesthesiology fellow in Thailand



## SPA Global Outreach

Supports international scholars attendance at the SPA meeting

- 2018 – Walid Habre MD, PhD; Geneva, Switzerland
- 2019 – Britta Von Ungern-Sternberg, MD MB BCh PhD; Perth, Australia
- 2020 – Clover-Ann Lee, MD; Johannesburg, South Africa
- 2021 – Jeong-Rim Lee, MD, PhD; Seoul, South Korea
- 2022 – Rodrigo Lopez Barreda MD; Santiago, Chile
- 2023 – Zipporah Gathuya, MBCHB, MMED Nairobi, Kenya



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## SPA Critical Events Checklists



- In 2007 the SPA Quality & Safety Committee created the Critical Event Checklists which are evidence-based and supported by expert consensus
- Current languages: Spanish, Chinese, French, Portuguese, Tagalog, Turkish, Ukrainian, Hebrew

<https://pedsanesthesia.org/critical-events-checklists/>

## SPA Critical Events Checklists



- The 26 checklists are continually updated based on the most recently available evidence/guidelines
- Focused on what a pediatric anesthesiologist needs to know to manage an emergency in the perioperative period

## SPA Critical Events Checklists



### Cardiac Arrest

#### Pulseless cardiac arrest

- Notify team, call for help and code cart/defibrillator
- Increase oxygen to 100%. Turn off anesthetics
- If ETT, 100-120 chest compressions/min + 10 breaths/min. Avoid hyperventilation.
- If no ETT, 15-2 compression:ventilation ratio (100-120 chest compressions/min + 8 breaths/min)
- For chest compressions, maximize EtCO<sub>2</sub> > 10 mmHg (see next card for more details):
  - Switch compressor every 2 min
  - Use sudden increase in EtCO<sub>2</sub> for ROSC. Do NOT stop compressions for pulse check
- Obtain defibrillator. Attach pads. If VF/VT, shock 2 joules/kg. Continue chest compressions x 2 minutes.
- Start timer. Designate team leader. Assign roles. Designate a scribe/recorder. Notify family. Continue with next items in yellow box.

Repeat sequence below until return of spontaneous circulation:

- If still in VF/VT, shock 4 joules/kg q 2 min (up to 10 joules/kg on subsequent shocks)
- Resume chest compressions immediately regardless of rhythm
- Epinephrine 10 MICROgrams/kg IV q 3-5 min while in arrest (MAX 1 mg)
- If still no ROSC after second dose of EPINEPHRINE, activate ECMO (if available)
- Check pulse & rhythm q 2 min during compressor change
- Check for reversible causes (Hs and Ts) early and often (see table below)
- Lidocaine 1 mg/kg bolus (MAX 100 mg); may repeat (total: 2 doses) OR amiodarone 5 mg/kg bolus; may repeat (total: 3 doses)
- Repeat sequence in this box until return of spontaneous circulation

#### Hs and Ts: Reversible Causes

- Hypovolemia
- Hypoxemia
- Hydrogen ion (acidosis)
- Hyperkalemia/Hypoglycemia
- Hypothermia
- Tension Pneumothorax
- Tamponade (Cardiac)
- Thrombosis
- Toxin (anesthetic, B-blocker)
- Trauma (surgical or nonsurgical bleeding)

### Cardiac Arrest: VF/VT

#### Shockable, pulseless cardiac arrest

- Start chest compressions (100 chest compressions/min + 8 breaths/min)
- Place pt on backboard, maintain good hand position; if prone, see "Prone CPR" card
- Maximize EtCO<sub>2</sub> > 10 mmHg with force/depth of compressions
- Allow full recoil between compressions
- Switch compressor every 2 min
- Use sudden increase in EtCO<sub>2</sub> for ROSC
- Do NOT stop compressions for pulse check
- Give 100% oxygen. Turn off anesthetics
- Start timer. Designate team leader. Assign roles
- Obtain defibrillator. Attach pads. Shock 2-4 joules/kg
- Resume chest compressions immediately
- Epinephrine 10 MICROgrams/kg IV q 3-5 min while in arrest
- Check pulse & rhythm q 2 min during compressor change
- Check for reversible causes (Hs and Ts) early and often (see previous "Cardiac Arrest" card)
- If VF/VT continue:
  - Shock 4 joules/kg
  - Resume chest compressions for 2 min regardless of rhythm
  - Check pulse & rhythm q 2 min during compressor switch
  - Repeat epinephrine 10 MICROgrams/kg IV q 3-5 min if VF/VT continue
- If VF/VT continue 2 min after previous defib attempt, shock 4-10 joules/kg and resume chest compressions for 2 min; check pulse with compressor change; repeat sequence until ROSC
- Lidocaine 1 mg/kg bolus OR amiodarone 5 mg/kg bolus; may repeat (total of 2 doses)
- If cardiac arrest > 6 min, activate ECMO (if available)



Cardiac Arrest: VF/VT

## PediCrisis App 2.0

- The SPA Critical Events checklists were adapted as a free smartphone app in 2013
- PediCrisis 1.0 featured 18 scenarios
- PediCrisis 2.0, the most recent version, features all 26 scenarios



## PediCrisis App 2.0

- Smartphone versions are available in English & Spanish
- PediCrisis has been downloaded over 25,000 times from 132 countries

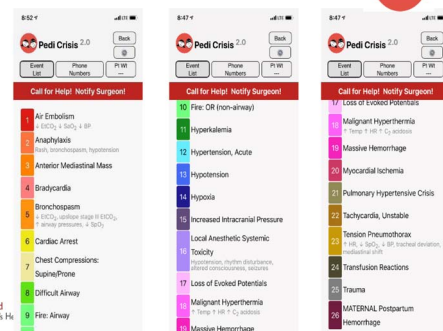


## PediCrisis App 2.0

- Download for free from Apple iOS and Android Store
- No internet connection needed after initial download



## PediCrisis App 2.0



## PediCrisis App 2.0

Navigate directly to:

- ☐ Event List
- ☐ Phone number
- ☐ Weight entry



## Objectives *At the end of this lecture the learner will be able to:*

- ✓ Describe the development of the Society for Pediatric Anesthesia (SPA)
- ✓ Discuss how the Society for Pediatric Anesthesia is contributing to improving the perioperative care of children
- ✓ Access and use the PediCrisis app developed by the SPA





# Randall Flick: The Future of Pediatric Anesthesiology around the World; We are Better Together

## PAIF


**Paediatric Anaesthesia International Forum**

Nigel Turner, Andrew Davidson and  
October 18, 2013

**PEDIATRIC ANESTHESIA INTERNATIONAL FORUM**

**Situation**  
The specialty of paediatric anaesthesia is new societies and increasing membership in Africa, Southeast Asia, China, industrialized and the developing world, cooperation between the world's societies.

**Recommendations**  
Considering the above we recommend that Pediatric Anaesthesia International Forum (PAIF) take the form of an extended common issues group with the following structure:  
1. The PAIF shall consist of representatives of the national organizations for pediatric anesthesiology with a maximum of one representative per country. If in a certain country there is no national organization for pediatric anesthesiology, the PAIF membership will appoint a member from the national organization for anesthesiology from that country to be PAIF. If in a certain country there is more than one national organization for pediatric anesthesiology, representation for the PAIF will be from the largest and most broadly representative Society as determined by the PAIF leadership.  
2. Every national organization referred to in the preceding paragraph shall be entitled to appoint one representative for the PAIF and shall inform the Executive Board thereof in writing or electronically, and do so on a regular basis.  
3. From among the members of PAIF shall be selected officers including a president, president elect and secretary-treasurer who shall serve as the executive board along with the past president. The terms of the officers shall be one year.  
4. Members shall serve 2 year terms that may be renewed a maximum of once by the nominating society. Length of service on the PAIF shall therefore not exceed four years except for those serving as officers who may serve a maximum of 8 years.  
5. The president shall also be the chairman of the meetings of the PAIF. If the president is lacking, the vice-president shall act as chairman. In the absence of both the president and the vice-president a person to be designated by the members from among the officers of the PAIF shall act as the chairman.  
6. It shall be the task of the PAIF to collect and discuss suggestions that are made by the national organizations. The findings of the PAIF shall be submitted for discussion to the meetings of the various member societies.  
7. The members of the PAIF shall receive no remuneration for their work as such. They may be entitled to compensation of the expenses incurred by them in the performance of their function at the discretion of their member society.  
8. The PAIF shall meet once a year in conjunction with a meeting of one of the member societies. Costs associated with the meeting shall be the responsibility of the hosting society or members of the PAIF.  
9. Further provisions about the composition, the method of appointment and the functions of the members of the PAIF may be laid down in the by-laws by the Executive Board with the approval of the members.  
10. Each society wishing to be represented on the PAIF shall be responsible to pay dues as determined by the PAIF leadership. Dues may be waived for members without a sponsoring Society and limited resources at the discretion of the executive committee.



## PAIF

### FIRST STEP TOWARD AN INTERNATIONAL SOCIETY

- Forum of leaders from societies around the world.
- One leader from each society participates.
- If no organized society – an individual from that country can be appointed by PAIF.
- PAIF membership will select leaders.
- Meeting will occur once per year in conjunction with a member society.
- Dues are paid by the member's society.



## World Federation of Societies for Pediatric Anesthesia



## INTERNATIONAL ASSEMBLY FOR PEDIATRIC ANESTHESIA

Spring 2027  
?????




## SPA-AAP PEDIATRIC ANESTHESIOLOGY 2024

A meeting co-sponsored by the Society for Pediatric Anesthesia and the American Academy of Pediatrics Section on Anesthesiology and Pain Medicine

April 12-14, 2024 | Anaheim Marriott | Anaheim, CA



## 2023 ANNUAL MEETING

October 13, 2023 | San Francisco, CA

[pedsanesthesia.org](https://pedsanesthesia.org)









# Asian Society of Paediatric Anaesthesiologists: Past, Present, and Future

Josephine Tan


KK Women's and Children's Hospital, Singapore



From the Beginning ...  
1999 - 2020

## Why do we need a paediatric anaesthesia society in Asia?




## Jet Lag / language ?




Asian paediatric anaesthesia society can arrange for anaesthesia meetings in asia.

Better for learning if you are awake....



## Paediatric Anaesthesiologists have to be recognized at home, by our surgical colleagues, hospital staff, and general public.




Children in the World by Country 2023

Country	2023 Population
India	1,428,627,663
China	1,425,671,352
United States	339,996,563
Indonesia	277,534,122
Pakistan	240,485,658
Nigeria	223,804,632
Brazil	216,422,446
Bangladesh	172,954,319
Russia	144,444,359

ASIA

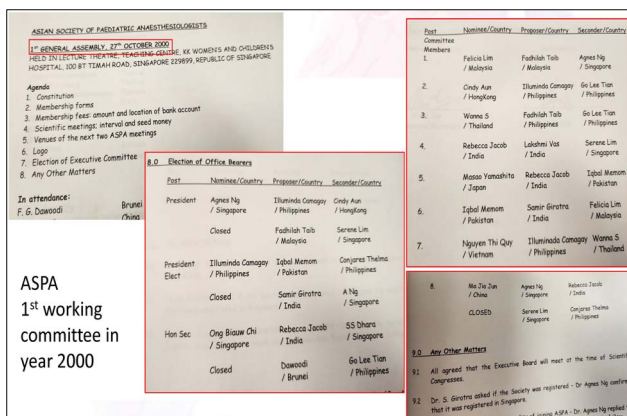
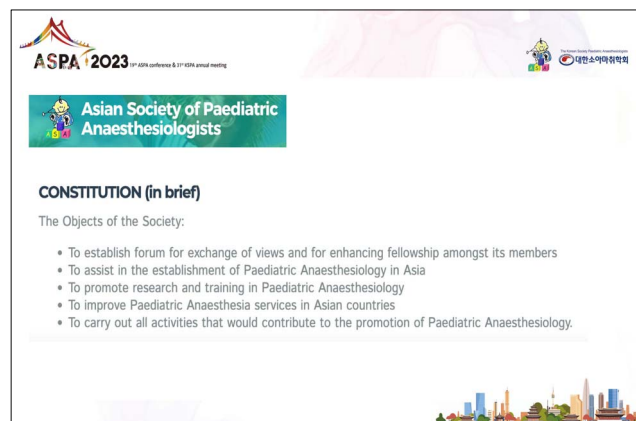
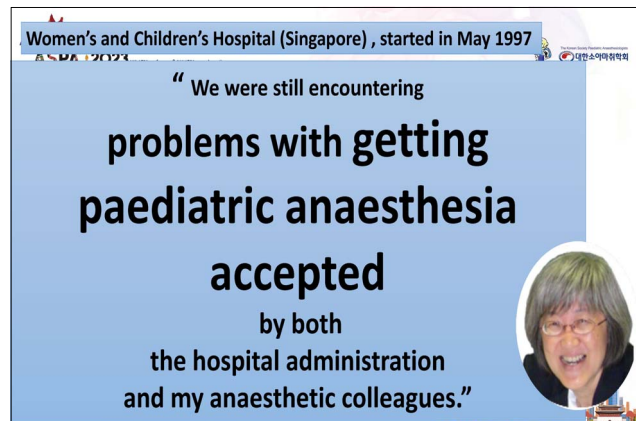
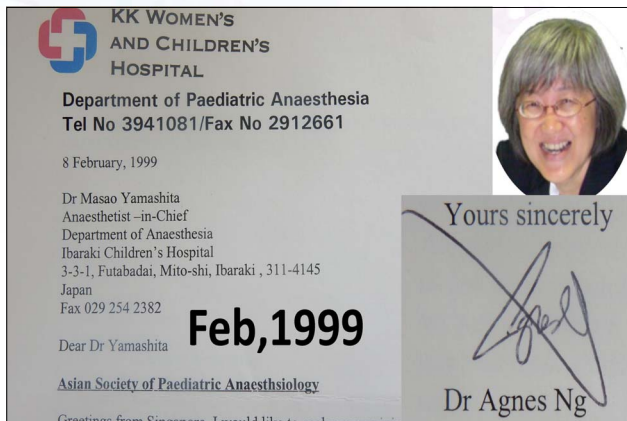



## Challenges in Asia

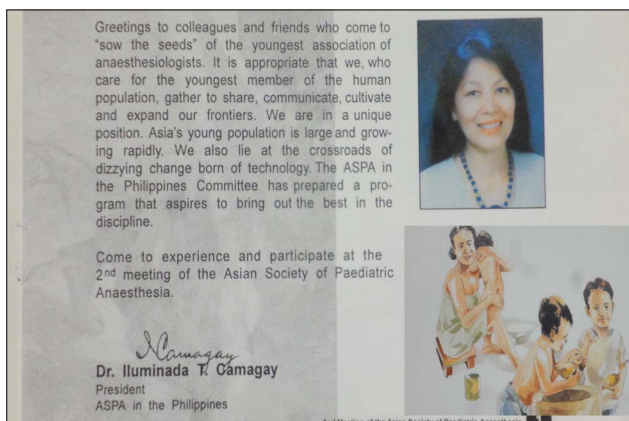
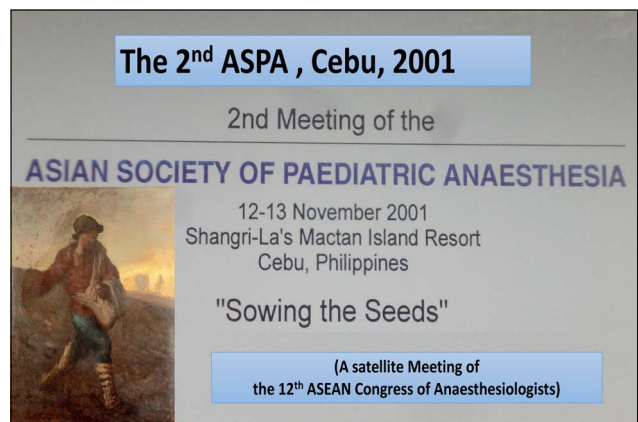
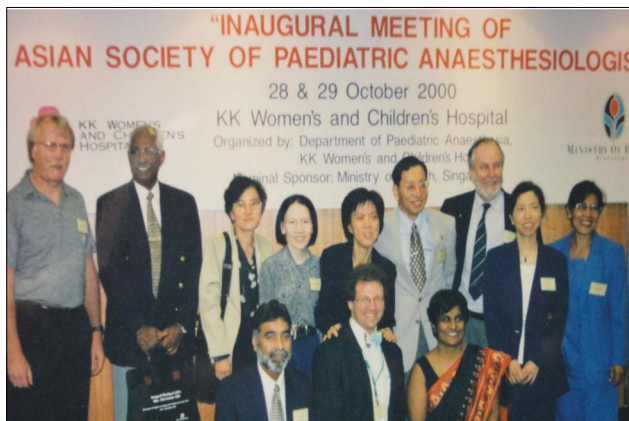


- Uneven distribution of medical resources
- In some countries or regions within countries, medically qualified anaesthetists may be a scarce resource.
- Physician and non-physician anaesthesia providers providing occasional anaesthesia to children



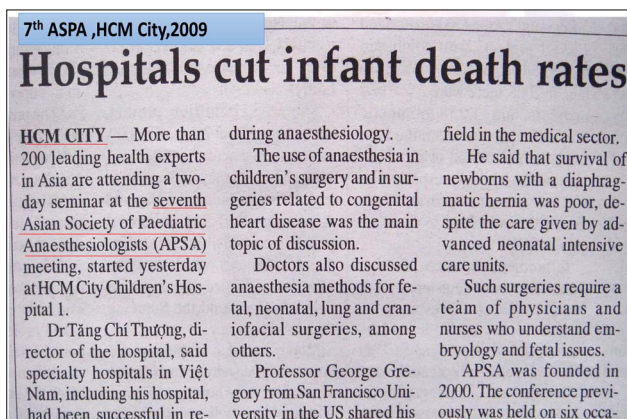
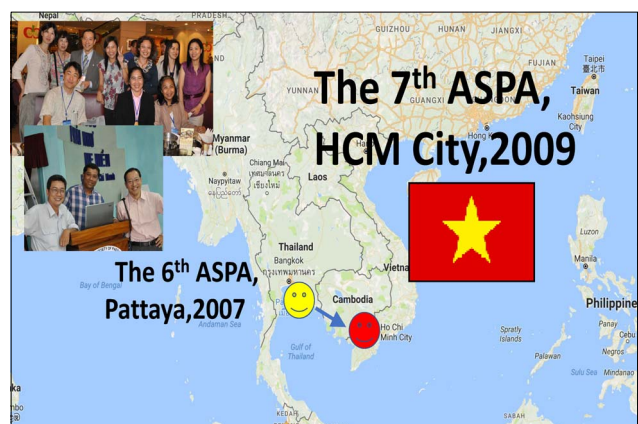
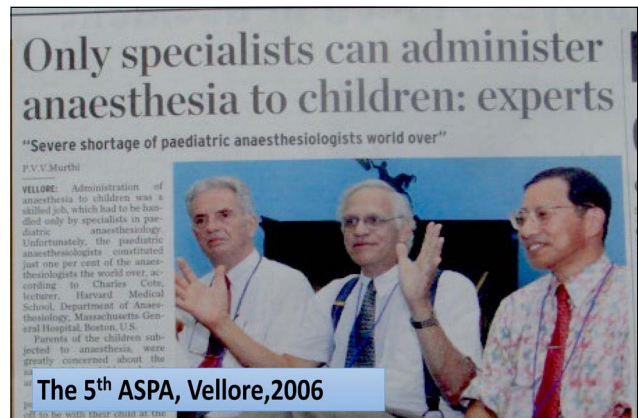








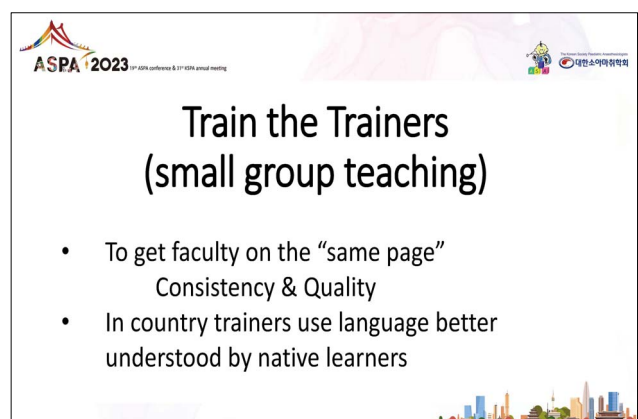
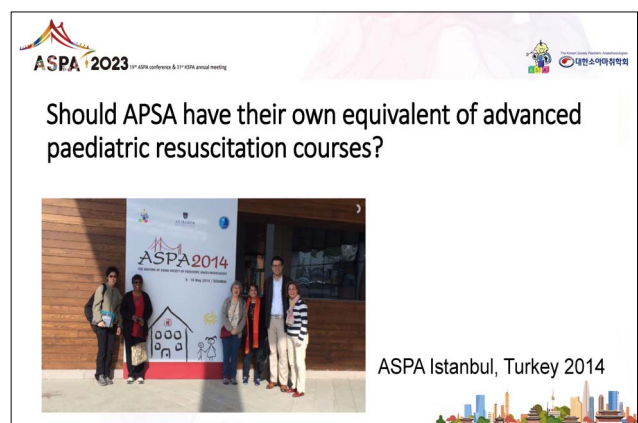
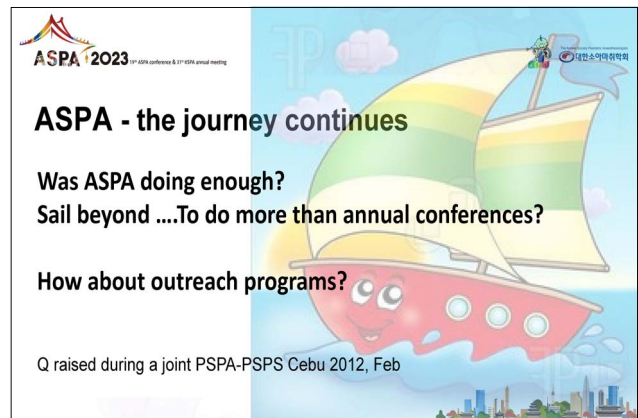
Josephine Tan: Asian Society of Paediatric Anaesthesiologists: Past, Present, and Future














**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**“Train the Trainers/TTT sessions”**



**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting



**Malaysian Society of Paediatric Anaesthesiologist PPLS – TTT course Jan 2018**

**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**Philippine Society of Pediatric Anesthesia PPLS and TTT, Feb 2018**



**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**ASPA Collaborations**  
International, National and Local societies & Healthcare organisations



**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**ASPA NOW....  
TODAY in 2023**

**ASPA 2023**  
Equity and Quality in Paediatric Anaesthesia

19th Conference of the Asian Society of Paediatric Anaesthesiologists  
31st Annual Meeting of the Korean Society of Paediatric Anaesthesiologists

16 (Fri) - 18 (Sun) June, 2023  
SC Convention Center, Seoul, Korea



**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**MEMBERSHIP**

• 596



Bhutan
Japan
Turkey
Maldives
Kenya
Bangladesh
USA
Uzbekistan
Myanmar
Sri Lanka
Mongolia
Kosovo
Nepal
UAE
Mauritius
Singapore
Philippines
China
Pakistan
Thailand
Cambodia
India
Hong Kong
Indonesia
Malaysia
Korea
Vietnam
Canada

**ASPA 2023** 17th ASPA conference & 17th KPSA annual meeting

**ASPA e-Education**  
Our Pursuit: To disseminate education for a holistic paediatric anaesthesia care.

**Now into 3rd season of webinars.....all available at ASPA website [aspa-2000.com](http://aspa-2000.com)**

**ASPA Education Committee**




**1st ASPA FLEX Webinar Series Launch**

**2nd ASPA FLEX Webinar Series Launch**

**3rd ASPA FLEX Webinar Series Launch**

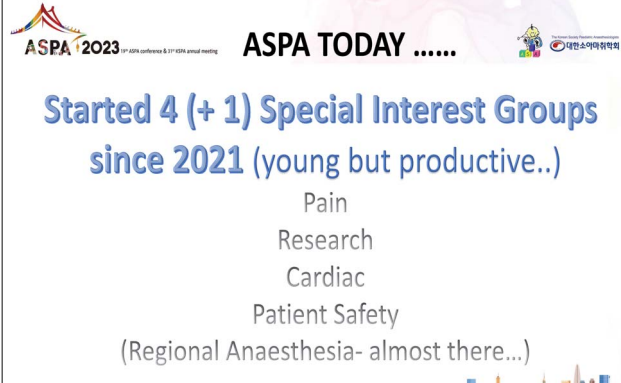
## Josephine Tan: Asian Society of Paediatric Anaesthesiologists: Past, Present, and Future



**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

Despite Covid restrictions...  
Still continuing with existing programmes --> PPLS

**e-PPLS Philippines**



**ASPA TODAY .....**

**Started 4 (+ 1) Special Interest Groups since 2021 (young but productive..)**

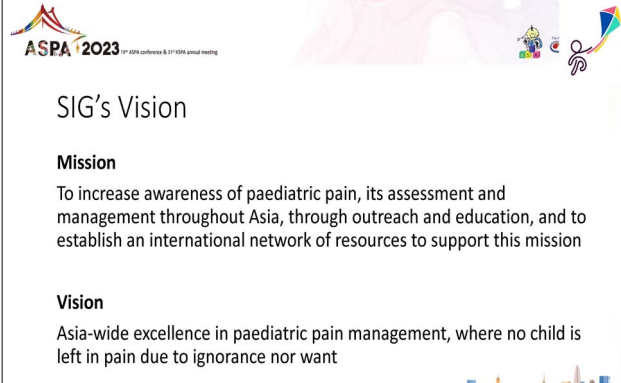
Pain  
Research  
Cardiac  
Patient Safety  
(Regional Anaesthesia- almost there..)



**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**ASPA Paediatric Pain Special Interest Group**

Honorary Advisor : Prof Allen Finley  
President : Angela Yeo  
President-Elect : Kathrina Epino  
Secretary : Teddy Fabila  
Treasurer : Jang Young-Eun  
Education : Andi Ade Ramlan  
Research : Ritu Pradhan  
Membership : Janice Ng  
Special Projects : Elvan Ocmen



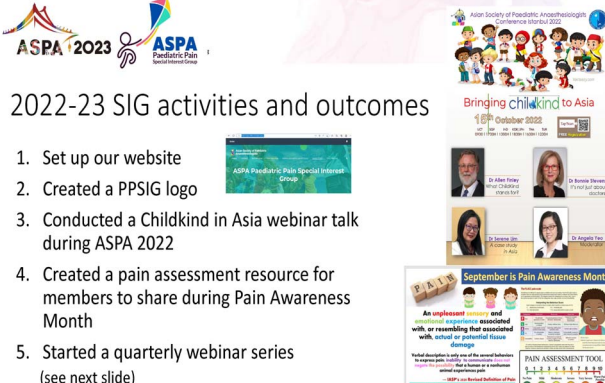
**SIG's Vision**

**Mission**

To increase awareness of paediatric pain, its assessment and management throughout Asia, through outreach and education, and to establish an international network of resources to support this mission

**Vision**

Asia-wide excellence in paediatric pain management, where no child is left in pain due to ignorance nor want




**2022-23 SIG activities and outcomes**

1. Set up our website
2. Created a PPSIG logo
3. Conducted a Childkind in Asia webinar talk during ASPA 2022
4. Created a pain assessment resource for members to share during Pain Awareness Month
5. Started a quarterly webinar series (see next slide)

Bringing childkind to Asia  
16<sup>th</sup> October 2022

September is Pain Awareness Month!



**2022-23 SIG activities and outcomes**

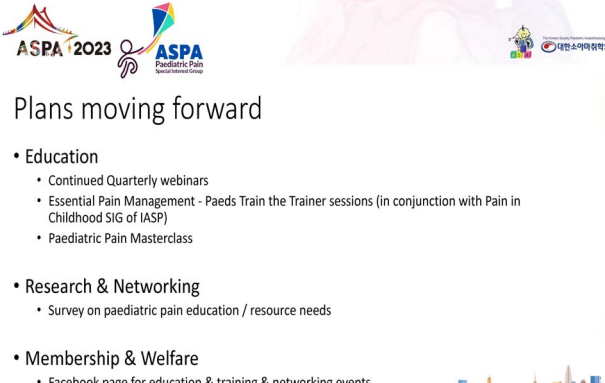
*Save the date!*

**8th July 2023 5pm SGT**

- Detecting neuropathic pain in children
- Managing neuropathic pain in children

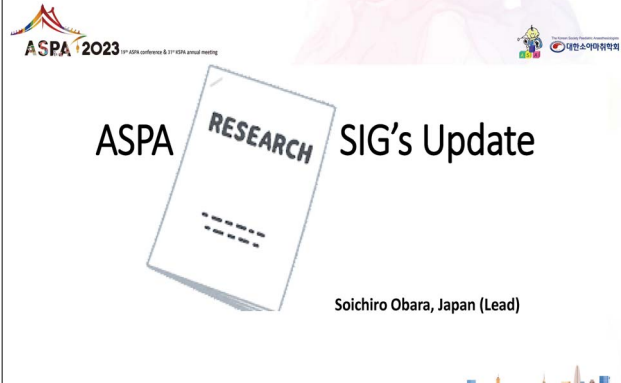
**14 Oct 2023 5pm SGT**

- Oncological pain
- Palliative pain
- Interventional Procedures in Chronic Cancer Pain



**Plans moving forward**

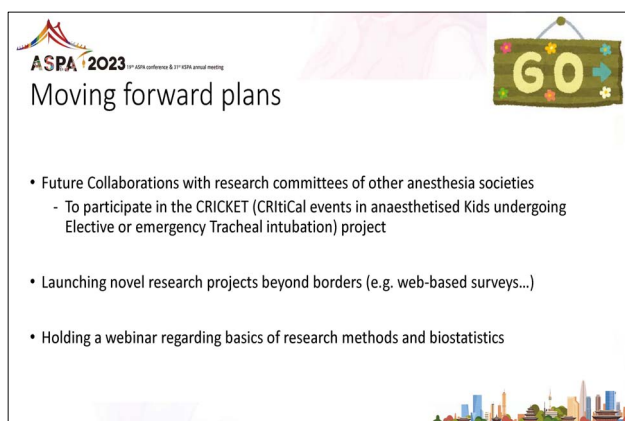
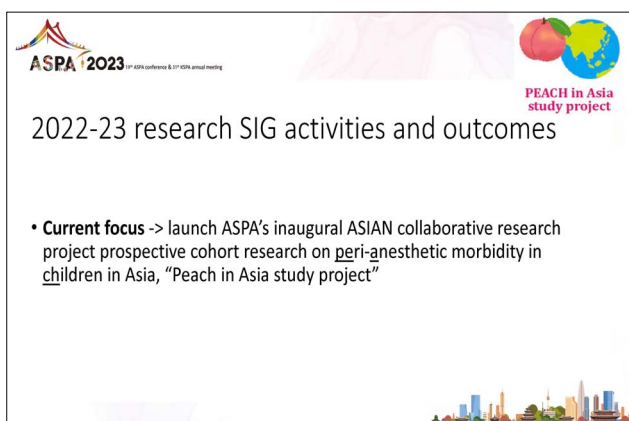
- Education
  - Continued Quarterly webinars
  - Essential Pain Management - Paeds Train the Trainer sessions (in conjunction with Pain in Childhood SIG of IASP)
  - Paediatric Pain Masterclass
- Research & Networking
  - Survey on paediatric pain education / resource needs
- Membership & Welfare
  - Facebook page for education & training & networking events



**ASPA RESEARCH SIG's Update**

Soichiro Obara, Japan (Lead)







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# Patient Safety


Special Interest Group

ASPA 2023 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

# Members

- Canan Bor (Turkey)
- Angelina Gapay (Philippines)
- Rebecca Jacob (India)
- Arif HM Marsaban (Indonesia)
- Siow Yew Nam (Singapore)
- **Erlinda Oracion (Philippines) - Lead**
- Sana Urooj Shaheer (Pakistan)
- Shu Ching Teo (Malaysia)
- Josephine Tan (Singapore)




ASPA 2023 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

# Patient Safety Module

**Learning Relevance:**


1. Participants recognize the importance of patient safety and the need to improve it in today's complex healthcare system.
2. The participants also know their role and individual responsibility for their patient's safety.
3. They understand that identifying the causes of critical incidents is the basis for developing proactive measures to improve patient safety.



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# ASPA FUTURE


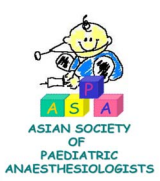

? Clinical Fellowship  
? Mentorship programme  
Collaborations & Partnerships



ASPA 2023 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

# To continue ASPA journey -

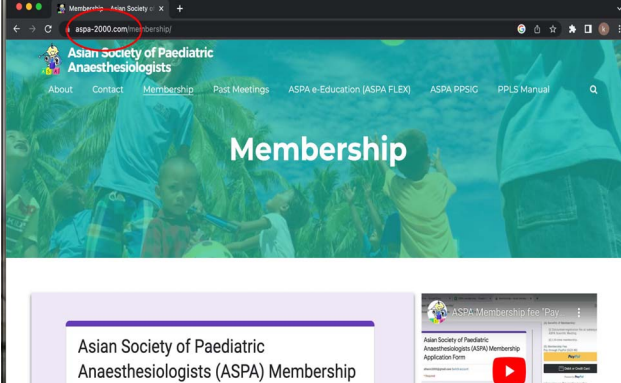
Younger members to step forward!

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# Membership

Asian Society of Paediatric Anaesthesiologists (ASPA) Membership Application Form



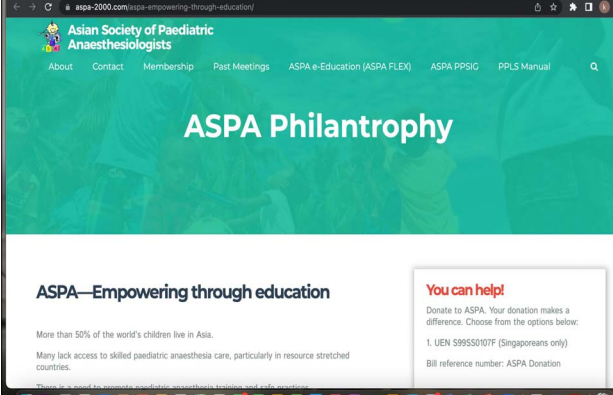
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# ASPA Philanthropy

ASPA—Empowering through education

More than 50% of the world's children live in Asia. Many lack access to skilled paediatric anaesthesia care, particularly in resource stretched countries.




**You can help!**  
Donate to ASPA. Your donation makes a difference. Choose from the options below:  
1. UEN S9553107F (Singaporeans only)  
Bill reference number: ASPA Donation



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# The Paediatric Anaesthesia Community:

# It's a small and wonderful world!



ASPA 2023 17th ASPA conference & 17th ASPA annual meeting



대한소아마취학회



Children in Asia receive  
safe anaesthesia care at  
any time, any place ...



# ESPA: How to Collaborate Internationally and Intercontinentally

Jurgen C. de Graaff

Erasmus Medical Center, Netherlands

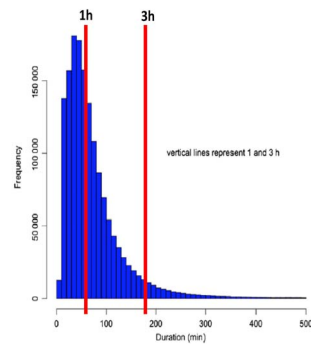
## Anesthesia in children is common!

- One in 7 children were exposed to general anesthesia before age 3 yrs.  
= 4 children per class/24 children



Shi et al. Ped Anesth, 2018; 15:51-519

## Most anesthetics in children are short



Bartels Ped Anesth 2018

## What do we measure Neonates ≠ Infants ≠ Children ≠ Adolescents

- Mortality
- Morbidity
  - less clearly defined compared to mortality

Overall perioperative  
Morbidity:

	Adults	Pediatrics
Mortality	1-4%	?
Myocardial infarction	1-3%	?
Stroke	0.1-0.7%	?
ARDS	0.2%	?
Acute kidney injury	1%	?

EuSOS-cohort, Pearse Lancet. 2012 Sep 22; 380(9847): 1059-1065.

## Pediatric perioperative outcomes are different... Neonates ≠ Infants ≠ Children ≠ Adolescents

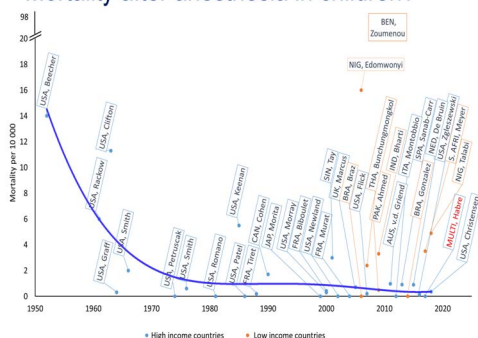
### Adults

- Mortality
- Myocardial infarction
- Kidney failure
- Perioperative stroke
- Thromboembolism
- Postoperative cognitive decline
- Return to work

### Children

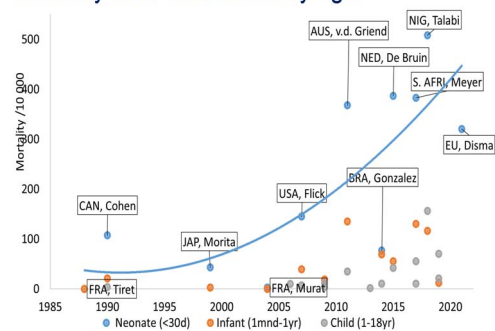
- Rare
- Rare
- Rare
- Rare
- Rare
- Postoperative behavior change
- Emergence delirium
- Parent proxy outcome measures
- Developmental/age-specific measures

## Mortality after anesthesia in children?



de Graaff Best Pract Res Clin Anesth 2021

## Mortality after anesthesia by age

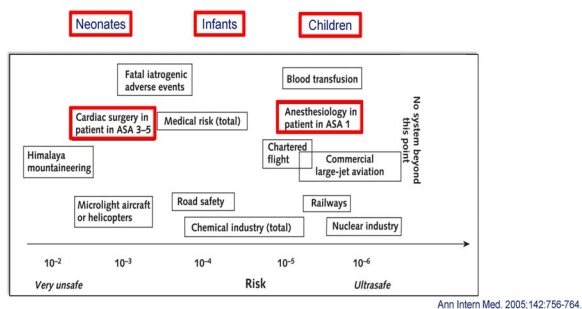


de Graaff Best Pract Res Clin Anesth 2021



## Five System Barriers to Achieving Ultrasafe Health Care

René Amalberti, MD, PhD; Yves Auroy, MD; Don Berwick, MD, MPP; and Paul Barach, MD, MPH

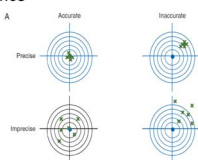


## Study design

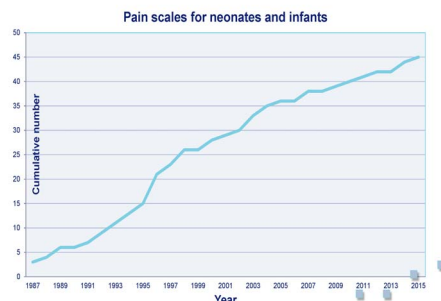
- Define aim study!
- Define primary outcome!
- Frequency outcome?
- Sample
  - Age
  - Location
- Sample size
- Tool outcome measure

## How do we measure outcome?

- Definition of outcome?
- Clinical relevance
- Defined minimal clinically important difference
- Metric properties
  - Validity
  - Reliability
  - Utility
  - Responsiveness



## Number of pain scales for neonates and infants



## Neonatal pain scales

Neonatal Infant Pain Scale (NIPS)			
N-PASS			
COVERS Scale			
FLACC scale			
Behavioral Observation Pain Rating Scale			
Categories	Scoring	0	1
Face	No particular expression or smile; distressed	Occasional grimace or frown, withdrawn	Frequent to constant frowns, clenched jaw, quivering chin
Legs	No position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or talking to. Distortable	Difficult to console or comfort

## Selection of pain instruments for (premature) neonates

Pain assessment instruments neonates	First author, year of first publication	Type of pain I procedural II postoperative III prolonged	Facial Expression	Body movement	Posture/ tone	Cry/ vocal	Behavioural state sleep pattern	Physiology	Consolability
NIPS	Lawrence et al. 1993	I	✓	✓✓	✓	✓	✓	✓	✓
BPS	Pokela et al. 1995	I	✓	✓	✓	✓	✓	✓	✓
CRIES	Krechei et al. 1995	II	✓	✓	✓	✓	✓	✓	✓
PIPP	Stevens et al. 1996	I / II	✓✓✓	✓	✓	✓	✓	✓	✓
DAN	Carbajal et al. 1997	I	✓	✓	✓	✓	✓	✓	✓
COMFORT-B	Van Dijk et al. 2000	II, sedation	✓	✓	✓	✓	✓	✓	✓
CHPPS	Buttner et al. 2000	II	✓	✓✓	✓	✓	✓	✓	✓
EDIN	Deblon et al. 2001	III	✓	✓	✓	✓	✓	✓	✓
BPNS	Cignacco et al. 2004	I	✓	✓	✓	✓	✓	✓	✓
BIIP	Holsti et al. 2007	I	✓✓✓✓	✓✓	✓	✓	✓	✓	✓
N-PASS	Hummel et al. 2008	II/III, sedation	✓	✓	✓	✓	✓	✓	✓
COMFORTneo	Van Dijk et al. 2009	II, III	✓	✓	✓	✓	✓	✓	✓
			100%	83%	67%	75%	42%	25%	

## Problems

- Large variability
- Large variation
- Difficult Meta-analysis
  - Variability undermines systematic reviews & meta-analyses
- Difficult combined outcome measures
- Selective outcome reporting
  - Report only outcomes of statistical or 'clinical' significance.

## Advantages of core outcome sets

- Increases consistency across trials
- Maximise potential for trial to contribute to systematic reviews of these key outcomes
- Much more likely to measure appropriate outcomes
- Major reduction in selective reporting

## Core outcome set:

An agreed standardized set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care



## Core Outcome Measures in Effectiveness Trials

[www.comet-initiative.org](http://www.comet-initiative.org)  
Twitter: @COMETinitiative



## Standardizing end points in perioperative trials: towards a core and extended outcome set

P. S. Myles<sup>1\*</sup>, M. P. W. Grocott<sup>1,2,3,4,5</sup>, O. Borczyk<sup>6,7</sup> and S. R. Moonesinghe<sup>1,5</sup>,  
on behalf of the COMPAC-SEP Group  
*British Journal of Anaesthesia* 116 (3): 586-9 (2016)

## Pediatric Perioperative Outcomes Group (PPOG)



## EDITORIAL

WILEY **Pediatric Anesthesia**

## Pediatric perioperative outcomes group: Defining core outcomes for pediatric anesthesia and perioperative medicine

Paul A. Stricker<sup>1</sup>   
Jurgen C. de Graaff<sup>2</sup>   
Laszlo Vutskits<sup>3</sup>  
Wallis T. Muhly<sup>1</sup>   
Ting Xu<sup>4</sup>  
Alexandra M. Torborg<sup>5</sup>  
Yifei Jiang<sup>6</sup>  
Suellen M. Walker<sup>7</sup>

## Goal Representation:

- Europe
- United Kingdom
- China
- South Africa
- Australia
- New Zealand
- United States
- India
- Colombia
- Canada

DOI: 10.1111/pan.12054

## EDITORIAL

WILEY **Pediatric Anesthesia**

## Pediatric perioperative outcomes group: Defining core outcomes for pediatric anesthesia and perioperative medicine

In 2015, the joint National Institute of Academic Anesthesia/James Lind Alliance Research Priority Setting published a top 10 list of research priorities for anesthesia and perioperative care in the UK.<sup>1</sup> These priorities were developed through a systematic process that engaged physicians, patients, and the public with the intent of identifying research questions broadly relevant to pertinent stakeholders. A subsequent editorial in this journal highlighted 4 priorities applicable to the care of children.<sup>2</sup>

One of the questions relevant to both adults and children was "What outcomes should we use to measure the success of anesthesia and perioperative care?" However, this research priority generates many more questions: What outcomes matter most to our patients and their families? What outcomes are most important to clinicians? What are the fundamental outcomes for clinical research? Are these outcomes aligned? Do we and can we routinely measure these outcomes, either in clinical practice or in clinical trials?

Care outcomes sets have been developed to address these questions across a wide range of medical disciplines. Consensus-based standardized outcomes are defined with the aim of reducing variability in the use and reporting of outcomes in clinical trials. In 2012, The Core Outcome Measures in Effectiveness Trials (COMET) initiative

the same "outcome" is used, variability in how that outcome is defined can make comparison of different trial results difficult. The use of standardized outcomes would greatly enhance the value of individual study results by enabling them to be seamlessly integrated into meta-analyses. The ability to combine results of multiple trials also helps address an ethical obligation of clinical research by enhancing the benefits and generalizability of data derived from human subject participation in research and minimizing unnecessary duplication.

Using COMET methodology, a core outcome set for adult perioperative medicine is being developed by a group of perioperative medicine clinicians and researchers. This initiative is described in greater detail elsewhere,<sup>3,4</sup> but in essence there are 2 parallel projects, COMPAC Core Outcome Measures for Perioperative and Anaesthetic Care is a collaborative effort that seeks input from patients, care givers, nurses, and physicians to determine what outcome domains should be included in a perioperative core outcome set. The parallel SEP (Standardizing Endpoints in Perioperative medicine) project is an expert-based Delphi consensus-driven effort to define how the specific outcomes within these domains should be measured.<sup>5</sup>

Both COMPAC and SEP focus on perioperative care of adults having major surgery, and as such many of the outcomes are more

## SPECIAL INTEREST ARTICLE

WILEY **Pediatric Anesthesia***Pediatric Anesthesia* 2020;30:1166-1182.

## A systematic review of outcomes reported in pediatric perioperative research: A report from the Pediatric Perioperative Outcomes Group

Wallis T. Muhly<sup>1</sup> | Elsa Taylor<sup>2</sup> | Cyrus Razzavi<sup>3,4</sup> | Suellen M. Walker<sup>5,6</sup> | Lei Yang<sup>7</sup> | Jurgen C. de Graaff<sup>8</sup> | Laszlo Vutskits<sup>9</sup> | Andrew Davidson<sup>10,11,12</sup> | Yunxia Zuo<sup>7</sup> | Carolina Pérez-Pradilla<sup>13</sup> | Piedad Echeverry<sup>13</sup> | Alexandra M. Torborg<sup>14</sup> | Ting Xu<sup>15</sup> | Ellen Rawlinson<sup>6</sup> | Rajeev Subramanyam<sup>1</sup> | Simon Whyte<sup>16</sup> | Robert Seal<sup>17</sup> | Heidi M. Meyer<sup>18</sup> | Sandhya Yaddanapudi<sup>19</sup> | Susan M. Goobie<sup>20</sup> | Joseph P. Cravero<sup>20</sup> | Aileen Keaney<sup>21</sup> | M. Ruth Graham<sup>22</sup> | Tania Ramos<sup>23</sup> | Paul A. Stricker<sup>1</sup> | on behalf of The Pediatric Perioperative Outcomes Group





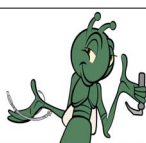
## How to collaborate?

- Clear Aim
- Accurate & precise international primary outcome
- Accurate sample size
- Define cohort
- Sample size
- Start simple, not too much!
- Work together and enjoy
- Have fun!



## JOIN THE CRICKET

CRITICAL EVENTS IN ANAESTHETIZED CHILDREN UNDERGOING TRACHEAL INTUBATION  
PROSPECTIVE, MULTI-CENTRE OBSERVATIONAL STUDY



### WHAT IS THE CRICKET STUDY

It is a prospective observational study looking at major complications occurring during tracheal intubation in children undergoing general anaesthesia.

### WHICH PATIENTS SHOULD BE INCLUDED

Children from 0 to 16 years requiring tracheal intubation for general anaesthesia performed by the anaesthesia team are eligible for the study. During the study period all children undergoing tracheal intubation should be included. Those experiencing a critical event will be followed up.

### HOW MANY PATIENTS SHOULD BE ENROLLED

Critical events are likely rare. For this reason we will need 100,000 (one-hundred-thousand) patients included. Then 500 centres are expected to participate the CRICKET study.

### WHICH CENTRES CAN TAKE PART TO THE CRICKET STUDY

All centres doing paediatric anaesthesia are welcome to join. They can be in all five continents. CRICKET is going to be a true worldwide international study.

## HOW CAN A CENTRE JOIN THE CRICKET STUDY

If you are interested in joining the study, scan the QR-code and fill in the online form.



[esac.org/research/research-groups/parnet/](https://esac.org/research/research-groups/parnet/)

## ESPA CONGRESS



## 13<sup>th</sup> European Congress for Paediatric Anaesthesiology

September 28–30, 2023  
Prague, Czech Republic

[www.espacongress.com](http://www.espacongress.com) | [www.euroespa.com](http://www.euroespa.com)





## **Session 2.**

# **WFSA Panel Discussion: Universal Coverage of Safe Pediatric Anesthesia All Over Asia**

**Chair(s): Erlinda Oracion (Philippines)  
Il-Ok Lee (Korea)**

# Universal Coverage of Safe Pediatric Anesthesia in Cambodia

Sokha Tep

National Pediatric Hospital, University of Health Sciences, Cambodia



## Contents

- Geography
- Introduction
- Current State of Pediatric Anesthesia in Cambodia
- Success Stories and Best Practices in Cambodia
- Barriers to Universal Coverage of Safe Pediatric Anesthesia in Asia
- Conclusion and Call to Action



## Overview of Cambodia



- Capital: Phnom Penh
- Currency: Cambodian riel
- King: Norodom Sihamoni
- Prime Minister: Samdach HUN SEN

[www.cambodia.org](http://www.cambodia.org)



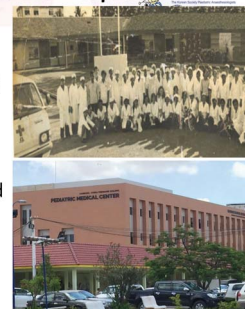
## Geography

- Location: Southeastern Asia
- Area: 181,035 sq km
- Climate: Tropical(Rainy, monsoon season)
- Population: 17,168,639 (July 2022 est.)
- Nationality: Cambodian
- Religions: Buddhist 97.6%
- Languages: Khmer (official)



## History of National Pediatric Hospital

- 1974: World Vision International(WVI) build the Hospital, Completed in March 1975.
- 1975 – 1979: Khmer Rouge Regime, not operational due to KR invasion.
- 1980: WVI and Ministry of Health renovated and opened on Oct 15<sup>th</sup>
- Now: National Pediatric Hospital(NPH)



## Cooperated by:

- KOICA: Pediatric Medical Center
- VITA AND FUTURA, CZECH REPUBLIC: GYNECOLOGY AND OBSTETRICS
- Foundation International Development and Relief/Japan(FIDR): PEDIATRIC SURGICAL PROJECT

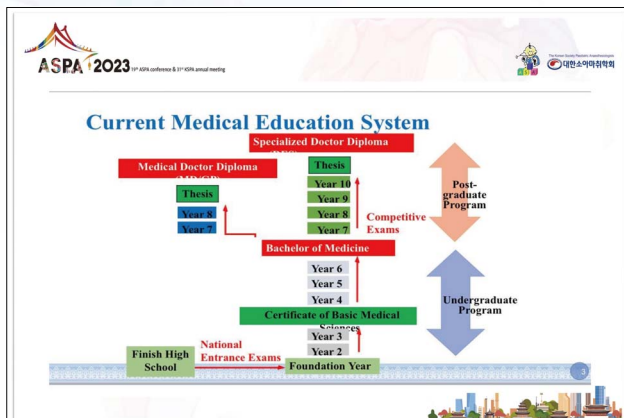


## Medical Universities in Phnom Penh, Cambodia

- 1- University of Health Sciences(UHS), 1946
- 2- International University(IU), Since 2002
- 3- Health Science Institute of Royal Cambodian Arm Force(RCAF), Since 1979
- 4- University of Puthisastra(UP), Since 2007







**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

### Introduction

Brief introduction to the Current State of Pediatric Anesthesia in Cambodia:

- => Continuous medical education and development practice
- => Limited some essential equipment and medications
- => Substandard patient monitoring
- => Postoperative pain management can practice in few hospitals only.
- => The limited of subspecialized training in Cambodia

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

### Current State of Pediatric Anesthesia in Cambodia(1)

- We have only 3 Pediatric hospitals that provide pediatric surgery services.
- Anesthesiologist provide pediatric anesthesia after short course training, or in hospital training only.
- We have limited some medication: neostigmine, naloxone, lipid emulsion(intralipid).
- Limit equipment using with small size in neonatal anesthesia.
- We still have nurse anesthetist providers in most hospital to care child under anesthesia.

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### Current State of Pediatric Anesthesia in Cambodia(2)

- We faced with old monitors because the new is expensive.
- We work with substandard equipment and try to provide the quality of child care services.
- We work and train medical doctor to be pediatric anesthetist in operative theater then send to other training center oversea.
- With pediatric anesthesia, we don't have specific curriculum in training yet.

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### Success Stories and Best Practices in Cambodia

- => FIDR(Foundation International Delovement/Relief:Japan): Pediatric Anesthesia Course :2010-2015
- => In-hospital training then apply to trainee in other country World Federation Society of Anesthesiologists as Bangkok Anesthesia Regional Training Center fellowship(1 year) to be anesthesiologist
- => Safe Pediatric anesthesia workshop training in Phnom Penh, Cambodia, 2022
- => Specialized 4 years training in University of Health Science after competitive exam from Medical Doctor/Bachelor of medicine.

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### Barriers to Universal Coverage of Safe Pediatric Anesthesia in Asia

- We have limited training of pediatric anesthesia in lower income countries( Cambodia, ...)
- Deficits in anesthesia infra structure, equipment and drugs.
- Asian countries doesn't have standard protocol practice.

**To be better in future:**

- We would like to request ASPA countries and members to support and anesthesia training in Asia regularly.
- Request Asian medical companies to supply low price.
- Asian countries should have standard protocols in pediatric practice and do training to all Asian anethetists regularly.

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### Conclusion and Call to Action

Safe pediatric anesthesia providing is a bit far from expectation, so each hospital have to guide:

- => Minimal standard monitor for pediatric anesthesia in Cambodia: ECG, HR, pulse oxymeter, blood pressure, Temperature
- => Minimized using equipment, drugs and reversal agents.
- => to do bedside teaching and training regularly
- => to join pediatric course Oversea as possible as they can
- => Asian countries should have standard protocols in pediatric practice and do training to all asian anethetists in low income countries.

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

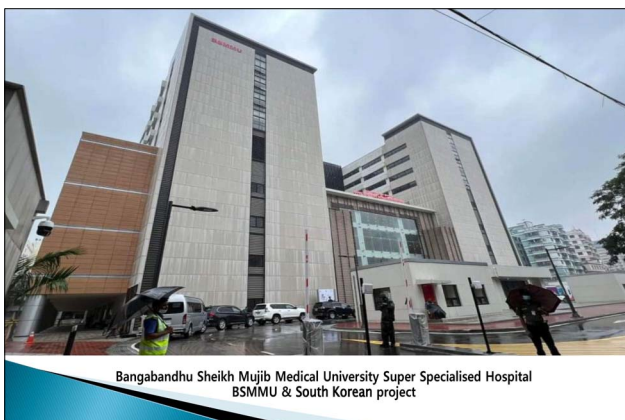
### LOCAL PEDIATRIC ANESTHESIA TRAINING



# Current Status of Pediatric Anesthesia In Bangladesh Challenges and Opportunities for Improvement

Debabrata Banik

Department of Anesthesia, Analgesia and Intensive Care Medicine,  
Bangabandhu Sheikh Mujib Medical University, Bangladesh



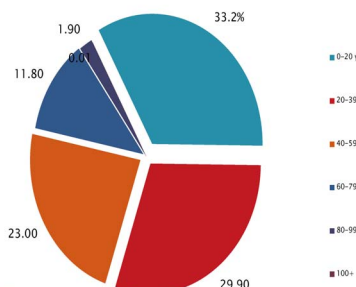
## Health care facilities and indicator

- ▶ Bangladesh has a good healthcare network covering both rural and urban areas, ( Health care facilities 3976 in public sector 975 in privates with 0.79 bed per 1000 ) and comparable to other Asian country with little difference in level of care – most difference in Skill due to lack of facility
- ▶ This country is hugely populated (1252 sq km with about 17 crore) which is 2.2 % whole world population

## Demography of Pediatric population in Bangladesh

Birth rate:	17.71 / 1000 population
Death rate	5.54/1000
Infant mortality :	22.9– 24.73/1000 live
Mortality under 5 year	27.27– 38/1000 live
Neonatal mortality	16 –20/ 1000 live birth
Anesthesiology Man power	1.2 / 100000
Pediatric Anesthesiologist	Not defined

## Population distribution / 1/3 pediatric population



Hospital facility for Pediatric surgical patient  
BSMMU : Different pediatric surgical subspecialty including pediatric cardiac surgery.

All government medical college (n=38) : Pediatric surgery  
Bed 10 to 30 bed /500 to 1000 bed hospital.

Child and maternal hospital  
(1) 30 bed Shishu hospital.  
(2) 50 bed.

Pediatric cardiac surgery Limited Bed

All above have a separate pediatric surgical unit

Private Clinic or Hospital: No definite pediatric surgical ward.

NICU And PICU : PICU very limited compare to NICU



## Every Anesthesiologist All over the world



## Anesthesia

- › Anesthesiology is one of the most demanding and essential specialty of modern medical science not only to provide anesthesia for surgical operation but also involve in the management of different medical condition.
- › Anesthesiology is the largest single hospital specialty.
- › But is probably the least well understood in the developing countries like Bangladesh



## Anesthesia

- › Anesthesiologists treat patients of all ages with a variety of medical problems.
- › Anesthesiologists provides anesthesia operate on wide range of cases, from heart and brain procedures to births and catastrophes.

## Anesthesia

- › In reality- Anesthesia is a rewarding and challenging specialty and acute in nature.
- › It is truly one of the few specialties where decisions made in critical situations can mean the difference between "life and death."
- › Among anesthesia specialty- pediatric anesthesia is more risky than other specialty

DS (Child) H J 2018; 34(1) : 3-4

### LEADING ARTICLE

## History of Pediatric Anesthesia in Bangladesh

Md. Shahidul Islam

Children are very special people who require special care in order to provide safe anesthesia. The history of pediatric anesthesia is the steps towards maintaining normal limits of neurologic, respiratory, cardiovascular and other body systems. The goal of the specialty of the pediatric anesthesiology is the reduction of perioperative morbidity and mortality and promotion of monitoring, resuscitation and supportive fields through teaching, research, organizational activity throughout the world.<sup>1,2</sup> Before discussing the history of pediatric anesthesia in Bangladesh I want to discuss what was the global condition. Before introduction of ether in 1846, circumcision,

believed that the development of modern pediatric anesthesia started in 1930.<sup>3</sup> The rapid growth of pediatric anesthesia was divided into two chronological categories. First were 1930 to 1950 and the second 1950 to present. During the first period the anesthesia techniques and equipment were developed. In the second phase with further techniques, equipment, refinement, modern anesthetics and vital system monitoring were introduced into everyday practice.<sup>9</sup> Ether and chloroform could be given for orthopedic and limb surgery but problems were with cleft lip, palate, abdominal, ENT and chest surgery.<sup>10</sup> Digital tracheal intubation with a soft rubber catheter was

## The history of pediatric anesthesia

- › The history of pediatric anesthesia in Bangladesh was miserable.
- › In early 1970 's the only agent was ether and chloroform to anesthetize the pediatric patient.
- › Pediatric endotracheal tube, laryngoscope, pediatric circuit and IV cannula was available late 1980
- › Pediatric surgeon and pediatric anesthetists were not available before 1980
- › Mortality rate was very high due to aspiration and respiratory depression in 1970-1980
- › The condition was horrible for the anesthetists and surgeon.

## The history of pediatric anesthesia in Bangladesh

- › Individual pediatric surgery started after 1980
- › Before 1980 all pediatric surgery was done by general surgeon
- › 1980 to 2000 pediatric anesthesia started to provided by qualified senior anesthesiologist

## Debabrata Banik: Current Status of Pediatric Anesthesia In Bangladesh Challenges and Opportunities for Improvement

## History of pediatric Anesthesia In Bangladesh

- ▶ But morbidity and mortality was high due to lack proper skill and institutional support.
- ▶ One study support only 13% qualified anesthesiologist provide safe pediatric anesthesia .
- ▶ Revolution for Specialty anesthesia started after 2000.
- ▶ When the patient safety is a pioneer and more medico legal issue came out -- Improved Action plan start

## Development of Specialty

- ▶ **Safety Issue:** Today high profile advances in surgical practice mostly depends on efficient and effective methods of anesthesia and intensive care medicine.
- ▶ More and more safety is a crucial point for surgical patient .
- ▶ So on this point surgical specialty divided into different surgical sub specialties and super specialties for more skill and successful outcome

## Development of Specialty

- ▶ The American College of Surgeons recognizes 14 surgical specialties:
- ▶ and in Royal college of Surgeon UK recognized 10 surgical specialties,
- ▶ With this changes in developed country was initiate the development of anesthesia subspecialty.
- ▶ Among them Pediatric anesthesia is most important subspecialty and it is different in all respect

## Development of Specialty

- ▶ In Bangladesh 17 surgical specialty with different division were created.
- ▶ Dental and medical faculty also divided into many subspecialty.
- ▶ However, in Bangladesh single Anesthesiologists have to performed wide range of clinical practice related to all surgical specialties for a long period
- ▶ So there is less scope to anesthesiologist to develop skill and Knowledge on a specific surgical specialty.

## Development of Specialty

- ▶ There were confidential report in Bangladesh that if anesthesia provided by specific subject specialty outcome is better in respect of morbidity and mortality.
- ▶ Pediatric Anesthesiologists works in more urgent and risky conditions specially neonatal surgery
- ▶ There is limited anesthetists are able to provide safe anesthesia for children.

*Pediatr Clin North Am 1994; 41: 1-14*



Journal of Anesthesia &amp; Critical Care: Open Access

Review Article



## Issues and challenges of pediatric anesthesia in Bangladesh

## Abstract

Geographically Bangladesh is located in an area where natural calamities like flood, cyclone, and drought are very common. The country is largely populated (125.5 Sq km) due to its fertile plain terrain with a good reserve of natural resources but as usual, we have a developing health management system. So, as a non-earning member of family women and children is the most vulnerable group of society. Children constitute more than one third (31.3 million) of total population on the other hand women constitute almost half (49.4%) as well. Due to low Gross Domestic Product (GDP), allocation of budget in health (0.92% of GDP) specifically for addressing children and maternal health is not sufficient. Despite the diversity in their geographical, linguistic, and political structures, Afghanistan, Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka face common health challenges. Moreover socioeconomic status of these countries differs very little, even though Bangladesh had achieved United Nations Award for successful reduction of infant (28.2/1000) and maternal mortality rate (170/1000) on Millennium Development Goals-4 during the 65<sup>th</sup> United Nations General Assembly.

Combined Military Hospital, Dhaka is a 1500 beds tertiary care teaching hospital which has 30 beds pediatric surgery ward, 130 beds pediatric medical ward, 10 beds neonatal ICU, 10 beds pediatric ICU and 30 beds adult ICU as well. On an average 100

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- ▶ After 2000 1<sup>st</sup> Pediatric anesthesia workshop was arranged with the help of WFSA and faculty was Prof Dilip Power from India
- ▶ Includes Pediatric anesthesia in Every post graduate training and course like DA, MD and FCPS
- ▶

## Pediatric anesthesia and Surgery - Outcome

Statistics of neonatal surgery in 2016 at Dhaka Shishu (Children) Hospital			Statistics of neonatal surgery from 2012 to 2016 at CMH, Dhaka		
Name of month	Total op	Total death	Year	Total op	Total death
January	78	12	2012	28	3
February	64	9	2013	31	5
March	62	13	2014	35	8
April	60	10	2015	43	7
May	67	14	2016	37	6
June	70	13	Total	174	29 (16.66)
July	74	11			
August	69	9			
September	72	10			
October	66	8			
November	57	6			
December	63	15			
Total	802	130 (16.20%)			



### High mortality rate in pediatric surgical patient

#### Causes of death in Dhaka children hospital 2016

- Delayed reporting sick and delayed intervention
- Complex medical diseases & co-morbidity
- Ongoing sepsis & multi-resistant organisms
- Hospital set-up is not well equipped
- Peripheral hospitals are neither well prepared & equipped
- Lack of trained staffs
- Maternal causes: poor nutrition, preterm, multiple pregnancies

Less skilled manpower specially anesthesiologist ?  
Overload of work for anesthesiologist

#### Causes of death in military hospitals 2012 to 2016

- Military hospitals having a very effective chain of evacuation system from field hospital to base hospital
- Good infrastructure with excellent instrumental support
- Trained manpower
- Qualify Anesthesiologist

But mortality is same compare to other hospital  
So patient factor and management protocol is very important  
Not all related to anesthesia

Pediatric Anesthesiologist is providing different surgery of following Diseases with different surgical specialty

- ▶ Pediatric surgery
- ▶ Hernia . Esophageal atresia with/without fistula / Intestinal atresia. Biliary atresia or deformity
- ▶ A diaphragmatic hernia , Eventration of diaphragm
- ▶ Mesenteric cyst , Myelomeningocele
- ▶ Gastroschisis , Omphalocele PUV UDT ARM
- ▶ Hirschsprung's disease, Intussusceptions, Rectal polyp
- ▶ IHPS. Hydrocephalus, Hypospadias, Tongue tie
- ▶ Appendicitis .Cholecystectomy . Child hood cancer etc.

### CURRENT STATUS OF PEDIATRIC ANESTHESIA IN BANGLADESH



Rare cerebrovascular disease MOYAMOYA mandates anesthesiologists to formulate an individualized anaesthetic plan for these patient



### Common Surgical procedure in pediatric patient in Bangladesh

Pediatric Anesthesia is providing in the different surgery with following Diseases or specialty

- ENT :- Adenoidectomy Tonsillectomy / Mostioidectomy
- ▶ Orthopedic :- Correction of structure abnormality, Trauma
- ▶ Neurosurgery :- Congenital Hydrocephalus ,Meningocele, Brain tumor
- ▶ Endo Leparoscopic :-Lap Chol,Appen, ERCP, Splenectomy
- ▶ Anesthesia outside operation theater:- CT scan MRI,Endoscope ,Bronchoscope
- ▶ Plastric Surgery :- Cleft lip,palette other structural abnormal or burn or burn contracture
- ▶ Pediatric kidney Transplant :- Kidney transplant
- ▶ Pediatric cardiac surgery : Correction of congenital cardiac disease . Open heart surgery ,Non invasive procedure

### Common anesthetic Technique in Pediatric surgery

Mostly Provide General anesthesia with or without tracheal intubation.

Regional anesthesia combined General anesthesia or independent in specific and limited surgery .

Among them caudal , spinal is commonly practice

Monitoring anesthesia or proper way of sedation anesthesia of pediatric patient is less practice

### Common anesthetic Technique in Pediatric surgery

#### Anesthetic Drugs

IV induction TPS, Propofol Ketamine

Inhalation :Halothan ,Isoflurane and Sevoflurane

Opioid : Pethidine and Fentanyl

Muscle relaxant ; Suxa, Rocurium,Vecurium Atracurium

Local Anesthetic : Lignocaine , Bupivacaine

Monitoring : Clinical.SPO2.BP ECG Limited ETCO2 Precordial Stethoscope

Per operative Fluid :open

Post operative Analgesic : Paracetamol, NSAID , Pethidine and caudal block

#### Original article

#### Paediatric Spinal Anaesthesia

MD. Kabir Rahman, S. S. Hossain, Kabir Rahman

Department of Anaesthesia, Dhaka Shadhin Hospital, Dhaka

Corresponding author: Email: kabbir@shadhin.gov.bd

#### Abstract

Spinal anesthesia is a valuable form of regional anesthesia that can be considered a useful practice for children. However, the use of spinal anesthesia has been an important anesthetic technique for providing the children (paediatric) general anesthesia and sedation. Spinal anesthesia provides good anesthesia in general anesthesia in children with congenital heart disease, and it is also useful for sedation and analgesia in children with congenital heart disease. It is a most commonly used a simple and safe technique. Spinal anesthesia is a valuable technique for children with congenital heart disease. Spinal anesthesia is a valuable technique for children with congenital heart disease.

Keywords: Paediatric, Spinal anesthesia, Regional anesthesia

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#### Review article

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## Debabrata Banik: Current Status of Pediatric Anesthesia In Bangladesh Challenges and Opportunities for Improvement

## CURRENT STATUS OF PEDIATRIC ANESTHESIA IN BANGLADESH

- Pediatric patient is not a miniature of adult
- So it needs special knowledge and skill to provide safe pediatric anesthesia
- Pediatric anesthesia can be divided into three group Intrauterine life, neonatal and infant to adolescent
- Considering this: BSA-CCPP and university take some initiative to improve by providing short term training and organised SAFE pediatric courses.
- One international workshop arranged - Faculty Prof Dilip Power in 2000 supported by WFSA.
- Arranged Three SAFE course: Faculty from UK, Australia and IRLAND supported by WSFA and AAI8 -2012 to2020
- After this there may reduced mortality but not morbidity which reflect in recent studies

## SAFE PEDIATRIC Course



## EAS Journal of Anaesthesiology and Critical Care

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Published By East African Scholars Publisher, Kenya

Volume 5 | Issue 1 | Jan-Feb-2023 |

DOI: 10.36348/easj.2023.v05i01.001

## Original Research Article

## Complication of Anesthesia in Children: A Prospective Observational Study

Dr. Asma Afroze<sup>1</sup>, Dr. Rehan Uddin Khan<sup>2</sup>, Dr. Chandra Shekhar Karmakar<sup>3</sup><sup>1</sup>Assistant Professor, Department of Anaesthesia, ICU & Pain Medicine, Shahed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh<sup>2</sup>Associate Professor, Department of Anaesthesia, ICU & Pain Medicine, Shahed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh<sup>3</sup>Assistant Professor, Department of Anaesthesia, ICU & Pain Medicine, Bangladesh Sheikh Mujib Medical University (BSSMU), Dhaka, Bangladesh

## Article History

Received: 08-11-2022

Abstract: Background: Any anaesthetic procedure, either regional or general, has some potential for complications. For this reason, careful preoperative assessment

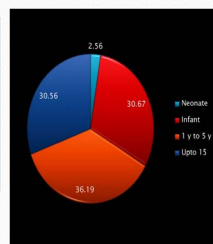
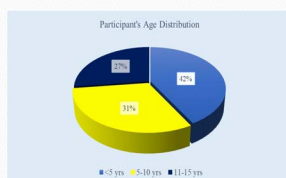
## Patient status according to ASA

Shahed Suhrawardy Medical College and Hospital,  
Dhaka, Bangladesh January 2018 to December 2018

BSMMU Year report 2021 to 2022

ASA Score	n	%	ASA Score	n	%
ASA I	42	68%	ASA I	1062	59.23%
ASA II	12	19%	ASA II	605	33.74%
ASA III	4	7%	ASA III	78	4.35%
ASA IV	2	3%	ASA IV	16	0.89%
ASA V	2	3%	ASA V	2	0.11%
	62	100%	Emergency	30	1.69%
				1793	100%

## Pediatric anesthesia in different aged group



Age - Shahed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh January 2018 to December 2018

BSMMU 2021 to 2022

## Pediatric anesthesia for different surgical speciality

Pediatric surgery bed 10			Pediatric surgery bed 40		
Surgical Procedures	n	%	Surgical Procedures	n	%
General surgery	30	48%	Pediatric surgery Dept	1305	72.78%
ENT	11	18%	ENT	115	6.41%
Orthopedics	8	13%	Orthopedics	31	1.72%
Maxillofacial	6	10%	Maxillofacial	2	0.11%
Ophthalmic	5	8%	Ophthalmic	68	3.79%
Cardiothoracic	2	3%	Cardiothoracic	30	1.67%
			Urology	20	1.11%
			Plastic Surgery	32	1.78%
			Outside OT/Procedural	190	9.92%
Total	62	100%		1793	100%

## Anesthetic technique

Anesthetic technique Medical college hospital			Technique		
Technique	n	%	Technique	n	%
General anesthesia	54	87.1%	General anesthesia	837	46.68%
General anesthesia & local infiltration	3	5%	General anesthesia & local infiltration	205	11.43%
General anesthesia & caudal block	4	6%	General anesthesia & caudal block	408	22.75%
Subarachnoid block	1	2%	Subarachnoid block/epidural	172	9.59%
			Monitoring anesthesia	171	9.53%

## Morbidity in Pediatric Anesthesia

Per-operative Complication Medical college hospital			Complications N 1703		
Complications	n	%	Complications	N	%
Bronchospasm	7	11%	Bronchospasm	50	2.78%
Bradycardia	6	10%	Bradycardia	69	3.38%
Hypotension	5	8%	Hypotension	67	3.73%
Hyperventilation	4	6%	Hyperventilation/induced hyperventilation	34	1.89%
Tachycardia	4	6%	Tachycardia	156	8.70%
Laryngeal spasm	4	6%	Laryngeal spasm	57	3.17%
Hypertension	4	6%	Hypertension	61	3.40%
Apnoea	4	6%	Apnoea	5	0.27%
Dysrhythmia	3	5%	Dysrhythmia	103	5.74%
Total Morbidity	41	64%	Hypothermia	67	3.73%
Cardiac arrest table	2	3%	Total	669	37.31%
			Cardiac arrest On table	6	0.32%



### Morbidity in Pediatric Anesthesia

Post-operative Complication Medical and/or hospital			Post-operative Complication : BSMMU		
Complications	n	%	Complications	n1793	%
Tachycardia	12	19%	Air way obstruction/hypoxemia	75	4.18
Prolonged unconsciousness	6	10%	Tachycardia	185	10.31
Hypoventilation	5	8%	Prolonged unconsciousness/delay recovery	45	2.50
Restlessness	3	5%	Hypocapnia/hypoxemia	105	5.85
Respiratory arrest	3	5%	Restlessness	209	11.65
Pain	3	5%	Respiratory arrest	21	1.17
Shivering	3	5%	Pain inadequate control	107	5.96
Hypotension	2	3%	Shivering	121	6.74
Hypertension	2	3%	Hypotension	81	4.51
Hemorrhage	2	3%	Hypertension	65	3.62
Laryngospasm	2	3%	Hemorrhage	43	2.39
Bronchospasm	2	3%	Laryngospasm	67	3.73
			Bronchospasm	75	4.18
			Total	1132	63.13

### Mortality Pediatric surgery IN BSMMU 2022

Age and group	N Operation done	Mortality	%
Neonatal	130	16	12.3%
Infant	579	3	0.51%
Pre school	583	2	0.34%
Aldocent	501	1	0.19%
Pediatric cardiac surgery	85	15	17.64%
On table mortality		2	All other in post operative period



BJA

British Journal of Anaesthesia, 126 (6): 1157–1172 (2022)

doi: 10.1016/j.bja.2021.02.016

Advance Access Publication Date: 1 April 2022

Paediatric Anaesthesia

#### PAEDIATRIC ANAESTHESIA

#### Morbidity and mortality after anaesthesia in early life: results of the European prospective multicentre observational study, neonate and children audit of anaesthesia practice in Europe (NECTARINE)

Nicola Dima<sup>1,\*</sup>, Francis Veyckemans<sup>2</sup>, Katalin Virag<sup>3</sup>, Tom G. Hansen<sup>4,5</sup>, Karin Becke<sup>6</sup>, Pierre Harlet<sup>7</sup>, Laszlo Vutsikits<sup>8,9</sup>, Suellen M. Walker<sup>10</sup>, Jorgen C. de Graaff<sup>11</sup>, Marzena Zielinska<sup>12</sup>, Dusica Simic<sup>13</sup>, Thomas Engelhardt<sup>14</sup> and Walid Habre<sup>4,5</sup>, for the NECTARINE Group of the European Society of Anaesthesiology Clinical Trial Network<sup>†</sup>

<sup>1</sup>Department of Anaesthesia, Unit for Research & Innovation, Istituto Giannina Gaslini, Genova, Italy; <sup>2</sup>Département d'Anesthésie-Réanimation pédiatrique, Hôpital Jeanne de Flandre, CHU de Lille, Lille, France; <sup>3</sup>Department of Medical Physics and Informatics, University of Szeged, Szeged, Hungary; <sup>4</sup>Department of Anaesthesia and Intensive Care - Paediatrics, Odense University Hospital, Odense, Denmark; <sup>5</sup>Department of Clinical Research - Anaesthesiology, University of Southern Denmark, Odense, Denmark; <sup>6</sup>Department of Anaesthesia and Intensive Care, Croft Children's Hospital/Hospital Hallerwiese, Nürnberg, Germany; <sup>7</sup>Research Department, European Society of Anaesthesiology.

### Audit report on pediatric anesthesia

Critical events requiring intervention occurred in 35.2% of cases--

- ▶ Mainly hypotension (>30% decrease in blood pressure) or reduced oxygenation (SpO2 <85%).
- ▶ Postmenstrual age influenced the incidence and thresholds for intervention.
- ▶ Risk of critical events was increased by prior neonatal medical conditions, congenital anomalies, or both.

### Audit report on pediatric anesthesia

- ▶ The incidence of peri-operative complications and mortality is higher in neonate and infant than in older children,
- ▶ Specific impact of anaesthesia technique and management has not been fully characterized.
- ▶ Alterations in perioperative physiological parameters have a significant factors affecting early and late neuro-developmental and health outcomes.

## Debabrata Banik: Current Status of Pediatric Anesthesia In Bangladesh Challenges and Opportunities for Improvement

**Challenges**

1. **Administrative and Financial**
  - a. Capacity building and organized health management system is still going on
  - b. Socioeconomic status of Bangladesh is developing
2. **Infrastructure** : a. Many of our Hospital are inadequate for specialized facilities,  
b. Universal precaution and awareness for infection control is insufficient in theater & PICU, NICU
3. **Shortage of Skill manpower** , **anesthesiologist** and supporting staff.
4. **Need Motivation** and remunerations ,reorganization
5. **Lack of Social awareness** with various superstitions
6. **Government planning**

**Opportunities For Improvement**

- › **Regional and international co-operation is essential** led by AAPA And WFSA
- › Arrange Short term training program for qualifying anesthesiologist and OT and post operative nurses Like **SAFE pediatric Courses**
- › Special training schedule in all post graduate program at least 3 month to one year.
- › Training exchange program within developed and developing Country
- › **One year fellowship program** organized by **BSMMU** and scholarship from **WFSA**

**Recommendation/Conclusion**

- › **Neonates and infants** have limited physiological reserve, and carries high risk of complications with general anesthesia specially **Premature neonates**
- › Present study quantifies the important physiological aberrations and their risk factors.
- › A high degree of training and skill are required for safe delivery of anaesthesia for neonates and infants for specialised pediatric surgery

# Universal Coverage of Safe Pediatric Anesthesia all over the World: WFSA pediatric Anesthesia Committee

Norifumi Kuratani

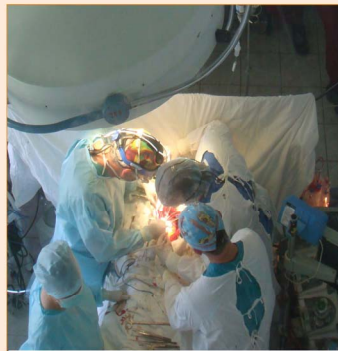
Saitama Children's Medical Center, Japan

## Outline

Inequity in safe pediatric anesthesia

WFSA

Pediatric committee



Pediatric Cardiac Surgery Mission, Kharkiv, Ukraine, 2012



0 ✓  
1

Inequalities in safe pediatric anesthesia

## GA for inguinal hernia repair



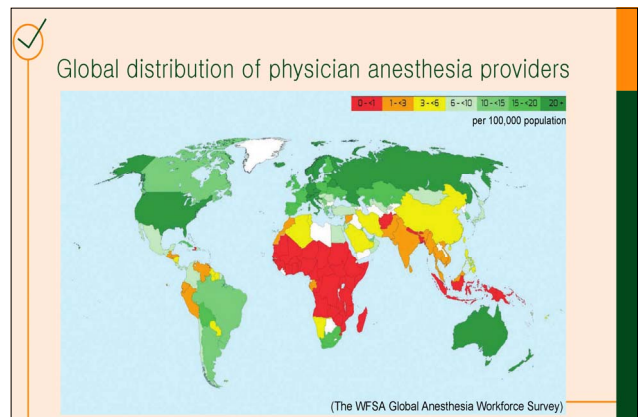
district hospital at Kampong Cham, Cambodia, 2010



district hospital at Kratie, Cambodia, 2019



PACU, National Children's Hospital, Mongolia,





Norifumi Kuratani: Universal Coverage of Safe Pediatric Anesthesia all over the World: WFSA pediatric Anesthesia Committee

Safe Pediatric Anesthesia *Inequalities*

## High income countries

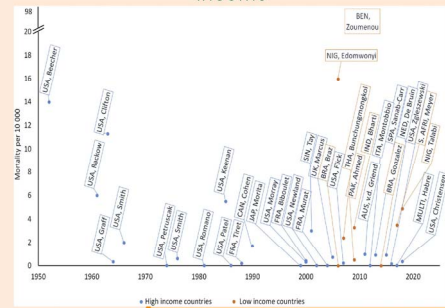
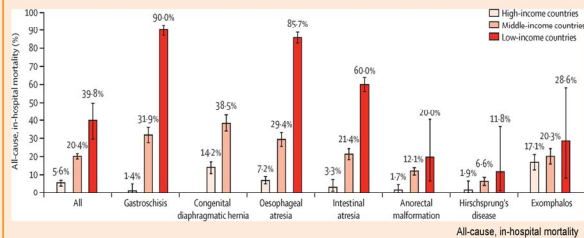
- Mortality is very low
- Good educational resources
- Good equipments and stable supply
- Latest medications
- Higher providers density



## Low-Middle income countries

- Mortality is higher? (Sparse data)
- Poor educational resources
- Old and less maintained equipments
- Older medications
- Lower providers density

## Anesthesia-related mortality stratified by country income

Disparities in outcome of common pediatric surgical diseases  
Lancet. 2021 Jul 24;398(10297):325-339.02  
WFSA

## Our Vision

Universal access to safe anaesthesia.

## Our Mission

To unite and empower anaesthesiologists around the world to improve patient care.

WFSA activities *in numbers*

136

Member Societies

450+

Anesthesia tutorials of the week

4827

Clinicians trained WFSA-lead courses



## 1. WFSA pediatric anesthesia committee member

Title	First name	Surname	Committee	Non Society
Professor	Desaien	Reddy	Pediatrics	Canada
Professor	Savadeh	Savadeh Asaf	Pediatrics	Canada
Professor	Zahra	Zahra	Pediatrics	Canada
Professor	Chandrasekhar	Chandrasekhar	Pediatrics	Canada
Dr.	Debarshi	Debarshi	Pediatrics	Canada
Dr.	Adisa	Advisi	Pediatrics	Canada
Dr.	Elana	Vivian Villanar	Pediatrics	Canada
Dr.	Nils	Denhardt	Pediatrics	Canada
Dr.	Maria Alejandra	Colotto	Pediatrics	Canada
Dr.	Yusuf	Yusuf	Pediatrics	Canada
Dr.	Shah	Vaso	Pediatrics	Canada
Dr.	Norumi	Kurata	Pediatrics	Canada
Dr.	Suzanne	Nabulindo	Pediatrics	Canada
Dr.	Indu	Kapoor	Pediatrics	Canada
Dr.	Manjula	Manjula	Pediatrics	Canada
Dr.	Larissa	Orang	Pediatrics	Canada
Dr.	Janet	Tumuhundu	Pediatrics	Canada
Dr.	Yvonne	Kovale	Pediatrics	Canada





## Ongoing Committee Projects

### SAFE Course

Implementing SAFE pediatric anesthesia course all over the world

### Textbook

Case-based pediatric anesthesia textbook authored by committee members

### Webinars

Working together with ASPA providing educational resources

### Fellowship

Development of new pediatric anesthesia fellowship program in Bosnia and Herzegovina

### PEACH

Epidemiologic study to learn the incidence of critical adverse events in pediatric anesthesia

### Cancer Care

Anesthesia is important in pediatric oncology care

## SAFE Pediatric Course

- WFSA, AAGBI, SAFE steering committee
- 3 days course
- Interactive course, few didactic lectures
- Education materials (manuals, video, tests...)
- SAFE for GBI version (for developed countries)
- train the trainer course → trainees to be a tutor



## SAFE pediatric anesthesia & ToT course in Cambodia

Nov. 18-20, 2022



## Anesthesia workforce data

### Anaesthesia Workforce Data

- PAP Density: 2.89
- Population: 15,578,000
- Physicians: 2,440
- Physician anaesthesia providers: 450
- Surgeons: No data
- Nurse anaesthesia providers: 100
- Other anaesthesia providers: 0
- No. of physician providers that have an anaesthetic qualification: 150
- Minimum duration of training (years) for physician anaesthesia providers: 3
- Typical duration of training (years) for nurse anaesthesia providers: 2
- Typical duration of training (years) for non physician / non-nurse anaesthesia providers: 0

Capital : Phnom Penh  
Population : 15M  
Life expectancy: 67y  
<5y mortality rate: 25.68



Faculties	SAFE pediatric course	Train the Trainer
<ul style="list-style-type: none"> <li>• Faculty leaders <ul style="list-style-type: none"> <li>➢ Lowri Bowen (UK, SAFE steering committee)</li> <li>➢ Nori Kuratani (Japan, WFSA pediatric chair)</li> <li>➢ Tep Sokha (Cambodia, SCARMU)</li> </ul> </li> <li>• UK:4, Japan:4, Cambodia:5</li> </ul>	<ul style="list-style-type: none"> <li>• 2 days course</li> <li>• 5 lectures, 19 modules</li> <li>• 26 local providers trained</li> </ul>	<ul style="list-style-type: none"> <li>• 1 day course</li> <li>• 10 new trainers</li> </ul>





## Ongoing Committee Projects

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## Pediatric Anesthesia fellowship program at Bosnia and Herzegovina



## Anesthesia workforce data

- PAP Density: 6.04
- Population: 3,810,000
- Physicians: 6,224
- Physician anaesthesia providers: 230
- Surgeons: 275
- Nurse anaesthesia providers: 0
- Other anaesthesia providers: 0
- No. of physician providers that have an anaesthetic qualification: 195
- Minimum duration of training (years) for physician anaesthesia providers: 5
- Typical duration of training (years) for nurse anaesthesia providers: 0
- Typical duration of training (years) for non physician / non-nurse anaesthesia providers: 0

Capital : Sarajevo  
Population : 3.8M  
Life expectancy: 77y  
<5y mortality rate: 5.86

## Norifumi Kuratani: Universal Coverage of Safe Pediatric Anesthesia all over the World: WFSA pediatric Anesthesia Committee

## Progress

- Requested by Dr. Adisa Šabanović Adilović, B&H society
- Draft program developed and discussed in pediatric committee
- Approved and endorsed by
  - Medical chamber Zenica-Doboj Canton
  - Cantonal Hospital Zenica
  - Association of anesthesiologists of the Federation of BiH
  - Faculty of Medicine Zenica
  - Ministry of Health Zenica-Doboj Canton
- Waiting for WFSA approval



## Program overview



### Practice

- 3 month
- Zenica hospital
- Dr. Adisa Šabanović Adilović
- To acquire competency



### Lectures

- Didactic lectures
- Case-conference
- Online by committee members
- To learn theoretical background



### Evaluation

- Formative and summative evaluation



### Site visit at Cantonal Hospital, Zenica, B&H

to view the actual education settings and conduct interviews with staffs, surgeons, directors, and fellow candidates.

(Oct. 18, 2022)

### Ongoing Committee Projects

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#### PEACH

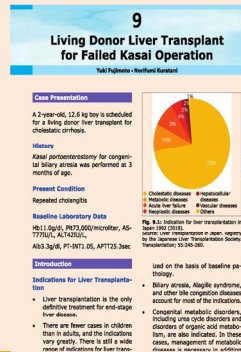
Epidemiologic study to learn the incidence of critical adverse events in pediatric anesthesia

#### Cancer Care

Anesthesia is important in pediatric oncology care

### Case-based Textbook in Pediatric Anesthesia

- Authoried by committee members and colleagues
- Focus on important cases (>40 topics) with an easy-to-read format
- Sections: Case presentation, disease pathophysiology, anesthesia considerations
- Encourages individual perioperative management plans
- Includes do's and don'ts, controversial areas (Pros and Cons), and author's anesthesia recipe



### Ongoing Committee Projects

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#### Cancer Care

Anesthesia is important in pediatric oncology care

### PEACH in Asia study

#### Design

- multinational, multicenter, prospective, observational study

#### Outcome measures

- Primary: Incidence of severe critical events

- laryngospasm, ② bronchospasm, ③ pulmonary aspiration, ④ drug error, ⑤ anaphylaxis, ⑥ cardiovascular instability, ⑦ neurological damage, ⑧ peri-anesthetic cardiac arrest, ⑨ post-anesthetic stridor

[Time Frame: Children will be followed for the duration of their anesthesia procedure and up to 60 minutes afterwards]

- Secondary:

- Risk factors for the occurrence of severe critical events
  - Consequences of the critical events: irreversible damage, in-hospital mortality
- [Time Frame: in-hospital and up to 30 days]

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*Pediatric Committee Webinar:*  
*"Anesthesia and Oncology Care in Pediatrics"*

- Anesthesia Consideration for Pediatric Oncology Patients: case presentation
- "Iterative Anesthesia," by  $\Delta$ Lucas Optiz (France)
- "Pain Management for Pediatric Oncology Patients"
- "Procedural Sedation for imaging and radiation therapy"

2023 ANNUAL THEME:  
**ANAESTHESIA AND CANCER CARE**  
 #OncoAnaesthesia

WFSA  
 WORLD FEDERATION OF SOCIETIES OF ANAESTHESIOLOGISTS

Satellite program of JSPA2023



## Conclusions

**Unmet need**  
 is common for safe pediatric anesthesia

**Education**  
 is key to change

**Work together**  
 to implement safe pediatric anesthesia all over the world



**SAFE**  **WFSA**  
 Safe Anesthesia From Education World Federation of Societies of Anesthesiologists



# Activities and Accomplishments of the WFSA BARTC Pediatric Fellowship Program

Patcharee Sriswasdi

Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, USA

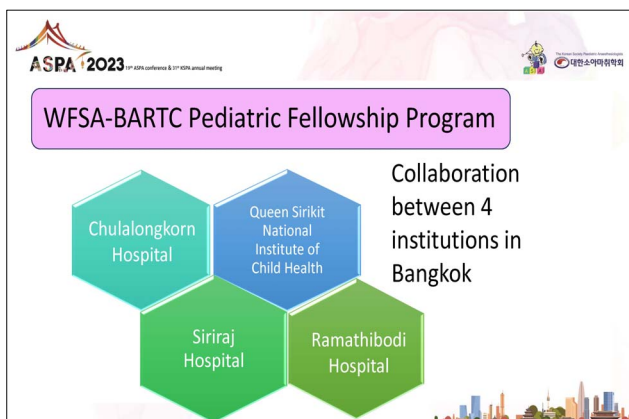
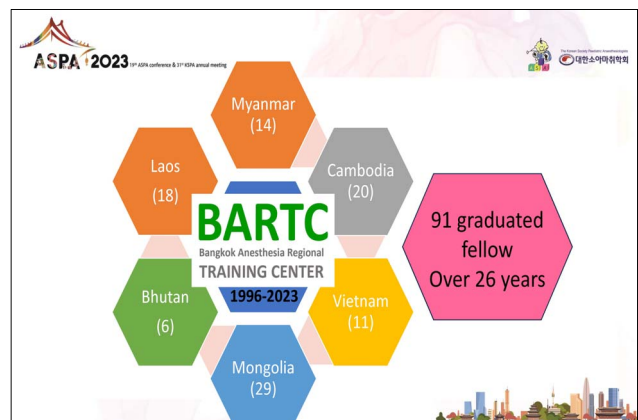
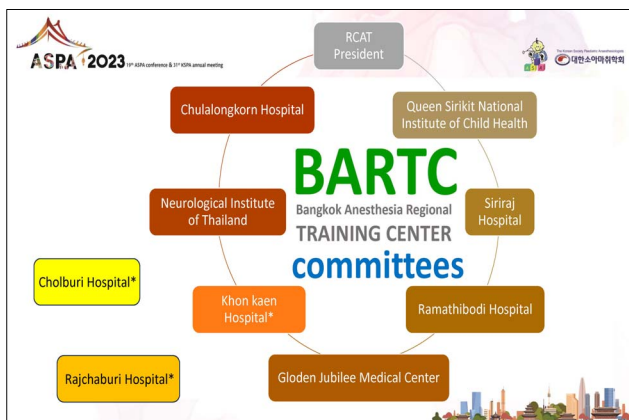


**BARTC**  
Bangkok Anesthesia Regional  
TRAINING CENTER

- Departments of Anesthesiology of 3 Teaching Hospitals
- A Pediatric Center Hospital
- 2 Provincial General Hospitals (Cholburi Hospital and Rajchaburi Hospital)
- 1 year training for fellows

• Professor Thara Tritrakarn  
• Founded in 1996  
• World Federation of Societies of Anesthesiologists (WFSA) and the Royal College of Anesthesiologists of Thailand (RCAT).

• Our goal is to promote safe anesthesia for patients in developing countries in Asia.  
• Our strategy is to train future trainers to form a critical mass and enable them to teach junior colleagues and students in their own countries.



**WFSA-BARTC Pediatric Fellowship Program**

- 1 year fellowship in pediatric anesthesia
- 1 fellow per year (12 months from January to December)
- Announce on <https://www.wfsa-bartc.org> in July – August
- Interview in September using Zoom
- Announce the result by the end of September



ASPA 2023 17th ASPA conference & 17th KSA annual meeting

## WFSA-BARTC Pediatric Fellowship Program

Applicant requirement

- He/she works in a Government hospital and will return to this institution work after the training. (with letter recommendation from the Head of Department where he/she works)
- Recommendation from the Society of Anesthesia in his/her country.
- Work as an anesthesiologist for at least 3 years




ASPA 2023 17th ASPA conference & 17th KSA annual meeting

## WFSA-BARTC Pediatric Fellowship Program

Applicant requirement


- The number of pediatric cases in the institute that he/she works per year
- List of the surgical services for pediatric patients in your institution.
- The total number of pediatric cases that he/she has anesthetized per year in the past.



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## 12 months Rotation

Institute	Month	Rotation	Topic discussion
Siring	15-31 January 2021	General surgery	Premature babies, neonates and infants: basic science, physiology, pharmacology, monitoring, psychology
Siring	1-14 February 2021	Urology	UTI, emergency delirium, airway obstruction, laryngospasm, laryngeal edema
Siring	15 February - 15 March 2021	Neuro-ENT	Anesthesia for neuro-surgery: craniotomy, myelomeningocele, spine surgery
Chula	16 March - 15 April 2021	Gen-Uro-Thoracic	Upper and lower abdominal, groin, perineal and anorectal surgery, endoscopic surgery, thoracotomy
Chula	16 April 2021	Outside OR	Anesthesia for eye surgery: retinopathy of prematurity, strabismus & muscle correction
Chula	1-31 May 2021	Plastic/ENT	Anesthesia for maxillofacial surgery: craniofacial reconstruction, cleft lip/palate surgery
Rama	1-30 June 2021	Gen-Uro	Common congenital anomalies: Down syndrome
Rama	1-15 July 2021	Outside OR	Anesthesia for outside OR procedure: CT, MRI, bone scan, cath lab, endoscopy
Rama	16 July -15 August 2021	Plastic/ENT/ Uro	Anesthesia for ENT: bronchoscopy, airway surgery, adenotonsillectomy, tympanoplasty, morbid obesity
Queen Sirikit	16 August -15 September 2021	Ortho/ENT	Anesthesia for orthopedics: scoliosis, limb deformity correction
Queen Sirikit	16 September-15 October 2021	Gen-Uro	Hypothermia, malignant hyperthermia, muscular dystrophy, Postoperative pain management (multimodal analgesia)
Queen Sirikit	16-31 October 2021	Neuro/Outside OR	Massive bleeding, phosce, fluid, electrolyte management
Siring	1-15 November 2021	GEN	Examination
	16 November 2021 - 10 January 2022		Elective in 4 institutes
	11-14 January 2022		Final Presentation on Graduation Day



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## Minimal case requirement 100 cases

Age group	Cases	ETT	SI	CU	RA	QS
• NEONATE	10					
• INFANT	40	15	5	5	5	5
• Age >1- 6 year	30					
• Age > 6 year	20	10	3	3	3	3
Type of patients						
• In-patient	70					
• Ambulatory patient	15					
• Anesthesia for outside OR	15					
Type of surgery						
• Anesthesia for Gen-Uro surgery	30	All				
• Anesthesia for Neuro	5	SI				
• Anesthesia for ENT	15	All				
• Anesth. for Plastic & maxillofacial	10	Cu Ra				
• Anesthesia for orthopedics	5	QS				
• Anesthesia for outside OR	15	Cu Ra				

Procedures	Cases	SI	CU	RA	QS
• Peripheral IV access	10	3	3	3	3
• Supraglottic airway device	10	3	3	3	3
• Undermask (General anesthesia)	10	3	3	3	3
• Setting mechanical ventilator	5	2	2	2	2
• Arterial line insertion	4	1	1	1	1
• Central line insertion	4	1	1	1	1
• Caudal block/ Epidural block/ Neuraxial block	5	2	1	1	2
• Peripheral nerve blockade/Perile/ Iliogastral/hypogastric block	5	1	2	2	1
• Acute pain	10	3	3	3	3
• Management of difficult airway	Work shop				
• PALS	Work shop				
• Postoperative care in ICU	8	2	2	2	2




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## WFSA-BARTC Pediatric Fellowship Program

- Started in January 2021: 1 Fellow from Nepal
- Stopped in January 2022 due to COVID
- July 2022- June 2023: 1 Fellow from Bhutan (Funding from Bhutan government)
- Restart in January 2023: 1 Fellow from Mongolia





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## Our current fellow




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- Our goal is to promote safe anesthesia for patients in developing countries in Asia.

Our first graduated fellow

First trained pediatric anesthesiologist in Nepal



# Improving Patient Safety Through the WFSA

Erlinda C. Oracion

WFSA Safety & Quality Of Practice Committee, Philippines

## ROADMAP

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- Introduction
- Education & Training
- Advocacy
- Safety
- Global Voice
- Summary

Uniting and empowering anaesthesiologists around the world to improve patient care.

---

“The last three years have been tough for anaesthesiologists around the world but 2022 felt like a turning point. Slowly but surely, we are regaining the momentum we lost during the pandemic.”

---

Wayne Morriss, WFSA President

## WFSA (WORLD FEDERATION OF SOCIETIES OF ANAESTHESIOLOGISTS)

---

- Global anaesthesia family
- Global advocacy
- Continuing medical education
- Capacity building & training

## IMPROVING PATIENT SAFETY THROUGH EDUCATION & TRAINING

---

## SAFE (Safer Anaesthesia from Education)

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- SAFE courses
  - Training of trainers
  - SAFE Online
  - SAFE Paediatric Anaesthesia
  - Safe Paediatric Anaesthesia - Cleft



## SAFE (Safer Anaesthesia from Education)

- VAST (Vital Anaesthesia Simulation Training)
  - Essential practices to perioperative teams
  - On-line learning + hands-on simulations
  - Resuscitation for OB, Pedia, Trauma
  - Pre- and post-operative care

“The WFSA is unique in terms of its positioning, global membership and reach. There are no other organizations in the perioperative space quite like it, and our role.... on the international stage is a powerful one.”

Kristine Stave, Chief Executive Officer

## ADVOCACY

- Engagement with decision makers
- Advance availability, safety, and quality of anaesthesia and perioperative services worldwide
- Amplify the voices of anaesthesiologists at the local, regional, and international levels
- Relationships
  - WHO (World Health Organization)
  - UN ECOSOC (United Nations Economic and Social Council)

“A concern of the WFSA in the early 1960's was anaesthesia workforce capacity building at the international level, in line with its objective of ‘providing better anaesthesia for all the peoples of the world.’  
In retrospect, it was the beginning of global anaesthesia, meaning that before globalization became a thing, there was a WFSA worldwide concept of anaesthesia.”

Dr. Bisola Onajin-Obembe, President of G4 Alliance's Permanent Council  
2022 WFSA Board Member

## GUIDING PILLARS

1. UNITY
2. ACCESS
3. SAFETY

## SAFETY

- WHO-WFSA International Standards for a Safe Practice of Anesthesia
- Minimum Capnometer Specifications 2021
- Consensus Statement on Environmentally- Sustainable Anaesthesia

## SAFETY & QUALITY OF PRACTICE COMMITTEE

- To promote the highest standards of safety and quality in anaesthesiology internationally
- Seek new methods to implement safe practices throughout the world
- Provide the necessary educational and human resources needed in the provision of access to safe anesthesia for essential surgery
- Deliver safe anesthesia care as a basic human right
- Collaborate with other WFSA committees incorporating patient safety and quality improvement in their plans and activities

## WORLD PATIENT SAFETY DAY September 17

- Advocate for improved global patient safety standards and practices
- 2022 – Medication Without Harm

## **WORLD ANAESTHESIA DAY October 16**

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- Celebrate the profession
- Unified global voice to advocate for safety in anaesthesia
- WAD2022
- Reduction of medication errors
- Improving patient safety practices

## **SUMMARY**

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- WFSA's strength – Member Societies
- Expertise and knowledge drawn together
- Diversity and global reach of members
- Unique organization
- Promoting safe anesthesia and perioperative care on a global scale
- WFSA Programmes



## Luncheon Symposium

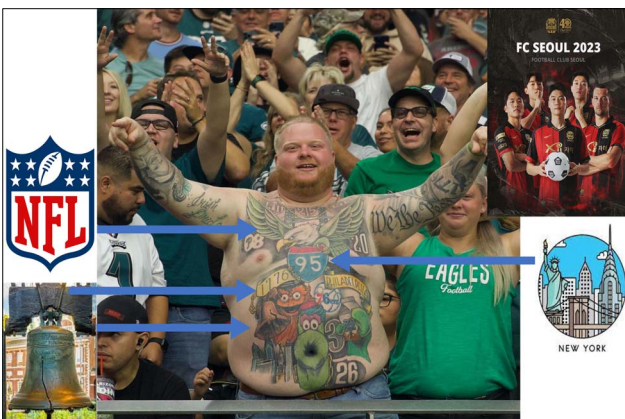
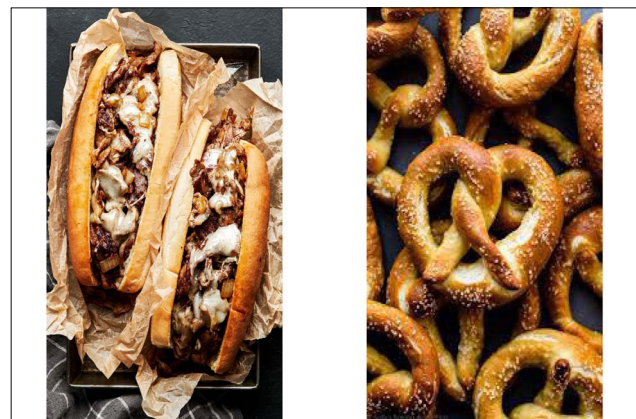
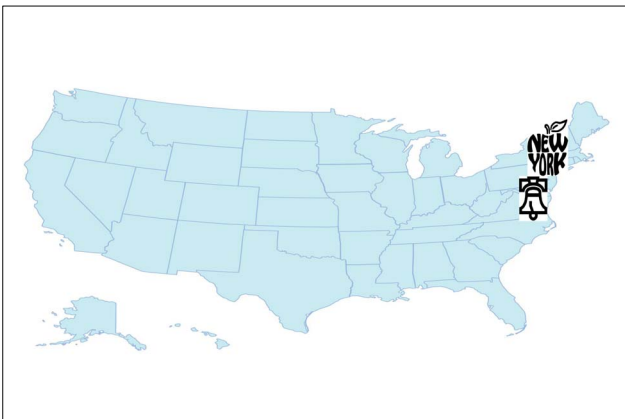
Chair(s): Dong Woo Han (Korea)



## EEG Guided Anesthesia in Young Children (Virtual)

Ian Yuan

Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia, University of Pennsylvania, USA



CHOP Childrens Hospital of Philadelphia

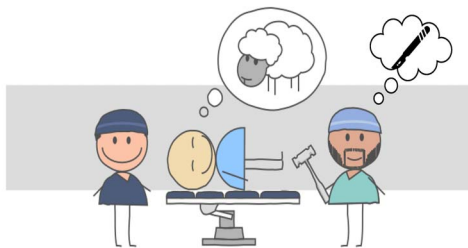
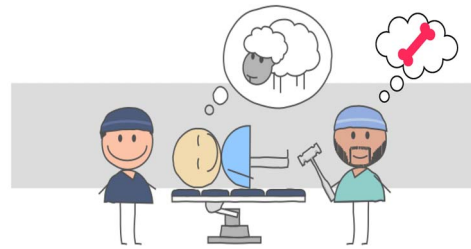
33k cases / year

75 Pediatric Anesthesiologist (9 Cardiac)

30 Nurse Anesthetists

11 Fellows

10 Residents

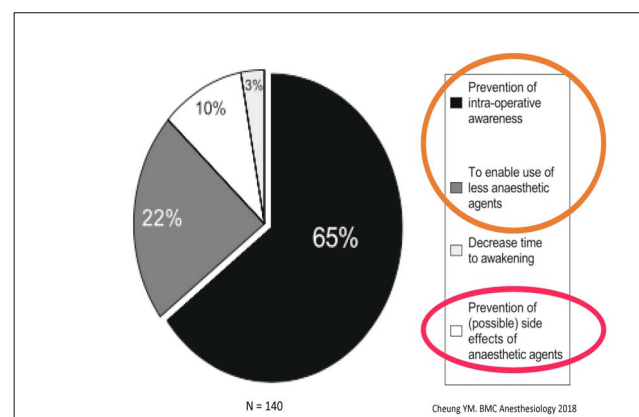
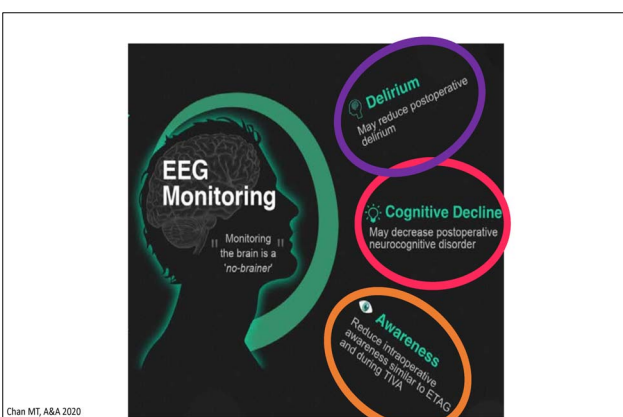
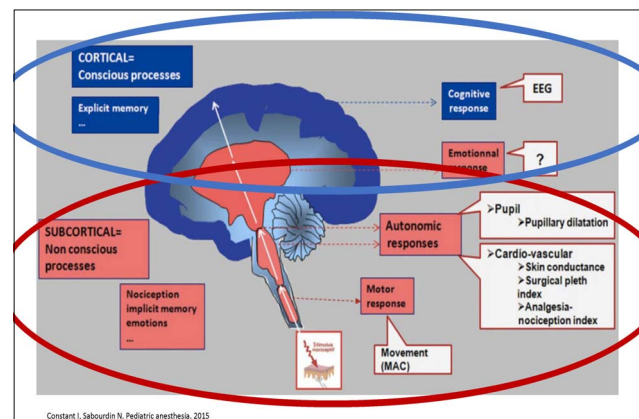
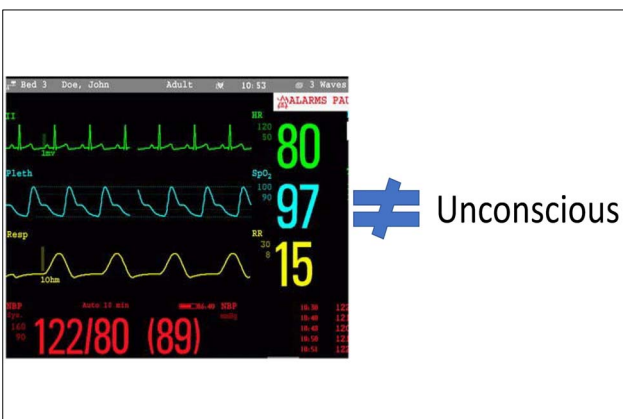


A. Increase the Sevoflurane

B. Bolus Propofol

C. Muscle relaxant

D. EEG



Young children sensitive to effects of excess anesthesia (hypotension)

Proprietary EEG indices (eg. BIS, PSI) not reliable

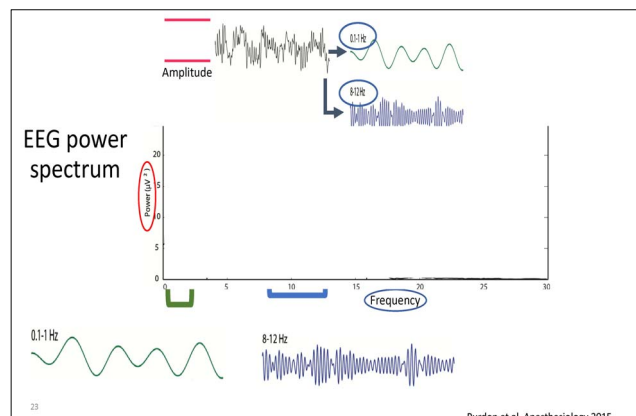
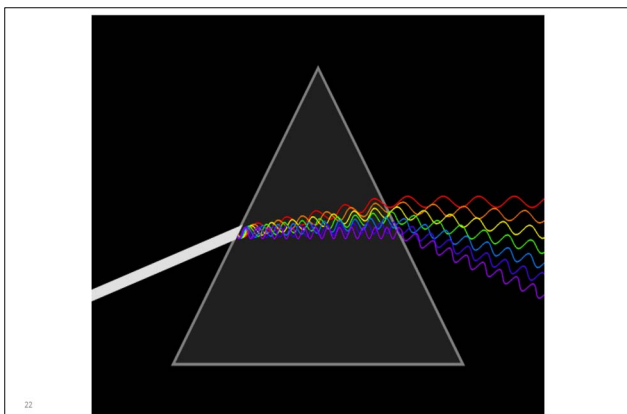
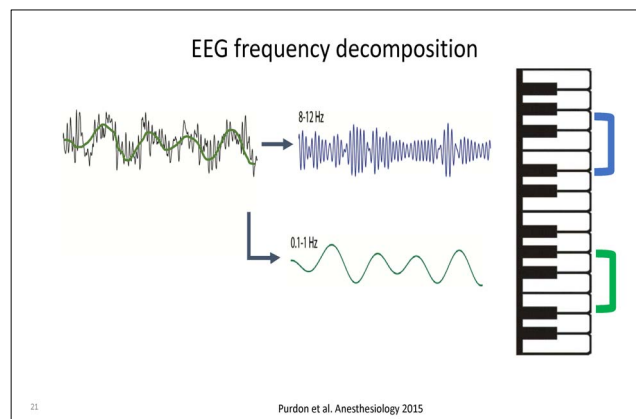
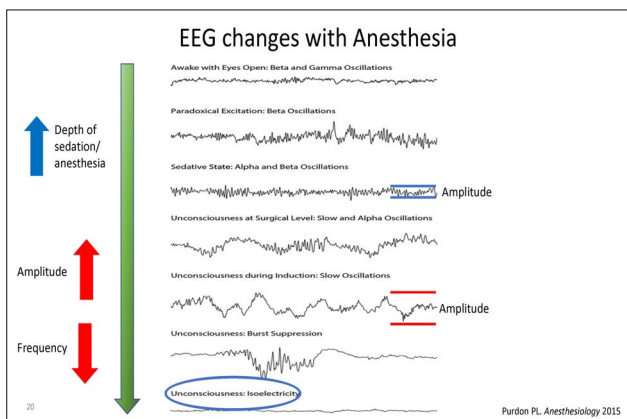
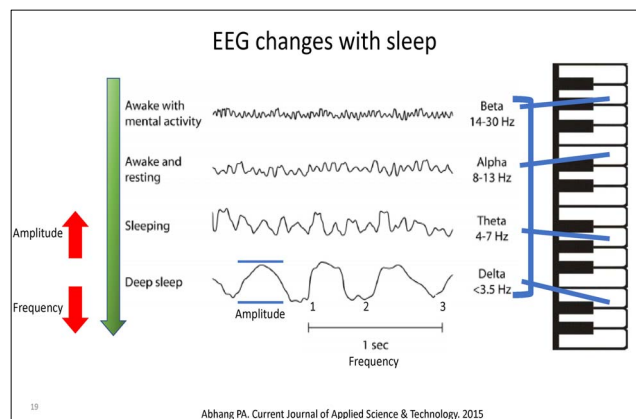
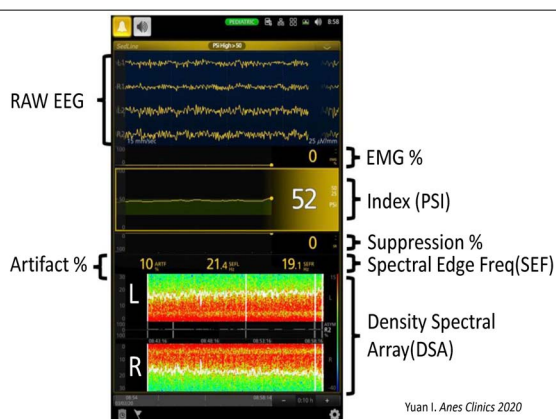
**How to use EEG to guide anesthesia in young children**

EEG guided anesthetic in young children

EEG waveforms and processed EEG parameters

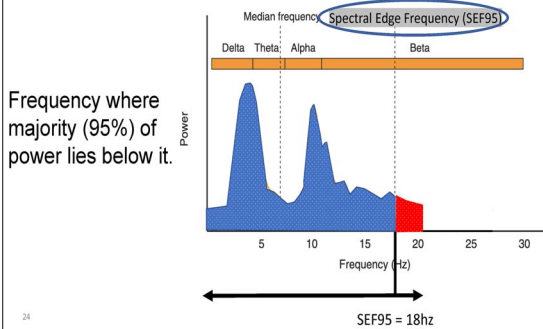
EEG changes with anesthetic and age

2 cases studies





## Spectral Edge Frequency (SEF)

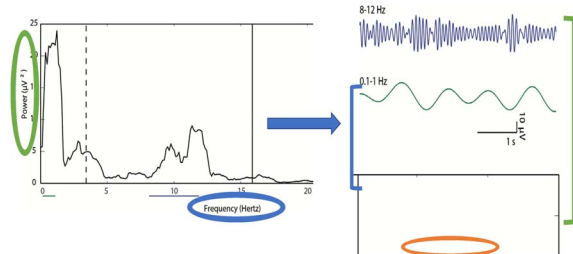


## SEF targets (> 3-6mo)

Anesthetic state	Clinical endpoint	SEF targets (hz)
Conscious	Emergence	> 20
Light anesthesia	Sedation	15-20
Surgical anesthesia	Surgical maintenance	10-15
Deep anesthesia	Incision/Laryngoscopy	6-9
Burst suppression		< 5

Yuan I. Anes. Clinics 2020

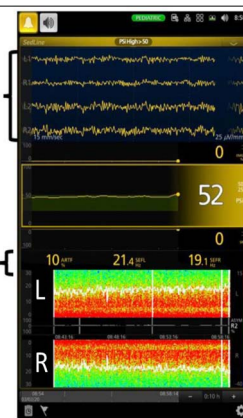
## DSA (Density Spectral Array)



EEG changes over time.

Purdon et al. Anesthesiology 2015

RAW EEG



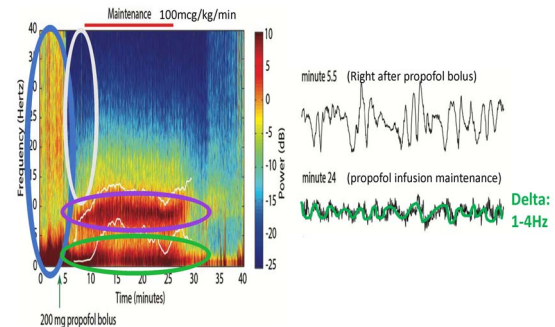
Yuan I. Anes Clinics 2020

## EEG guided anesthetic in young children

EEG waveforms and processed EEG parameters

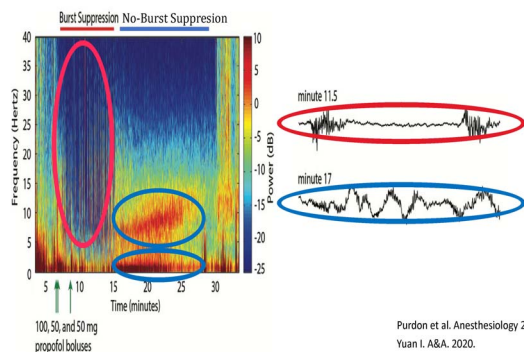
EEG changes with anesthetic and age

## Propofol: Delta (1-4hz) & Alpha (8-13hz)



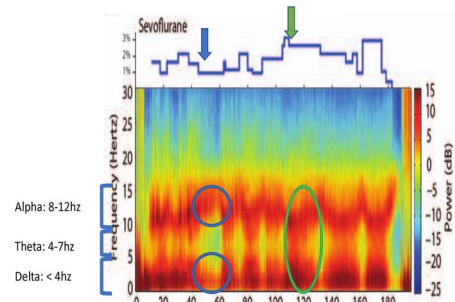
Purdon et al. Anesthesiology 2015

## Too much propofol...

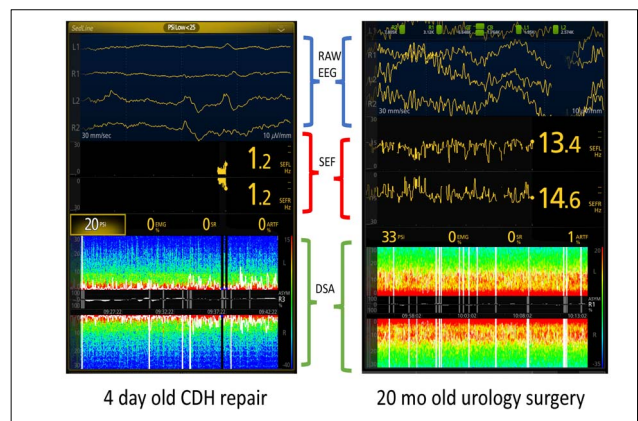
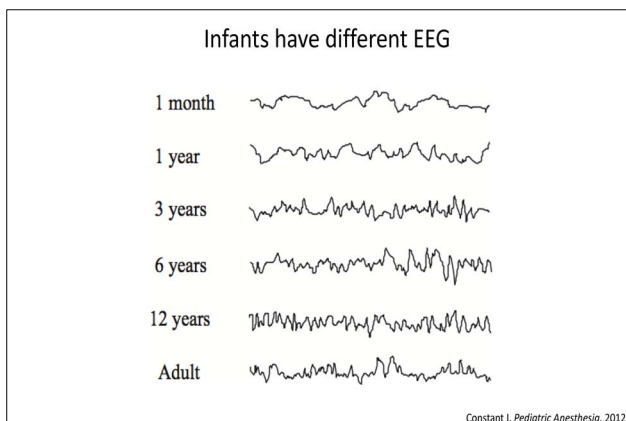
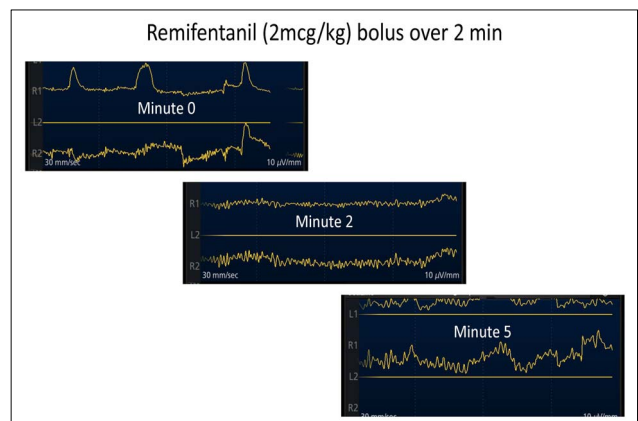
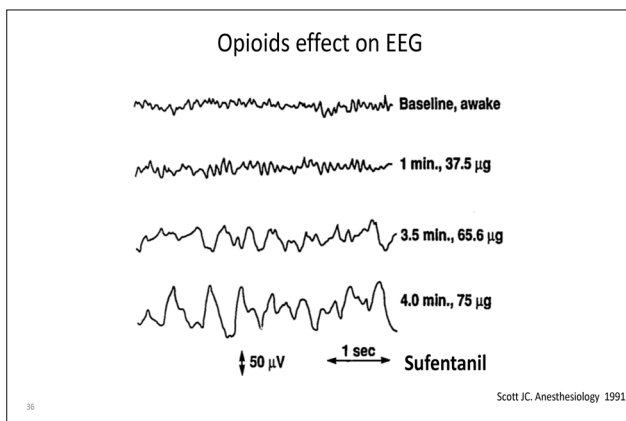
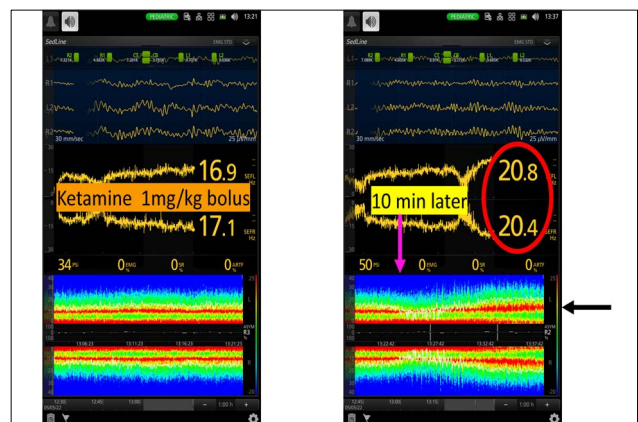
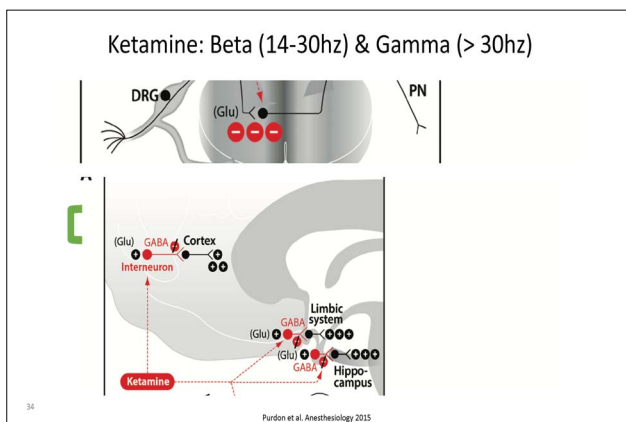
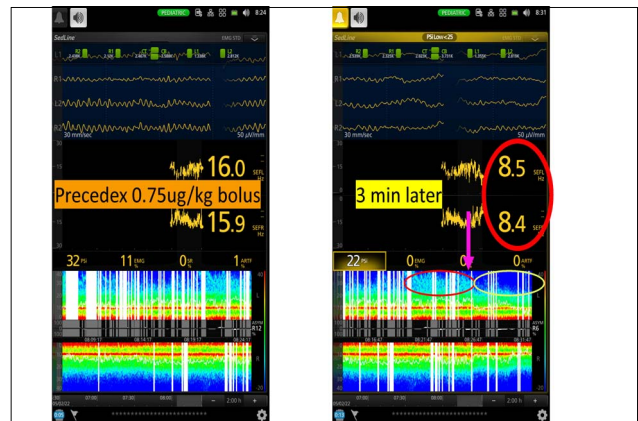
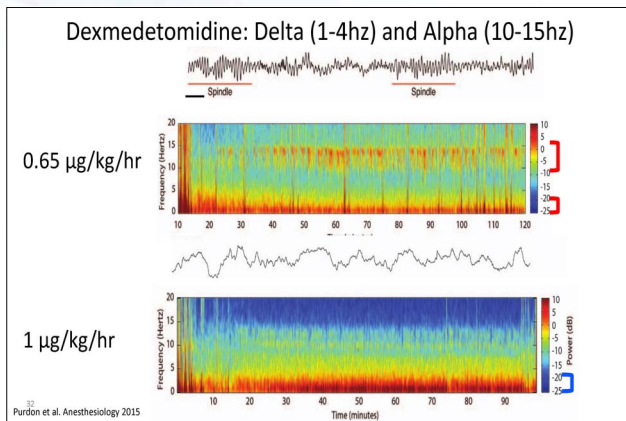


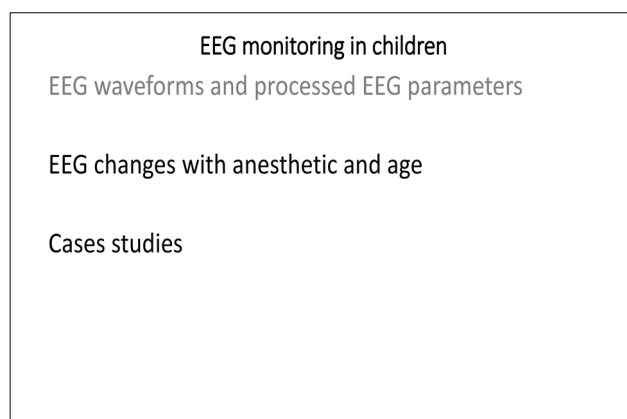
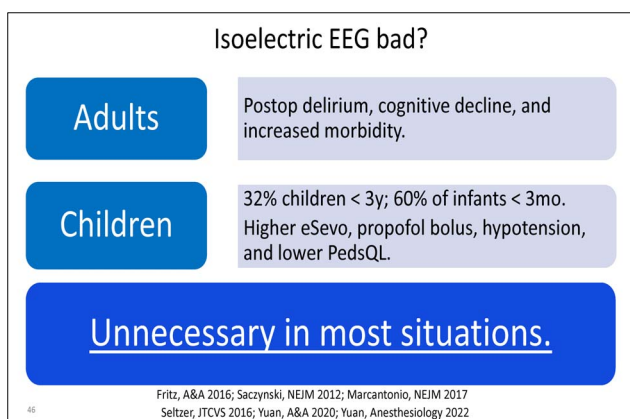
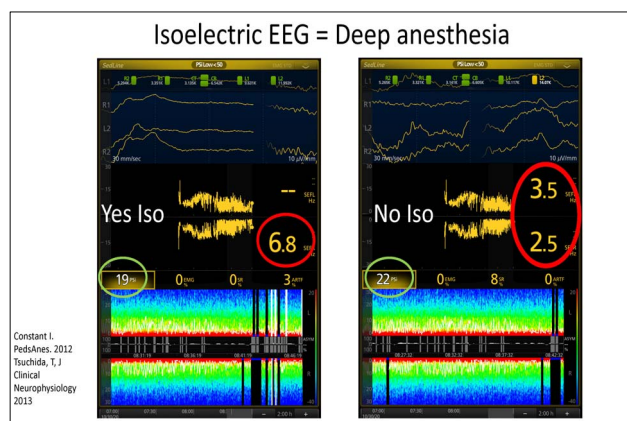
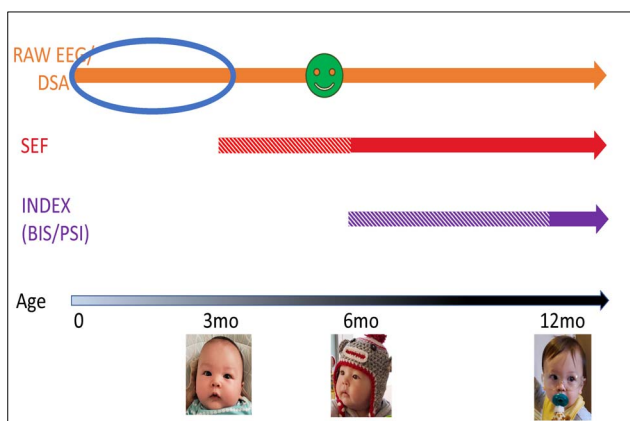
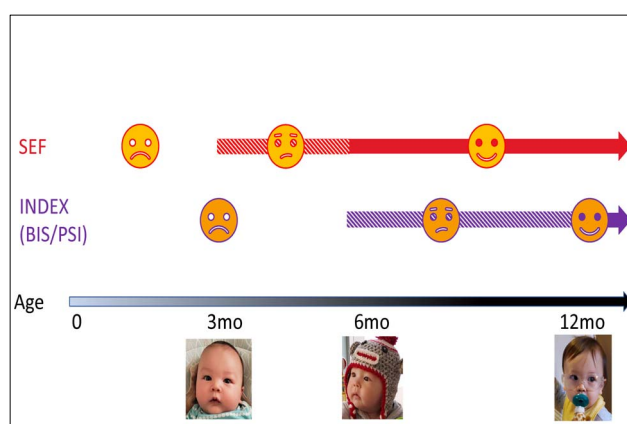
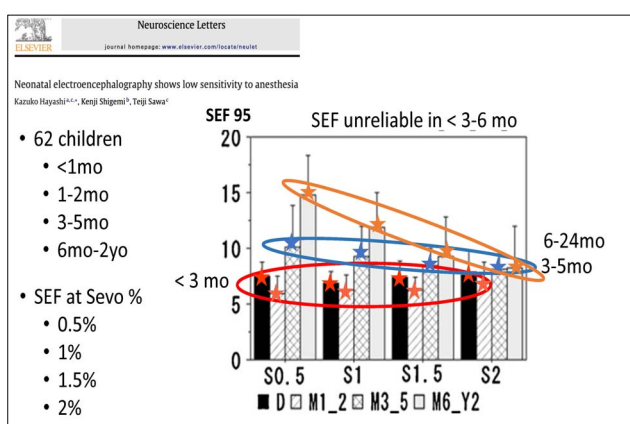
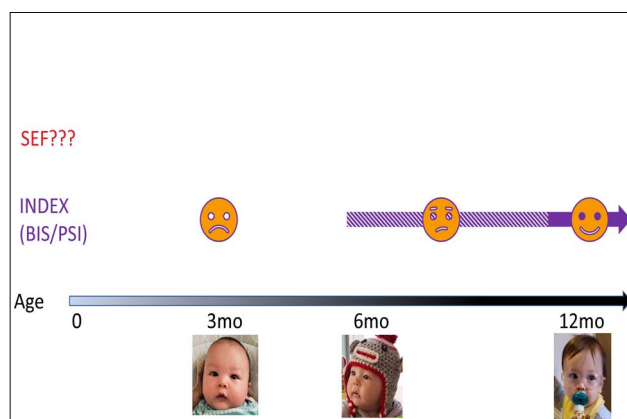
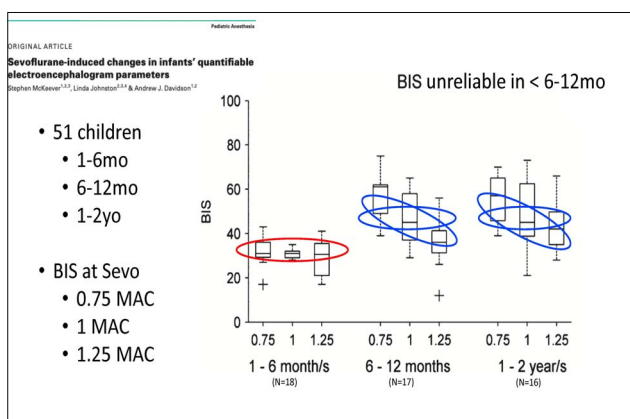
Purdon et al. Anesthesiology 2015  
Yuan I. A&A. 2020.

## Volatile anesthetics: Delta (<4 hz), Theta (4-7hz), Alpha (8-13hz)



Purdon et al. Anesthesiology 2015





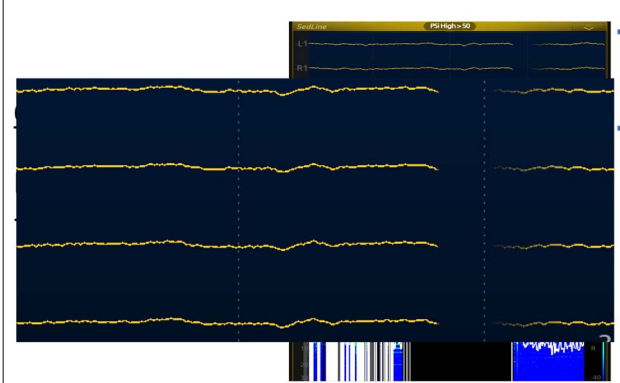


Case#1: 2mo old

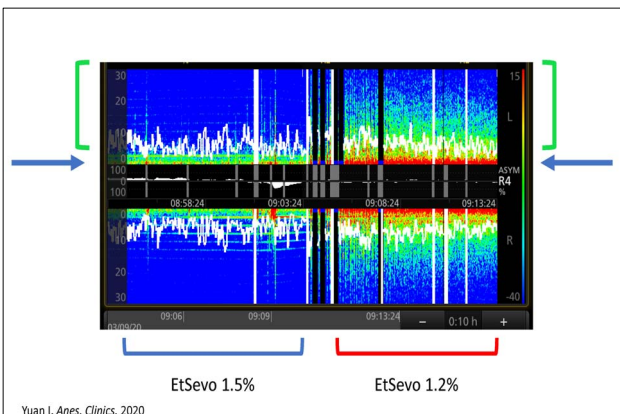
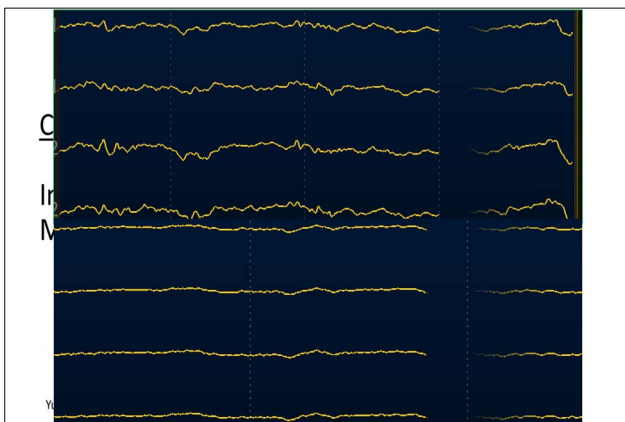
Sevo induction



Yuan I. Anes. Clinics. 2020



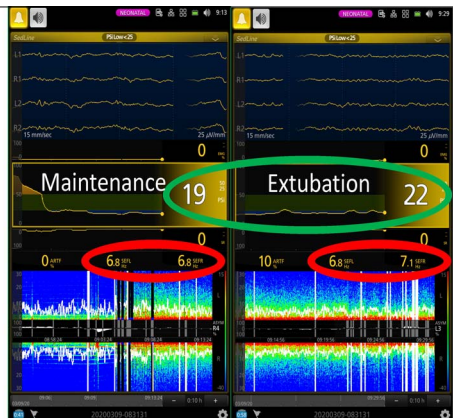
Yuan I. Anes. Clinics. 2020



Yuan I. Anes. Clinics. 2020

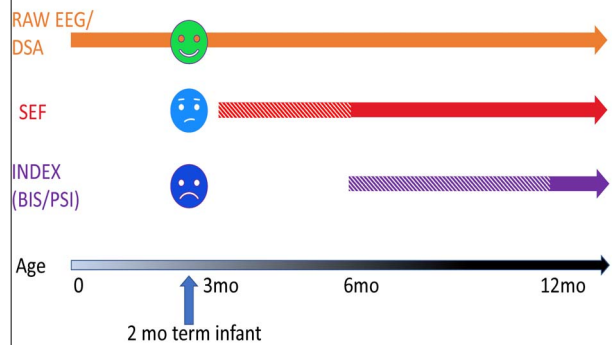
Case#1: 2mo

Extubation



Yuan I. Anes. Clinics. 2020

## Case 1 summary

Case#2: 10mo TIVA

TIVA with propofol and remifentanyl



Yuan I. Anes. Clinics. 2020

## Propofol dosing table

Age group	0-1 mo	1-3 mo	3-6 mo	6-12 mo	1-3 yrs	3-12 yrs
Propofol bolus (mg/kg)	3.5	3	3	3	3	2.5
Propofol 0-15 min (µg/kg/min)	183	200	200	208	217	250
Propofol 16-30 min	167	183	192	200	200	217
Propofol 30-60 min	150	167	175	183	192	183
Propofol 60-120 min	133	158	167	175	183	167
Propofol 120-180 min	117	150	158	167	175	150
Propofol 180-300 min	100	133	150	158	167	142

Yuan I. Anes. Clinics. 2020  
 Steer RJ. Ped Anes 2004  
 Morse L. Ped Anes 2019  
 Eleveld DJ. Br J Anaes 2018

Propofol Ce 3 µg/ml

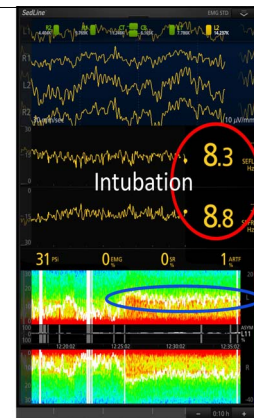
## Recommended SEF ranges (> 3-6mo)

Clinical endpoint	SEF range (hz)
Emergence	> 20
Sedation	15-20
Surgical maintenance	10-15
Incision/Laryngoscopy	6-9
Burst Suppression	< 5

Yuan I. Anes. Clinics 2020

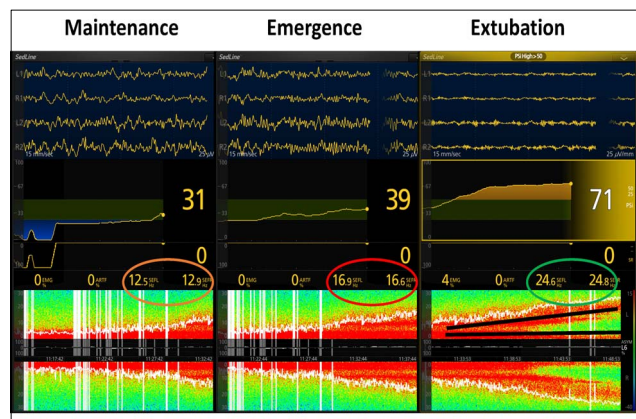
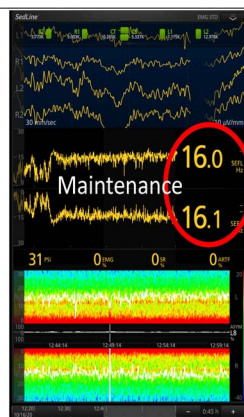
## Case#2: 10mo TIVA

Intubation



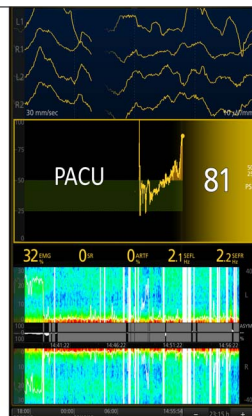
## Case#2: 10mo TIVA

Incision -> Maintenance

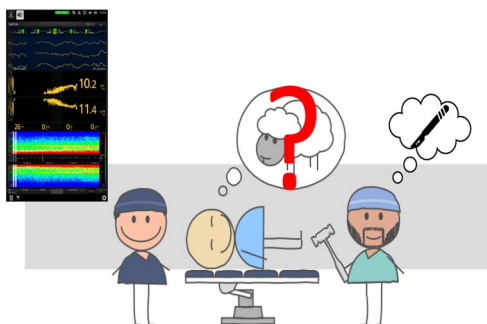
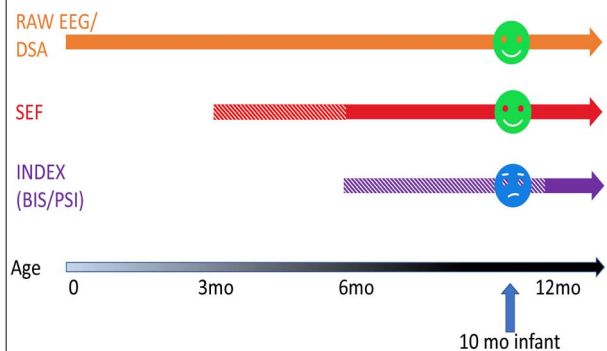


## Case#2: 10mo TIVA

PACU



## Case 2 summary





## **Session 3.**

# **Preparing for the Future**

**Chair(s): Choon Looi Bong (Singapore)**  
**Jun Heum Yon (Korea)**  
**Seong-Hyop Kim (Korea)**



# Thoughts on Leadership Professional Development and Career Success: Building the Future of Pediatric Anesthesiology Thoughts on Leadership

Randall Flick

Mayo Clinic Children's Center, USA

**Leadership**

**AS PHYSICIANS  
YOU ARE ALL  
LEADERS**

**YOUR... PROFESSIONAL  
SUCCESS DEPENDS ON THE  
CAPACITY TO LEAD.**

**TODAY... I WILL TOUCH ON A  
FEW LESSONS I HAVE LEARNED  
OVER A LONG CAREER.**




**Lesson #1  
Identify "Heroes"**

- \* Heroes are people who you look up to and want to emulate
- \* They are not perfect and often may be quite flawed.
- \* Heroes are often composites of several or many individuals

*\* There are also anti-heroes!*

*\* Be your own hero... but keep it to yourself*



**Lesson #2**


**WHAT DO YOU WANT  
TO BE WHEN YOU  
GROW UP?**

FLICK 2016

Most of us begin as clinicians not planning or aspiring to leadership.

Perspectives and careers change over time.

Periodic reassessment helps define direction and goals



**Lesson #2 , continued.**

**WHAT DO I WANT TO  
BE MOST PROUD OF  
WHEN I RETIRE?**

As you progress in your career the perspective changes.

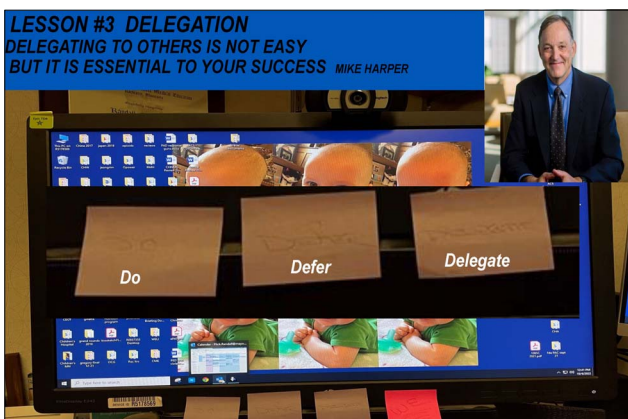
Forward looking...when I grow up perspective

Backward looking...when I retire perspective



**LESSON #3 DELEGATION**

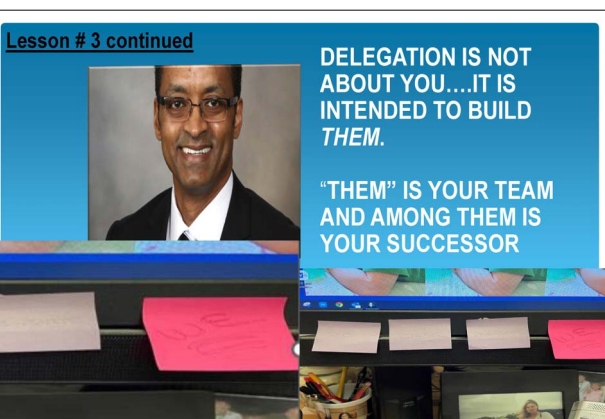
**DELEGATING TO OTHERS IS NOT EASY  
BUT IT IS ESSENTIAL TO YOUR SUCCESS** MIKE HARPER



**Lesson #3 continued**

**DELEGATION IS NOT  
ABOUT YOU....IT IS  
INTENDED TO BUILD  
THEM.**

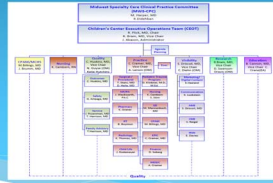
**"THEM" IS YOUR TEAM  
AND AMONG THEM IS  
YOUR SUCCESSOR**



**Lesson # 4****WE ...NOT I  
MAYO CLINIC CULTURE**

"The keynote of progress ... is system and organization — in other words, 'team-work.'" 1916

Rarely, if ever, do we ever do anything without help.  
There is always someone else who deserves credit  
**GIVE CREDIT EXPLICITLY**

**Lesson # 4****A culture of "We"**

"If the only tool you have is a hammer, it is tempting to treat everything as if it were a nail." Abraham Maslow 1966

**TEAMS AND PROCESSES**

DON'T JUST BE PROBLEM SOLVER (MANAGER)...

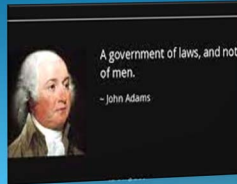
...BE A PROCESS BUILDER

Success of an organization is dependent on processes not on individual people...

...but on people (leaders) who build processes using teams of people.

Managers fix problems... often with a hammer

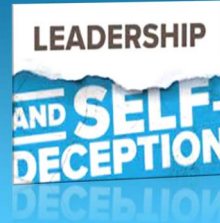
Leaders address challenges not with a hammer... but with a team

**Lesson # 5****RULES TO LIVE (LEAD) BY**

Transparency  
Equity  
Inclusion  
Process

Establish clear, equitable, inclusive and transparent processes...  
...when you do that, you empower **all** to be leaders and **all** to be held accountable to the rules that **we** made...

...rather than a ruler who makes rules unilaterally

**Lesson # 6**

THE PEOPLE ON YOUR TEAM ARE...PEOPLE.

PEOPLE WHO HAVE HOPES DREAMS FEELINGS STRENGTHS WEAKNESSES...

JUST LIKE YOU AND I

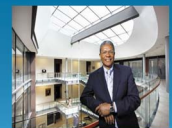
The Concept of Self-Betrayal and Self-Deception

**Lesson # 6 continued**

"AS FAR AS I AM CONCERNED THE PROBLEM IS ME..."

Seeing problems in others is easy.  
Seeing the role we play in those problems is much harder...  
...and much more important!

The Outward Mindset

**Lesson # 7****THE ANSWER IS ALWAYS....YES!**

This is advice that was given to me early in my career. I gave to my division members and have carried forward in my career.

My successor has made this a centerpiece of his leadership

**Lesson # 8****LEADERSHIP IS NOT ABOUT BEING RIGHT OR KNOWING MORE...**

John, I am thinking of getting an MBA...

John Noseworthy 2014

**...The need add value**

Resist the need to add value to every conversation

Adding value is another way of showing how much you know.

Good leaders are not necessarily the smartest people in the room.

More valuable is the ability to identify talent and use it effectively

**Lesson # 9**

BEING RIGHT DOES MATTER

KNOWING THINGS ALSO MATTERS



If you listen,...

...your team will teach you what you need to know and often what you don't know you need to know

BUT...YOU CANNOT KNOW MORE THAN ALL THE PEOPLE WHO **YOU** CHOSE TO HAVE ON THE TEAM.

REMEMBER THEY ARE JUST LIKE YOU. THEY WANT TO HAVE A CHANCE TO LET YOU AND THE TEAM KNOW HOW MUCH THEY CAN CONTRIBUTE.



### Lesson # 9



## LISTEN! MIKE HARPER 2015

Listening tells those engaged that you want to hear from them and their input is important.

### Take notes!

Taking notes sends a message that what is being said is important enough to write down.

Taking notes also forces you to listen

### Lesson # 10



*The data are what they are. It is our job to produce good science.*

*Let others opine and criticize.*

David Warner 2009

### Lesson # 11 Dealing with Complaints/Concerns

"Lincoln's Hot letters"

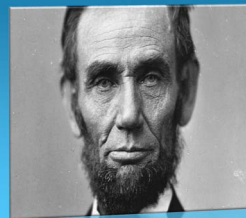


**WRITE A RESPONSE.  
SEND IT TO YOURSELF.  
LEAVE IT FOR A DAY OR TWO  
DECIDE WHETHER TO SEND, EDIT  
OR DISCARD**

*Randy; you don't need to respond to every concern or complaint. File it. Ignore it...if its serious they will send another note or give you a call* Jukka Rasanen



### Lesson # 11 continued



## THIS TOO SHALL PASS...AWAY

*Whatever the urgent issue is today.*

*It is transient and will be replaced by something else tomorrow.*

**Put it on a single sheet of paper and send it to me.**

### Lesson # 12



## THE IMPORTANCE OF TRUSTED CONFIDANTS

As leaders you need individuals whom you trust enough to seek advice before you introduce change.

If you are unsure or even if you are sure, it is never a bad idea to seek input from a trusted colleague

It (they) can keep you out of trouble.

### Lesson # 13



## ASSUME BENIGN INTENT

*Often we assume that the behavior of others is directed toward us especially when it seems negative*

**QUESTIONS  
& ANSWERS**





# How to Prepare for the Next Pandemic?

Nicola Disma

Research & Innovation Unit at Istituto Giannina Gaslini, Italy

## Conflict of interests declaration

- No conflict of interests to declare

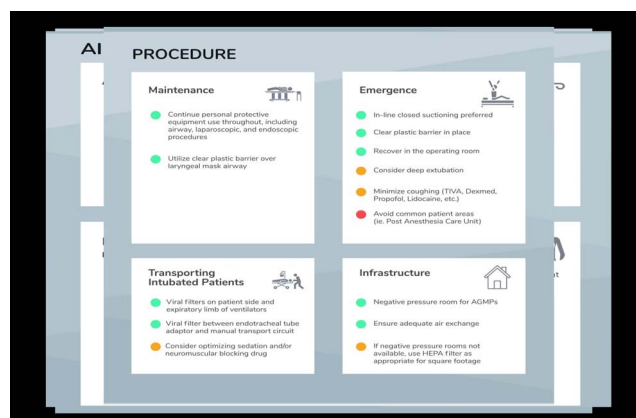
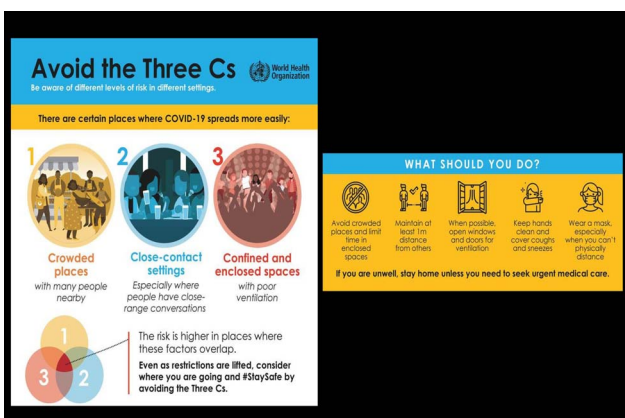
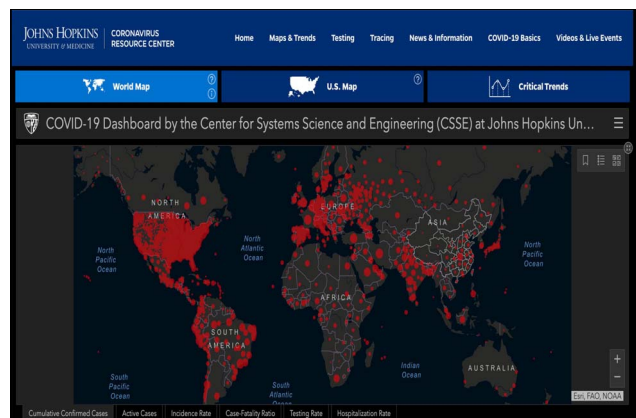
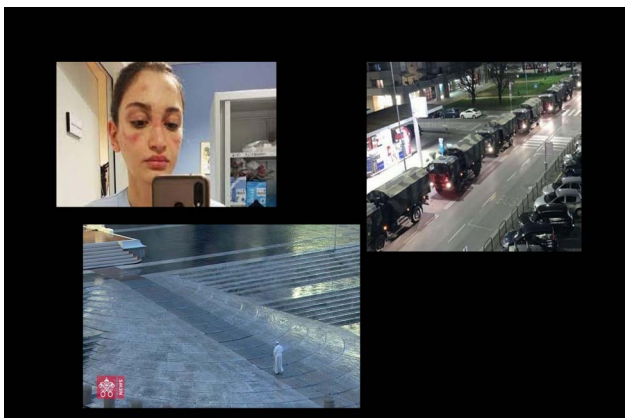
## The background.....

- January 30, 2020, two Chinese tourists where tested positive in Rome
- Feb 20, 2020, 16 cases in Lombardy
- **March 11, 2020** The World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak a global pandemic

Then the “whole world gone crazy»

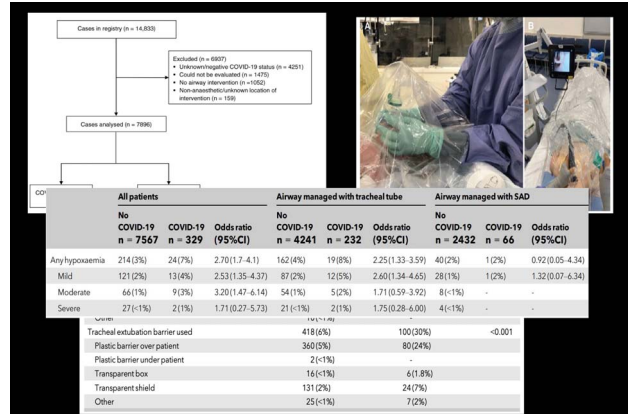


Karlsson J SARS-CoV-2 airway reactivity in children: more of the same? Anaesthesia 2022



## PEDIATRIC AIRWAY MANAGEMENT COMPLICATIONS DURING THE COVID-19 PANDEMIC.

An International, Multicenter, Observational Registry: The PAWS-COVID-19 (Pediatric AirWay complicationS COVID-19) Registry



## Aftermaths (very personal)

- Stress test for NHSs
- Research & Innovation
- Long term consequences
- URTI

## Aftermaths (very personal)

- Stress test for NHSs
- Research & Innovation
- Long term consequences
- URTI

## Pandemics

- HIV/AIDS (2005-2012)
  - Death Toll: 36 million
- FLU PANDEMIC (1968)
  - Death Toll: 1 million
- ASIAN FLU (1956-1958)
  - Death Toll: 2 million
- Polio (1950s)
  - Death Toll: >100k
- SPANISH FLU (1918-1920)
  - Death Toll: 100 millions



## Aftermaths (very personal)

- Stress test for NHSs
- Research & Innovation
- Long term consequences
- URTI

## Dissemination of knowledge

- Advanced informatics
- Rapid publishing
- Social media
- Data repositories



## Pubmed search 20 Sept 2022

- **296,187 published papers in 2020**
  - ((wuhan[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND 2019/12[PDAT] : 2030[PDAT]) OR 2019-nCoV[All Fields] OR 2019nCoV[All Fields] OR COVID-19[All Fields] OR SARS-CoV-2[All Fields]
- **30,801 articles for children**
  - ((wuhan[All Fields] AND ("coronavirus"[MeSH Terms] AND "coronavirus"[All Fields])) AND 2019/12[PDAT] : 2030[PDAT]) OR 2019-nCoV[All Fields] OR 2019nCoV[All Fields] OR COVID-19[All Fields] OR SARS-CoV-2[All Fields] AND children

## Nicola Disma: How to Prepare for the Next Pandemic?

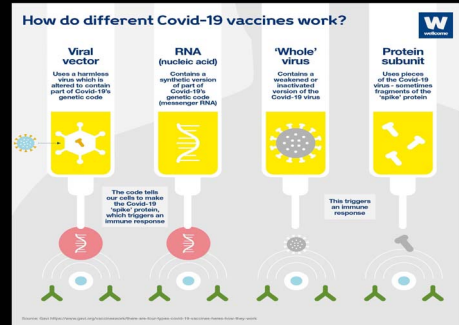
Scientific quality of COVID-19 and SARS CoV-2 publications in the highest impact medical journals during the early phase of the pandemic: A case control study

Marko Zdravkovic<sup>1,2</sup>, Joana Burger-Estilla<sup>1,2</sup>, Bogdan Zdravkovic<sup>1</sup>, David Berger<sup>1,2</sup>

PLOS ONE

Table 3. Google Scholar citations of original articles published between March 12 and April 12, 2020.

Study date	Date	Original articles citations		P value <sup>a</sup>
		COVID-19 (n = 13)	nonCOVID-19 (n = 52)	
All publications	Web-design	33 (14-212)	2 (1-3)	<0.001
	Case series	45 (30-244)	2 (1-4)	<0.001
	Opinion	65 (41-290)	2 (1-4)	<0.001
	Review	88 (48-328)	2 (1-5)	<0.001
	May 15	123 (59-390)	2.5 (1-5)	<0.001
Original articles	May 20	139 (64-435)	3 (1.3-6)	<0.001
	May 25	149 (73-512)	3 (1.3-7)	<0.001
	Well-designed controlled trial without randomization; prospective comparative cohort study	2	0 (0)	1 (1.9)
	Case-control study; retrospective cohort study	3	2 (0.4)	7 (13.5)
	Case series without or with intervention; cross-sectional study	4	9 (0.2)	4 (11.5)
Original articles	Opinion papers, case reports	3	1 (7.7)	0 (0)
	Animal or in-vitro research	4	0 (0)	0 (0)



## Innovation

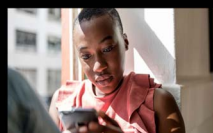
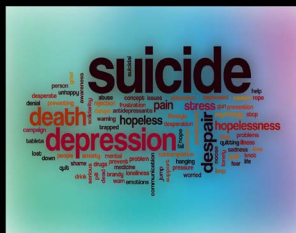
- Pre-anaesthesia evaluation
  - Telemedicine
- Apps
- Videoconferences
- Faster discharge
- Treatment at home



## Aftermaths (very personal)

- Stress test for NHS
- Research & Innovation
- Long term consequences
- URTI

## CHILDREN AND YOUTH MENTAL HEALTH UNDER COVID-19



### Systematic Review

## Interventions to Ameliorate the Psychosocial Effects of the COVID-19 Pandemic on Children—A Systematic Review

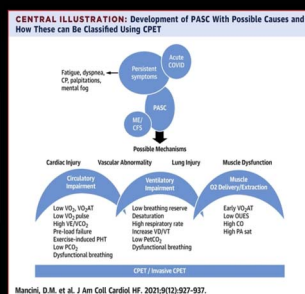
Katharina Boldt<sup>1,2</sup>, Michaela Coenen<sup>1,2</sup>, Ani Movsisyan<sup>1,2</sup>, Stephan Voss<sup>1,2</sup>, Eva Rehfuess<sup>1,2</sup>, Angela M. Kunzler<sup>3,4</sup>, Klaus Lieb<sup>3,4</sup> and Caroline Jung-Sievers<sup>1,2,\*</sup>

- Exercise
- Education
- Socialization
- Financial support programmes

Mitigate the impact of these crises on the mental health status of children

## Long-COVID

Adults	Children/adolescents
1% asymptomatic	6% asymptomatic
99% symptomatic	94% symptomatic
81% mild	99% mild
19% severe	1% severe
10-61% post COVID-19 condition	1-30% post COVID-19 condition



## MISC

## Multisystem inflammatory syndrome

### 4 things you need to know about Multisystem Inflammatory Syndrome in Children (MIS-C)

- Appears to be a rare condition in children
- May show up weeks after COVID-19 infection
- Causes inflammation across multiple organs, including:
  - Heart
  - Lungs
  - Kidneys
  - Brain
  - Skin
  - Eyes
  - Gastrointestinal
- Produces varying symptoms in children, but they can include:
  - Fever
  - Abdominal pain
  - Vomiting
  - Diarrhea
  - Neck pain
  - Rash
  - Bloodshot eyes
  - Feeling extra tired

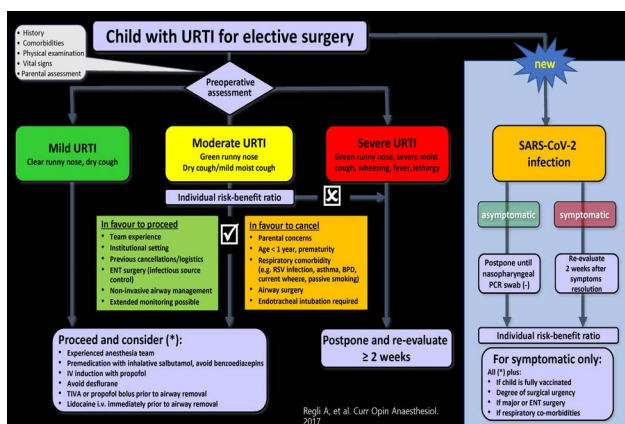


## Aftermaths (very personal)

- Stress test for NHSs
- Research & Innovation
- Long term consequences
- URTI

## Paediatric infectious disease – “The perfect storm”

- COVID-19 variants, RSV, influenza A and B, haemophilus influenzae, rhinovirus, and pneumococcal variants, etc....
- Precautionary measures like
  - rapid point of care testing
  - appropriate methods for securing the airways
  - techniques designed to limit the spread of disease



## Reflections

1. What is the relevance of *paediatric anaesthesia network* during a rapidly evolving pandemic?
2. How and where *new devices and techniques* should be tested?
3. How to rapidly *implement clinical practice*, when scientific evidence is weak?
4. What is the role of paediatric anaesthesia services in redefining *hospital organization and patients' flow*?

“Has the whole world gone crazy?”



“I can't be worried about that.... anymore. Life goes on, man!”

Karlsson J. SARS-CoV-2 airway reactivity in children: more of the same? Anaesthesia 2022

# Time to Obtain Epidemiologic Data on Pediatric Anesthesia in Asia Itself: Introduction of PEACH in Asia Study

Soichiro Obara

Tokyo Metropolitan Otsuka Hospital, Japan

## Learning Objectives

1. Describe the rates of pediatric anesthesia related mortality and morbidity (serious adverse events) in developing and developed countries, although those definitions varies among studies
2. Review a number of large national or international epidemiological studies regarding the morbidity in children undergoing anesthesia and sedation which have been conducted or trialed in Europe, North America, Latin America, and Africa in recent years
3. Discuss the need for data describing the morbidity and mortality throughout Asia and the ongoing ASPA epidemiological research project, PEACH in Asia study

## 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

### Incidence of morbidity and mortality in pediatric anesthesia

- Pediatric anesthesia-related mortality
  - ↓ 0.01-0.05% in high-income countries
  - × 2-3 in developing countries
- Pediatric anesthesia-related severe adverse events
  - 2-8% in developed countries
 the definitions of "severe adverse events" varies among studies

## 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

Previous studies related to severe critical events in pediatric anesthesia in developed countries **outside Asia**

	Philadelphia, USA	Cincinnati, USA	Perth, Australia	Utrecht, Netherlands	Paris, France
Study design	Retrospective, case-control, Single center	Prospective, single center	Prospective, single center	Retrospective, single center	Prospective, single center
Study period	30 months (2010-2012)	6 years (2007-2012)	1 year (2007-2008)	6 years (2007-2013)	30 months (2000-2002)
Number of registered cases	55,070	19,059	9,297	35,190	24,165
Severe critical events [%]	0.4			3.4	7.9
Respiratory critical events [%]	0.26	2.8	15.0	1.6	4.1
Cardiac arrest [%]					0.033

## 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

Previous studies related to severe critical events in pediatric anesthesia **in Asia**

	Pakistan	Singapore	Thailand	South Korea	Japan
Study design	Retrospective, single center	Retrospective, single center	Prospective, 20 centers	Retrospective, single center	Clinical audit, 739 centers
Study period	25 years (1992-2016)	11 years (2000-2010)	1 year (2003-2004)	6 years (2014-2019)	5 years (1999-2003)
Number of registered cases	48,828	75,331	25,098	53,541	342,840
Severe critical events [%]	0.08	3.34	1.88	0.55	
Respiratory critical events [%]	0.027	2.33		0.32	
Cardiac arrest [%]	0.026	0.015 (near cardiac arrest)	0.051	0.047	0.0511 – 0.103, depending on institution type

## 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

**Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe**



Wald Hobe, Nicola Disma, Katalin Viny, Karin Becke, Tom G Hansen, Martin Jühr, Brigitte Leva, Neil S Morton, Petronella M Vermeulen, Marzena Zielinska, Kristina Boda, Francis Voeyckmans, for the APRICOT Group of the European Society of Anaesthesiology Clinical Trial Network\*

• Design: a **prospective, international, multicenter, observational study**

• Aims:

1. To establish the incidence of severe critical events in children undergoing anesthesia
2. To describe the differences in pediatric anesthesia practice
3. To study the potential impact of this variability on the occurrence of severe critical events
  - ① laryngospasm, ② bronchospasm, ③ pulmonary aspiration, ④ drug error,
  - ⑤ anaphylaxis, ⑥ cardiovascular instability, ⑦ neurological damage,
  - ⑧ peri-anesthetic cardiac arrest, ⑨ post-anesthetic stridor

Lancet Respir Med 2017  
March 28, 2017  
[http://dx.doi.org/10.1016/S2213-2600\(17\)30116-9](http://dx.doi.org/10.1016/S2213-2600(17)30116-9)

## 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

**Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe**



Results:

- Recruitment period: 10 months (Apr 2014 – Jan 2015)
- No. of participating institutions: 261, across 33 European countries
- No. of anesthetics included: 31,127
- Incidence of severe critical events: **5.2% (95%CI 5.0–5.5)**
- Incidence of respiratory critical events: **3.1% (95%CI 2.9–3.3)**
- The experience of the anesthesiologist in charge reduced respiratory and cardiovascular severe critical events



# 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

## Morbidity and mortality after anaesthesia in early life: results of the European prospective multicentre observational study, neonate and children audit of anaesthesia practice in Europe (NECTARINE)

Nicola Disma<sup>1,\*</sup>, Francis Veyckemans<sup>2</sup>, Katalin Virag<sup>3</sup>, Tom G. Hansen<sup>4,5</sup>, Karin Becke<sup>6</sup>, Pierre Harlet<sup>7</sup>, Laszlo Vutsits<sup>8,9</sup>, Suellen M. Walker<sup>10</sup>, Jurgen C. de Graaff<sup>11</sup>, Marzena Zielinska<sup>12</sup>, Dusica Simic<sup>13</sup>, Thomas Engelhardt<sup>14</sup> and Walid Habre<sup>6,9</sup>, for the NECTARINE Group of the European Society of Anaesthesiology Clinical Trial Network<sup>1</sup>

- Design: a **prospective, international, multicenter, observational study**
- Patients: Up to 60 weeks' postmenstrual age undergoing anesthesia for surgical or diagnostic procedures
- Aims:
  1. To identify thresholds of pre-determined physiological variables that triggered a medical intervention
  2. To evaluate morbidities, mortality at 30 and 90 days, or both, and associations with critical events



# 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

## Morbidity and mortality after anaesthesia in early life: results of the European prospective multicentre observational study, neonate and children audit of anaesthesia practice in Europe (NECTARINE)

Results:

- Recruitment period: 11 months (Mar 2016 – Jan 2017)
- No. of participating institutions: 165, across 31 European countries
- No. of recruited neonates included: 5,609
- Incidence of critical events: **35.2% of cases**
  - mainly hypotension (>30% decrease in BP) or reduced oxygenation (SpO<sub>2</sub> <85%)



# 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

Systematic Review / Meta-analysis

## Global mortality of children after perioperative cardiac arrest: A systematic review, meta-analysis, and meta-regression

Semagn Mekonnen Abate<sup>a,\*</sup>, Solomon Nega<sup>b</sup>, Bivash Basu<sup>a</sup>, Kidanemariam Tamrat<sup>c</sup>

<sup>a</sup> Department of Anaesthesiology, College of Health Sciences and Medicine, Dilla University, Ethiopia

<sup>b</sup> Department of Internal Medicine, College of Health Sciences and Medicine, Dilla University, Ethiopia

<sup>c</sup> Department of Anaesthesiology, College of Health Sciences and Medicine, Hawassa University, Ethiopia

Annals of Medicine and Surgery 74 (2022) 103285

- 38 studies with 3.35 million participants were included
- The global incidence of perioperative cardiac arrest: **0.254%** (95% CI: 0.223-0.284)
- The global incidence of perioperative mortality: **4.118%** (95% CI: 3.568-4.668)
- Significant difference in anesthesia-related mortality between low middle income countries and high income countries

# 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

**You can't manage  
what you don't measure**

**- Peter F. Drucker**

# 1. Epidemiology of peri-anesthetic complications in pediatric anesthesia

## Large multicenter collaborative projects regarding pediatric peri-anesthetic adverse events

**APRICOT  
NECTARINE**

**ASOS  
Paeds**

African  
Surgical Outcomes Study



PEACH in Asia  
study project

**Wake Up Safe**

**LASOS**

Latin American  
Surgical Outcomes Study



ANZCA reporting system

# 2. PEACH in Asia study

## What is "PEACH in Asia study"?

**Peri-Anesthetic morbidity in Children in Asia (PEACH in Asia) study:**

a prospective international multicenter observational study on epidemiology of severe critical events in pediatric anesthesia in Asia



PEACH in Asia  
study project

# 2. PEACH in Asia study

Design: **multinational, multicenter, prospective, observational study**

Outcome measures:

- Primary: Incidence of severe critical events
  - ① laryngospasm, ② bronchospasm, ③ pulmonary aspiration, ④ drug error,
  - ⑤ anaphylaxis, ⑥ cardiovascular instability, ⑦ neurological damage,
  - ⑧ peri-anesthetic cardiac arrest, ⑨ post-anesthetic stridor

Time Frame: Children will be followed for the duration of their anesthesia procedure and up to 60 minutes afterwards

• Secondary:

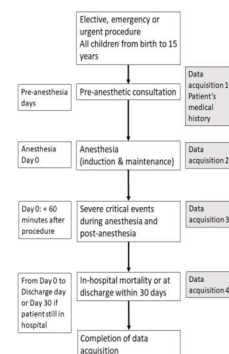
1. Risk factors for the occurrence of severe critical events
2. Consequences of the critical events: irreversible damage, in-hospital mortality

Time Frame: in-hospital and up to 30 days

# 2. PEACH in Asia study

## Data acquisition

- Each participating institutions collect data over a period of **two week including weekends and after-hours**
- The 2-week recruitment period will be chosen by each institution
- Participating institutions will be provided with data collection sheets
- The data will be filled in the electronic case report form (e-CRF)
- e-CRF has already been created on the internationally affiliated and safe cloud system, UMIN-INDICE



**Data collection flow chart**



## Soichiro Obara: Time to Obtain Epidemiologic Data on Pediatric Anesthesia in Asia Itself: Introduction of PEACH in Asia Study

## 2. PEACH in Asia study

## Study population

## Children from birth to 15 years

- ✓ admitted for an inpatient or outpatient procedure under general anesthesia with or without regional analgesia
- ✓ admitted for a diagnostic procedure under general anesthesia (such as endoscopy, radiology, bone marrow puncture, etc.)
- ✓ admitted out-of-hours for emergency procedures

## Exclusion criteria:

- Children admitted directly from the ICUs to the ORs
- Anesthesia procedures in the NICU or the PICU

## 2. PEACH in Asia study

## Sample size estimation

the European APRICOT

- mean 5.2% [95% confidence interval(CI) 5.0-5.5]

In several Asian countries

- 3.3% in Singapore, 8.9% in India, and so on



A minimum of **7,600** patients → a 95% CI of 1.0%

(assuming that the incidence of severe critical events is 5.2%, (ie, 95% exact CI is 4.7-5.7%) , or

A minimum of **30,000** patients → a 95% CI of 0.5%

## 2. PEACH in Asia study

## Publication policy

- After submitting grant proposal, recruitment of patients, data acquisition, cleaning and analysis of the data obtained, **authorship will be distributed according to differences in investment.**
- Each participating center including at least 5 patients can designate one collaborator that will be mentioned in the publication. Furthermore, for each additional 50 patients included, one more collaborator can be designated.
- **These collaborators will be mentioned in the manuscript and will be traceable via Pubmed.**
- Also, on request, centers will be allowed to use their data. Proposals for secondary analyses can be submitted to the Steering Committee that will need to approve those analyses and that will revise all papers originating from final analysis prior to submission.

## 2. PEACH in Asia study

## Current protocol issued on medRxiv



THE PREPRINT SERVER FOR HEALTH SCIENCES

<https://www.medrxiv.org/content/10.1101/2022.11.13.22282262v3>



**PEACH in Asia: PEri-Anesthetic morbidity in CHildren in Asia: A prospective multinational multicenter observational study to investigate epidemiology of severe critical events in pediatric anesthesia in Asia**

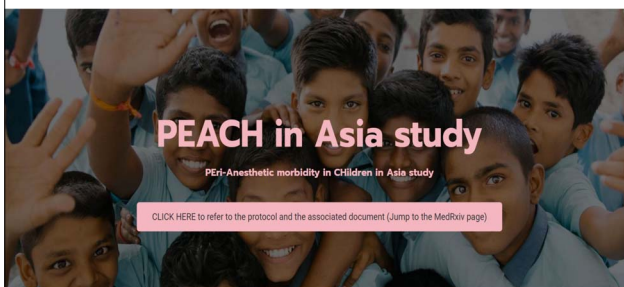
Soichiro Obara, Choon Looi Bong, Norifumi Kuratani, Zehra Serpil Ustalar Ozgen, Mahin Seyedhejazi, Shemila Abbasi, Ekta Rai, Elsa Varghese, Evangeline K Villa, Andi Ade W Ramlan, Ina Ismiarti Shariffuddin, Patcharee Sriswasdi, Pheakdey Nhong, Vivian Yuen, Hyo-Jin Byon, Josephine S K Tan

doi: <https://doi.org/10.1101/2022.11.13.22282262>



## 2. PEACH in Asia study

## The dedicated website will be updated soon



## 2. PEACH in Asia study

## Updated information available on newsletters

As of May 12<sup>th</sup>, 2023

**Questions and Answers**  
**for the PEACH in Asia study**

Soichiro Obara, the principal investigator of the PEACH in Asia study

Thank you all the national coordinators for contributing to the progress of our study project!  
Our PEACH in Asia study is now recruiting the patients for the pilot study.

## 2. PEACH in Asia study

## "User's guide for data entry in electronic case report form"

For all the national or local coordinators

**Data Entry into e-CRF on the UMIN INDICE system for the pilot study of the PEACH in Asia study: User Guide**

Contact: Soichiro Obara, MD, DrPH (Japan) soichoba@umc.ac.jp

## 2. PEACH in Asia study

A pilot study on-going in May to June 2023  
(facilities scheduled to participate as of mid-May)

Country/ Region Name	Country/ Region Code	Hospital Name	Hospital Code	Coordinator Name
Singapore	029	KK Womens' and Children's Hp	001	Choon Looi Bong, Siti Nuru Diyanah
Turkey	034	University of Acibadem	001	Z Serpil Ustalar Ozgen
Indonesia	010	Dr. Cipto Mangunkusumo Hp	001	Andi Ade W Ramlan
Malaysia	018	University of Malaya	001	Ina Ismiarti Shariffuddin
India	009	Christian Medical College	001	Ekta Rai
Pakistan	024	Aga Khan University Hp	001	Shemila Abbasi
Hong Kong	038	Hong Kong Children's Hp		Vivian Yuen, Jasmin Tong
Japan	013	Tokyo Metropolitan Otsuka Hp	001	Soichiro Obara
Japan	013	Saitama Children's Medical Center	002	Norifumi Kuratani

**Asian PEdiatric Anesthesia Research (A-PEAR) team**  
(contributing to our research project)



Shemila Abbasi (Pakistan)

Josephine Tan (Singapore)

Choon Looi Bong (Singapore)

Soichiro Obara (Lead) (Japan)

Norifumi Kuratani (Japan)

Patcharee Srisawasdi (Thailand)

Hyo-Jin Byon (South Korea)

Pheakdey Nhoung (Cambodia)

Elsa Varghese (India)

Ekta Rai (India)

Z Serpil Ustalar Ozgen (Turkey)

Andi Ade W Ramlan (Indonesia)

Mahin Seyedhejazi (Iran)

Ina Ismiarti Shariffuddin (Malaysia)

Teresita A Batanes (Philippines)

Evangelina Villa (Philippines)

## 2. PEACH in Asia study

### Research SIG's Vision

- To work on determination of the important research questions in our field of pediatric anesthesia, to hopefully trigger research endeavors in this area
- To foster the generation and propagation of research ideas in pediatric anesthesia beyond borders throughout Asia
- To collaborate with research committees of other anesthesia societies



## 2. PEACH in Asia study

### 2022-23 research SIG activities and outcomes

- Our main project: launching the internationally collaborative research project regarding prospective cohort research regarding peri-anesthetic morbidity in children in Asia, **PEACH in Asia study** project
- The Protocol was published on a pre-print server (MedRxiv)
- IRB review and approval were obtained at multi-national/regional centers in spring 2023
- A pilot study has been on-going in May to June 2023



## 2. PEACH in Asia study

### Peri-Anesthetic morbidity in Children in Asia (PEACH in Asia) study:

- will provide strategic framework for evidence-based policy-making, accountability and implementation guidance
- will work as a powerful roadmap to develop and implement data-driven education/training plans in Asia

**The main study will start recruitment this summer**



## 2. PEACH in Asia study

**Any hospital caring neonates and children is welcome to participate!**

**Your participation is highly appreciated!**

**Let us work on this project together!**

Kindly feel free to contact: **Soichiro Obara**

E-mail address: [soichoba1975@gmail.com](mailto:soichoba1975@gmail.com)



Or, kindly contact the A-PEAR tem members



PEACH in Asia study project

# The Future of Anesthesia-Related Neurotoxicity Studies: Update on the TREX Trial

Dean B. Andropoulos

Texas Children's Department of Anesthesiology, USA

## Disclosures

- SmartTots Medical Officer: private-public partnership of U.S. FDA and International Anesthesia Research Society
- U.S. FDA IND holder for dexmedetomidine studies (#118058)
- SmartTots grant funding for U.S. centers
- Australian National Medical Research Council funding the DCC in Melbourne, Australia
- Italian Medicines Agency funding all sites in Italy
- Dexmedetomidine is not labeled for pediatric use by U.S. FDA

## Learning Objectives

- Review the pharmacology and physiologic effects of dexmedetomidine
- Discuss dexmedetomidine neurodegenerative effects
- Describe human dexmedetomidine safety and pharmacokinetics in infants
- Detail the rationale and design for the TREX Trial

## Premise for Dexmedetomidine Studies

- Gamma-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) binding anesthetic agents consistently cause increased neuroapoptosis and other neurodegeneration, and adverse long-term neurocognitive/behavioral deficits in animal models of the developing brain, including non-human primates
  - Sevoflurane (GABA) is the most commonly used inhaled general anesthetic in infants and children world-wide
- Sevoflurane anesthetics in human infants and children are associated with behavioral changes (not cognitive) after single or multiple exposures
- Dexmedetomidine does not produce the same neurodegenerative changes in animals, and could serve as an adjunct, or sole sedative, during general anesthesia in infants and children

Ing C, et al. *Anesthesiology* 2022;136:500-512

**REVIEW ARTICLE**

**ANESTHESIOLOGY**

**Anesthesia and Developing Brains: Unanswered Questions and Proposed Paths Forward**

Caleb Ing, M.D., M.S., David G. Warner, M.D., Leticia S. Sun, M.D., Ravi Patel, P.H.D., M.D., M.P.H., Andrew J. Davidson, M.B.B.S., M.D., F.A.N.Z.C.A., F.A.H.M.S., Lucio Valente, M.D., Ph.D., Mary Ellen McCann, M.D., James O'Leary, M.D., David C. Salinger, Ph.D., M.Sc., Virginia Raab, Sc.D., Beverly A. Davis, M.D., Ph.D., F.R.C.P.C., Benjamin Green, M.D., **Dean B. Andropoulos, M.D., M.B.B.C.**

*Anesthesiology* 2022; 136:500-12

**ABSTRACT**

Anesthetic agents that alter neurodevelopment in animal models, but evidence in humans is mixed. The neurologic and behavioral changes observed across many species predict that children should be seen in humans, but identifying a potential of injury to children has been challenging. This review asks the field to consider a list of urgent questions, including: **What are the mechanisms of neurodevelopmental injury in animal models? How can we identify children at risk of neurodevelopmental injury? How can we identify children at risk of neurodevelopmental injury? How can we identify children at risk of neurodevelopmental injury?**

**DEFINING THE PROBLEM**

When the mixed results of the studies in children, the fundamental questions of the safety of commonly used anesthetics and whether this line of research inquiry should continue remains a source of intense debate. The purpose of this report is to provide expert consensus opinion regarding the state of the current preclinical and clinical evidence, the remaining questions, suggestions for future research, and improvements to the evolution of research of other suspected neurotoxicants, with the ultimate goal of ensuring that the millions of children who undergo procedures requiring anesthetic agents do so safely.

**Preclinical Data from Animal Models and Translation to Humans**

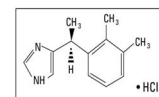
Animal studies convincingly show that general anesthetic medications induce a variety of morphofunctional alterations during brain development. Although most ani-

Approach	Advantages	Disadvantages
Further randomized controlled trials	Randomized controlled trials are the gold standard for proving causal effect of anesthetic exposure.	Randomized controlled trials are expensive and time consuming. Children cannot be randomized to no anesthetic, and what constitutes a "safe" anesthetic is unclear. The current feasible study designs are not optimal.
Observational studies and causal theory	Randomized controlled trials may not be feasible in all situations. Causal theory is commonly applied to other areas such as environmental toxicity.	Observational studies are limited by the inability to distinguish effects of anesthesia from surgery and other perioperative factors, as well as issues with confounding by indication. Application of causal theory relies on well-designed observational studies.
Intermediate outcomes and biomarkers	Injury could be identified at an earlier stage. Objective pre- and postoperative testing could be performed. Endophenotypes could be identified.	No consistent biomarkers have been identified. A phenotype of injury and the ideal outcomes to evaluate are unclear. The effects of anesthesia from uterine perfusion, inflammation, and other fetal distress cannot be distinguished.
Perinatal exposures	Translation between animal models and humans could be improved. Children may be more vulnerable to perinatal exposure. Less confounding by indication in the child as exposure is typically due to a condition in the mother rather than underlying conditions in the child. This is the animal model that is most similar to humans.	A randomized controlled trial is unlikely to be able to randomize a mother to general anesthesia or spinal anesthesia. The one study that evaluated the same outcome in humans and nonhuman primates found differences in nonhuman primates but not children, although nonhuman primates had significantly longer exposures.
Nonhuman primate studies	This model can be used to evaluate questions that cannot be studied in humans.	Translation between humans and animal models is challenging. The one study that evaluated the same outcome in humans and nonhuman primates found differences in nonhuman primates but not children, although nonhuman primates had significantly longer exposures.

*Anesthesiology* 2022; 136:500-12

## Dexmedetomidine

- Dexmedetomidine (DEX) is a novel sedative/hypnotic/anesthetic agent
  - $\alpha$ -2 receptors: locus ceruleus and spinal cord
  - $\alpha$ -2:  $\alpha$ -1 selectivity 1600:1 (clonidine 200:1)
- Minimal respiratory depression
- Reduces post-cardiac surgical tachyarrhythmias
- Reduce doses of volatile anesthetic agents (VAA), opioids, benzodiazepines
- Less neuroapoptosis in the developing brain
- Blocks neuroapoptosis by anesthetic agents
- Neuroprotective in hypoxia-ischemia
- Neuroprotective in inflammatory states



Human Data

Animal Data

*Anesth Analg* 2010;110:1383, *Anesthesiology* 2009; Ann Thorac Surg. 2011;92:964; Br J Anaesth. 2015;115:171-110;1077; Acta Anaesthesiol Scand 2010;54:710; Neurosci Lett 2008;409:128; Oxid Med Cell Longev 2016; 5303371



**SYSTEMATIC REVIEW** WILEY *Pediatric Anesthesia*

## A systematic review and narrative synthesis on the histological and neurobehavioral long-term effects of dexmedetomidine

*Pediatric Anesthesia*. 2019;29:125–136.

Camille E. van Hoorn<sup>1</sup> | Sanne E. Hoeks<sup>1</sup> | Heleen Essink<sup>1</sup> | Dick Tibboel<sup>2</sup> | Jorgen C. de Graaff<sup>1</sup>

**Conclusion:** In animals, dexmedetomidine was found not to induce histologic injury and to show a beneficial effect when administered with another anesthetic. No clinical results on the long-term effects in children have been identified yet.

**TABLE 2** Study characteristics

Article	Study design	Single dose dex (µg/kg)	Total dose dex (µg/kg)	Additional drugs	Histologic injury by dex?	Dex decreases injury caused by other anesthetic	Impaired function after dex	Less impairment after dex (Behavior)
Duan 2014 <sup>17</sup>	dex-ket vs dex-con	25	75	ket: ip 75 mg/kg	Yes	Yes	Yes	Yes
Goyagi 2016 <sup>23</sup>	dex-sevo vs sevo-con	6.6-12.5-25	6.6-12.5-25	sevo: 3.0% 4 h	---	---	---	---
Han 2013 <sup>24</sup>	dex-iso vs iso-con	25	75	iso: 0.75% sevo: 1.2% 4 h	---	---	---	---
Ibrahim 2015 <sup>25</sup>	dex-sevo vs prop-dex	3	3	sevo: 4%; prop: iv 4 mg/kg	Yes	No	---	---
Koo 2014 <sup>26</sup>	dex vs con	30-30	39-390	ket: 20 mg/kg 20-50 mg/kg 12 h	Yes	---	---	---
Lee 2012 <sup>27</sup>	dex-sevo vs dex vs sevo	1.5-2.5-50-100 <sup>a</sup>	3-15-75-150-300	sevo: 2.5% 6 h	---	---	---	---
LLJ 2016 <sup>28</sup>	dex-prop vs dex-iso vs dex	2.5-5.0-10	5-10-20	prop: iv 8.0 mg/kg+1.2 mg/kg/min	Yes <sup>a</sup>	Yes	---	---
LiY 2014 <sup>18</sup>	dex-iso vs iso-con vs dex	25-50-75	25-50-75	iso: 0.75% 6 h	No	Yes	---	---
Liu 2014 <sup>29</sup>	dex-iso vs iso-con	25-50-75	75-150-225	iso: 0.75%	No	Yes	---	---
Liu 2016 <sup>30</sup>	dex-ket vs dex vs con	10-25-50	50-125-250	ket: ip 20 mg/kg per dose	Yes	No	---	---
Lu 2017 <sup>31</sup>	dex-prop vs con	25-50-75	25-50-75	prop: ip 100 mg/kg	---	---	---	---
Obitany 2015 <sup>32</sup>	dex-iso vs iso	1	2	iso: 1.3%-2.0% 2-3 h 6 h	---	---	---	---
Pencano 2016 <sup>33</sup>	dex vs ket vs con	30-45	30-45	---	Yes	---	---	---
Perez 2017 <sup>34</sup>	dex-sevo vs con	1.5-10-25-50	3-15-30-75-150	sevo: 2.5% 6 h	---	---	---	---
Sanders 2009 <sup>28</sup>	dex-iso vs iso-con	1-10-25	3-30-75	iso: 0.75% 6 h	---	---	---	---
Sanders 2009 <sup>28</sup>	dex-iso vs iso-con	25-50-75	75-150-225	iso: 0.75% 6 h	---	---	---	---
Su 2015 <sup>35</sup>	dex-iso vs dex+O2 vs con	10	20	iso: 1.5% 4 h	---	---	---	---
Tachibana 2011 <sup>36</sup>	dex vs con	5-10	5-10	---	---	---	---	---
Wang 2016 <sup>37</sup>	dex-prop vs con	75	525	prop: ip 7 days 3x20 mg/kg/d	---	---	---	---
Zeng 2013 <sup>38</sup>	dex vs dex-iso vs iso	25-50-75	25-50-75	iso: 0.75% 6 h	---	---	---	---

*Pediatric Anesthesia*. 2019;29:125–136.

## Why Dexmedetomidine?

- Clinician's perspective:
  - Familiarity
  - Feasibility for research and adoption into clinical practice
- Widely used in pediatric anesthesia and ICU
  - Post-surgical, medical ICU, premed, opioid sparing for tonsillectomy, TIVA for spines, emergence agitation, procedural sedation
- Significant body of clinical research/clinical publications in infants/children
  - 456 in infants birth-23 months
  - 1191 in children 0-18 years
- U.S. FDA labeled for adults 18+
  - ICU sedation intubated patients
  - Procedural sedation: non-intubated patients; surgical and other procedures

**BJA** British Journal of Anaesthesia, 123 (6): 839–852 (2019)

doi: 10.1016/j.bja.2019.06.026  
Advance Access Publication Date: 14 October 2019  
Paediatric Anaesthesia

## PAEDIATRIC ANAESTHESIA

### Results of a phase 1 multicentre investigation of dexmedetomidine bolus and infusion in corrective infant cardiac surgery

Athena F. Zuppa<sup>1</sup>, Susan C. Nicolson<sup>1</sup>, Nicole S. Wilder<sup>2</sup>, Juan C. Ibla<sup>3</sup>, Erin A. Gottlieb<sup>4,5</sup>, Kristin M. Burns<sup>5</sup>, Mario Stylianou<sup>6</sup>, Felicia Trachtenberg<sup>7</sup>, Hua Ni<sup>7</sup>, Tera H. Skeen<sup>8</sup>, Dean B. Andropoulos<sup>4,5</sup> on behalf of Pediatric Heart Network Investigators

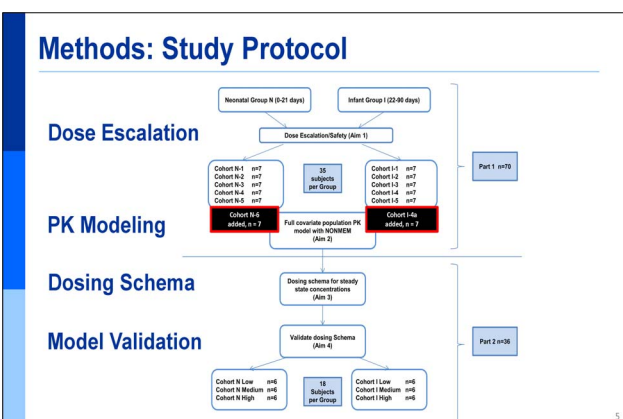
 

## Methods: Subject Recruitment, N = 124

- Inclusion criteria: Neonates/Infants 0-180 days
- Stratification: Neonates 0-21 days; Infants 22-180 days
- Corrective two-ventricle surgery with CPB:
  - Arterial switch for dextrotransposition of the great arteries (D-TGA)
  - Ventricular septal defect without arch obstruction
  - Tetralogy of Fallot
- Major exclusion criteria
  - <37 weeks (neonates), <36 weeks (infants), extracardiac anomalies affecting safety/PK, previous DEX/clonidine, AV block, bradycardia, renal/liver dysfunction, cardiac arrest/ECMO
- Enrollment in 4 U.S. centers
  - Texas Children's Hospital, Children's Hospital of Philadelphia, C.S. Mott Children's Hospital, Boston Children's Hospital

## Results: Safety Events

- 5 adjudicated safety events (4.1%, 95% CI 1.8-9.2%)
  - Two junctional bradycardia (65-109 BPM)
  - Two 2<sup>nd</sup>-3<sup>rd</sup> degree AV block (85-95 BPM)
    - All 4 with temporary pacing (30 minutes to 48 hours)
    - 3 of 4 receiving digoxin, amiodarone, or β-adrenergic blocking drugs
  - One hypotension: multifactorial etiology
- All safety outcomes in Infant age group
- No consistent relationship with DEX plasma level (126-977 pg/ml)



## Results: PK Parameters, N=119 Subjects

Parameter	Allometric weight normalised model		Linear weight normalised model	
	Point estimate (NONMEM SE%)	95% CI from LLP	Point estimate (NONMEM SE%)	95% CI from LLP
CLpre (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	1240 (14)	1030, 1470	2580 (14)	1950, 3400
CLcpb (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	74.1 (42.1)	59, 126	142 (53.5)	130, 300
CLpost (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	623 (7.9)	560, 670	1240 (8.39)	1020, 1400
V1pre (L 70 kg <sup>-1</sup> )	132 (26.4)	109, 152	139 (25.8)	94.6, 202
V1cpb (L 70 kg <sup>-1</sup> )	115 (14.7)	106, 136	116 (14.9)	103, 146
V1post (L 70 kg <sup>-1</sup> )	155 (7.61)	141, 167	159 (7.92)	123, 185
Qpre (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	2300 (96.1)	50, 6800	4120 (107)	100, 400 000
Qcpb (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	2980 (18.7)	2410, 3710	6160 (16.9)	4300, 8400
Qpost (ml min <sup>-1</sup> 70 kg <sup>-1</sup> )	209 (18.6)	161, 270	422 (20.3)	280, 700
V2pre (L 70 kg <sup>-1</sup> )	78.9 (36)	19.5, 154	69.6 (43)	5, 90
V2cpb (L 70 kg <sup>-1</sup> )	144 (12.4)	135, 162	147 (12.4)	101, 149
V2post (L 70 kg <sup>-1</sup> )	105 (9.4)	92.3, 113	97 (10.6)	78.6, 130
Age CLpost 50% mature (days)	1.77 (25.4)	1.11, 2.28	1.29 (33.9)	0.4, 2
Temp effect V1cpb	-1.6 (6.6)	-1.69, -1.41	-1.57 (6.43)	-1.73, -1.21

## Dean B. Andropoulos: The Future of Anesthesia-Related Neurotoxicity Studies: Update on the TRES Trial

## Results: Dosing Recommendations

Age Group	Target Plasma Concentration (pg/ml)	Initial Loading Dose (mcg/kg)	Infusion 1: pre-CPB, first 60 min CPB (mcg/kg/hr)	Loading Dose to CPB Prime (mcg/ml)	Infusion 2: after 60 min CPB until end CPB (mcg/kg/hr)	Infusion 3: 60 min after CPB (mcg/kg/hr)
Neonate	200	0.24	0.22	0.004	0.04	0.14
Neonate	500	0.6	0.55	0.01	0.1	0.35
Neonate	700	0.84	0.77	0.014	0.14	0.49
Neonate	1000	1.2	1.1	0.02	0.2	0.7
Infant	200	0.29	0.26	0.005	0.05	0.17
Infant	500	0.72	0.66	0.012	0.12	0.42
Infant	700	1.01	0.92	0.017	0.17	0.59
Infant	1000	1.44	1.32	0.024	0.24	0.84

Based on CPB low temp of 32°C and 90-minute CPB time

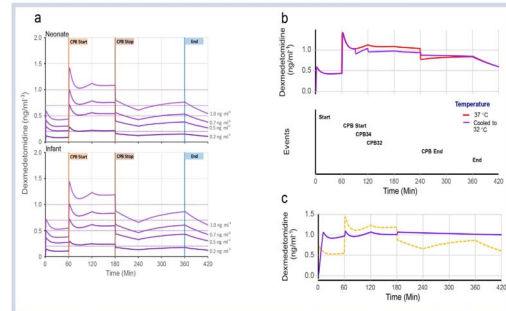
British Journal of Anaesthesia, 123 (6): 839–852 (2019)

12

## Playing with dexmedetomidine pharmacokinetics!

Gregory Hammer<sup>1</sup> and Steven L. Shafer<sup>1,2,\*</sup>

British Journal of Anaesthesia, 124 (3): 238–240 (2020)

<sup>1</sup>Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University, Palo Alto, CA, USA and <sup>2</sup>Department of Bioengineering and Therapeutic Sciences, University of California, San Francisco, CA, USA

## Rationale for TRES Trial

- Opioids and alpha-2 agonists do not cause the same neurodegenerative changes seen in animal models with other GAs or sedatives
- Neurodevelopmental outcome data in longer anesthetic exposures, i.e. >2-3 hours, is lacking
  - Short single exposures, multiple exposures: behavioral but not cognitive changes
  - GAS, MASK, PANDA studies
- A pilot study of dexmedetomidine/remifentanyl/combined with caudal anesthetic for anesthetics greater than 2 hours was feasible in 60 subjects less than 1 year of age
- For the randomized trial, low-dose sevoflurane was added to dexmedetomidine/remifentanyl because of high rate of light anesthesia in the pilot study
- Standard dose sevoflurane is commonly utilized in daily practice for these anesthetics

## TRES Pilot Study: (Toxicity of Remifentanyl-DEXmedetomidine)

Received: 16 March 2018 | Revised: 31 October 2018 | Accepted: 8 November 2018  
DOI: 10.1111/pan.13544

## RESEARCH REPORT

WILEY Pediatric Anesthesia

## An open label pilot study of a dexmedetomidine-remifentanyl-caudal anesthetic for infant lower abdominal/lower extremity surgery: The T REX pilot study

Peter Szumuk<sup>1,2</sup> | Dean Andropoulos<sup>3</sup> | Francis McGowan<sup>4</sup> | Ansgar Brambrink<sup>5</sup> | Christopher Lee<sup>6</sup> | Katherine J. Lee<sup>7</sup> | Mary Ellen McCann<sup>8</sup> | Yang Liu<sup>3</sup> | Rita Saynhalath<sup>1</sup> | Choon Looi Bong<sup>9</sup> | Brian J. Anderson<sup>10</sup> | Charles Berde<sup>8</sup> | Jurgen C. De Graaff<sup>11</sup> | Nicola Disma<sup>12,13</sup> | Dean Kurth<sup>4</sup> | Andreas Loepke<sup>4</sup> | Beverley Orser<sup>14</sup> | Daniel I. Sessler<sup>2</sup> | Justin J. Skovno<sup>15</sup> | Britta S. von Ungern-Sternberg<sup>16</sup> | Laszlo Vutskits<sup>17</sup> | Andrew Davidson<sup>18</sup>

Pediatric Anesthesia. 2019;29:59–67.

## TRES Pilot Study (Toxicity of Remifentanyl-DEXmedetomidine)

- 8 sites enrolled subjects: (1-20), N = 60, age < 1 year
- Eye-opening times about 7 minutes
- Most had excellent analgesia in PACU, most discharged <60 minutes
- No protocol abandonment in 56 subjects
- No serious adverse events: mild/moderate hypotension (25%) and bradycardia (16%)
- 80% had "rescue" treatment for light anesthesia (movement/hypertension)**
- Protocol is feasible: 87.5% of patients with functioning caudal required no sevoflurane or propofol rescue**

Pediatric Anesthesia. 2019;29:59–67.

## Dexmedetomidine/Remifentanyl/Low Dose Sevo vs. Standard Dose Sevoflurane RCT: TRES Trial

- Children <2 years undergoing 2 hours or longer of surgery time, 2+ hours of anesthesia time
- Dexmedetomidine/remifentanyl/low dose sevoflurane (0.3-0.6%ET), vs. standard higher dose sevoflurane (2.5-3.0%ET)
- Age 3 years: battery of neurodevelopmental tests
- Up to 20 sites in USA, Australia, Europe
- Weschler Full-scale IQ is primary outcome; difference of 5 points significant
- 450 needed to enroll to yield 380 evaluable subjects

## TRES: Toxicity of Remifentanyl-DEXmedetomidine Trial

- Phase III randomized, active controlled, parallel group, assessor blinded, multicenter, superiority trial of:
  - Low-dose sevoflurane/DEX/remifentanyl: DEX 1 mcg/kg load, 1 mcg/kg/hr infusion; remifentanyl 1 mcg/kg load, 0.1 mcg/kg/min or greater infusion; sevoflurane 0.3-0.6% ET or less
  - Standard dose sevoflurane: 2.5-3.0% ET or greater
- Neuraxial/regional/local anesthesia, morphine (end of case) allowed
- Inclusion: < 2 years, surgery time of 2 hours, total anesthesia/OR time 2+ hours
  - Decreased from 2.5 hours due to slow enrollment
- Exclusion: Previous or future GA >2 hours before age 3 years; neurodevelopmental issues, cardiac or neuro disease

## TRES: Primary Objective

- Determine if low dose sevoflurane/dexmedetomidine/remifentanyl is superior to standard dose sevoflurane anesthesia in terms of global cognitive function assessed by the full-scale IQ score of the Weschler Preschool and Primary School Intelligence Scale assessed at 3 years of age

### TREX Secondary Objectives

- A range of other neurodevelopmental tests performed at 3 years of age including subscales of general cognitive functioning, language, executive function, memory, adaptive behavior, clinical behavior and social skills
- Diagnosis of any neurodevelopment disorder at 3 years of age
- Additional secondary outcomes:
  - Incidence of intraoperative hypotension and bradycardia
  - Postoperative pain
  - Time to recovery

### TREX Enrollment

- 450 subjects have been enrolled, 190 in each group required to have 90% power to detect a difference of 5 points based on 2-sided test with alpha = 0.05
  - 15% loss to follow-up anticipated
- Enrollment started August 2017
- Pandemic slowed enrollment but additional centers started, especially Italy
- 450 target enrolled on April 21, 2023
- More than 100 with 3-year follow-up completed
- Anticipate completing most all neurodevelopmental assessments end of 2025
- No serious adverse events related to the study

### Participating Centers and Enrollment

- United States:
  - Children's Medical Center, Dallas: 85
  - Texas Children's Hospital, Houston: 60
  - Boston Children's Hospital: 25
  - Children's Hospital of Philadelphia: 4
  - Cleveland Clinic: 4
- Australia:
  - Perth Children's Hospital: 23
  - Queensland Children's Hospital: 25
  - Children's Hospital Westmead: 19
  - Royal Children's Hospital, Melbourne: 13
  - Flinders Medical Centre: 14
  - Women and Children's Hospital, Adelaide: 11
  - Sydney Children's Hospital: 13

### Participating Centers and Enrollment (cont'd)

- Italy:
  - Istituto Giannina Gaslini: 60
  - Azienda Ospedaliero Universitaria Pisana: 12
  - Azienda Ospedaliero-Universitaria Meyer: 21
  - Ospedale Bambino Gesù: 4
  - Azienda Ospedaliero-Universitaria di Bologna: 7
  - Presidio Ospedale Infantile C. Arrigo Azienda Ospedalier, Italy: 15
  - Vittore Buzzi Children's Hospital, Italy: 29
  - Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico - Clinica Mangiagalli, Italy: 6

### Conclusions

- Dexmedetomidine does not induce the same histologic injury, and ameliorates the effects of other anesthetics in pre-clinical models
- Dexmedetomidine pharmacokinetics and safety are well established in infant populations, including congenital heart disease
- A dexmedetomidine-based anesthetic, with low-dose sevoflurane is safe and feasible
- The TREX Trial enrollment is complete and will add human neurodevelopmental outcome data with a dexmedetomidine-based anesthetic vs. conventional sevoflurane anesthetic





## **Session 4.**

# **Issues We Are Facing & Need to Overcome**

**Chair(s): Vibhavari Naik (India)**  
**Hee-Soo Kim (Korea)**

## Environmental Impact of Anesthesia (Virtual)

Diane Gordon

Children's Hospital Colorado, USA

### Learning Objectives

1. Describe the chemical properties of volatile anesthetic agents and nitrous oxide that are responsible for their detriment to the atmosphere
2. Summarize the arguments supporting use of low fresh gas flows when using volatile agents, including the science that refutes higher flow suggestions for sevoflurane.

Department of Anesthesiology and Critical Care Medicine, Children's Hospital Los Angeles,  
University of Southern California Keck School of Medicine, USA

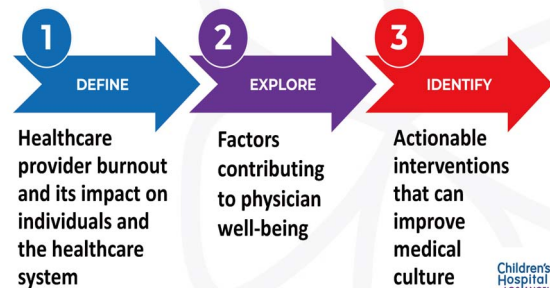


## DISCLOSURE

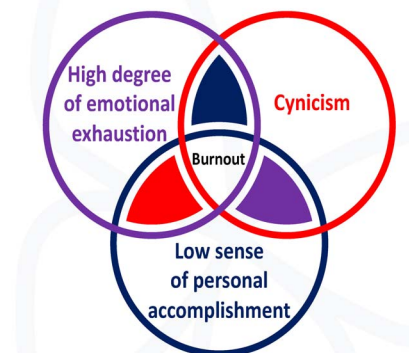
I have no actual or potential conflict of interest in relation to this presentation



## Objectives



## Definition of Burnout



## Drivers of Burnout



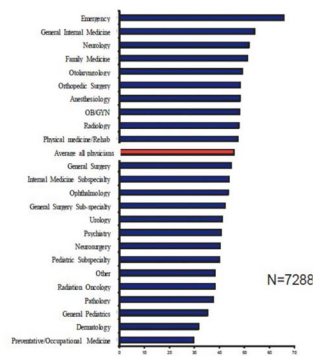
Shanafelt TD, Noseworthy JH. Executive Leadership and Physician Well-being: Nine Organizational Strategies to Promote Engagement and Reduce Burnout. *Mayo Clin Proc*. 2017 Jan;92(1):129-146. doi: 10.1016/j.mayocp.2016.10.004. Epub 2016 Nov 18. PMID: 27871627.



## Scope of problem

### Burnout and Satisfaction With Work-Life Balance Among US Physicians Relative to the General US Population

Tait D. Shanafelt, MD; Sonja Boone, MD; Lijun Tan, PhD; Lene N. Dyrbye, MD, MSFT; Wayne Satele, PhD; David Sordy, BS; Colin P. West, MD, PhD; Jeff Shuren, PhD; Michael E. Cushman, MD



## Burnout: A public health crisis



## Leading health care organizations declare physician burnout as 'public health crisis'



HealthAffairs

## Physician Burnout Is A Public Health Crisis: A Message To Our Fellow Health Care CEOs

 NATIONAL ACADEMY OF MEDICINE





## What can we do?

- Stop the glorification of excessive self-sacrifice
- Stop blaming and shaming doctors
- Normalize peer and mental health support
- Stop the strip mining
- Empower physicians to be the architects of their own environment

[Barnes] • Anesthesiol Clin. 2022; Jan;60(2):210-225. doi: 10.1016/j.anclin.2022.07.001. Epub 2022 Aug 4.  
**The Wicked Problem of Physician Well-Being**  
Jana L. Slinkey<sup>1</sup>, Rebecca D. Margolis<sup>2</sup>, Amy C. Orsini<sup>3</sup>

Children's Hospital LOS ANGELES

## Stop the Glorification of excessive self-sacrifice

Shapiro DE, Desautels C, Abbott DM, Babinew T, Pearl A, Haddad P. Beyond Burnout: A Physician Wellness Hierarchy Designed to Prioritize Interventions at the Systems Level. Am J Med. 2019 May;132(5):556-563. doi: 10.1016/j.amjmed.2018.11.028. Epub 2018 Dec 13. PMID: 30538832.

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## Stop blaming and shaming doctors

**Impact of lawsuits**  
Physicians involved in a lawsuit are at ↑ risk for stress, personal consequences, and burnout

**Litigation and patient safety & quality**  
Litigation has not been shown to improve patient safety or quality of care

**Liability reform**  
Liability reform is necessary to uphold patient safety while minimizing trauma to doctors

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## Normalize peer and mental health support

Proactive support mechanisms for provision of relief, connection to mental health support, longitudinal legal & risk management

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## The Impact of Perioperative Catastrophes on Anesthesiologist: Results of a National Survey

Gazoni, Farnaz M. MD; Amato, Peter E. MD; Malik, Zahra M. MD; Durieux, Marcel E. MD, PhD

Category	Percentage
Needed time to recover	88%
Never did	19%
Considered change in career	12%
Subsequent care compromised over the next 4 hrs	67%
Needed time to recover	7%

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## Addressing Postpandemic Clinician Mental Health

*Annals of Internal Medicine*  
 A Narrative Review and Conceptual Framework  
 Rachel Schwartz, PhD; Jina L. Slinkey, MD; Uma Asand, PhD, LP; and Rebecca D. Margolis, DO

**Societal**

- Broad funding and policies to support enhanced mental health programs

**Organizational**

- Addressing HCWs basic needs
- Specialized training for new job roles
- Recognition and communication from leadership
- Addressing moral injury
- Programs to encourage peer support/connection

**Individual**

- Resilience and stress reduction training

Figure. Proposed framework of clinician well-being resources

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## Stop the strip mining

- Harness intrinsic motivators
- Clinicians are a finite resource and must be valued as such
- Healthcare institutions must adopt long-term strategies focused on retention by investing in and supporting employees

Lukarsky DA, French MT, Gilson HS, Rosen LE, Ullmann SG. Why Money Alone Can't (Always) "Bribe" Physicians: The Role of Behavioral Economics in the Design of Physician Incentives. Anesthesiology. 2015;130(1):154-170. doi:10.1097/ALN.0000000000000273

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## Empower physicians to be the architects of their own environment

- Early leadership training
- Leadership roles must come with protected time

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## Challenges in providing safe anaesthesia to children in LMIC's

**Rebecca Jacob**

(Retired) Christian Medical College, India

Access to safe anaesthesia and surgery for patients of all ages should be considered a basic human right, but this is not available to a large segment of the world's population. Many developing and underdeveloped countries spend a very small portion of their GDP on health care, and this is the greatest barrier to providing good anaesthetic services and surgical care. Different countries have different problems and there are often regional variations within the same country. Some LIC's have very well equipped and staffed hospitals in major cities while the rural poor suffer. Often the problem is maldistribution of supplies rather than absolute shortage

Surgery is critical to the health of the population and safe anaesthesia is a mandatory component of safe surgical care. There is much that can be done to make sure that the existing resources are used efficiently. The WHO, acknowledging the fact that the global volume of surgery is significant and adverse events resulting from surgeries constitute a significant public health concern, launched the Patient Safety Initiative in 2004 and the Safe Surgery Saves Lives initiative in 2008. With these initiatives, they have set a core set of safety standards that can be applied to all countries in all settings. The Surgical Safety Check List, together with the WHO-WFSA International Standards for a Safe Practice of Anesthesia (2010) enhanced patient safety cultures but Pediatric Anaesthesia in LMIC's has not kept pace with advances made in developed countries and International standards for Safe Anaesthesia Practice adopted by the WFSA are seldom met.

The element of safety is particularly important in anaesthesia because anaesthesia is not in itself therapeutic and is intrinsically hazardous.

### Problems faced in delivering safe anaesthesia in LMIC's

- The patients
- Spectrum and nature of the disease
- Personnel – staffing
- Facilities
- Equipment and supplies
- Drugs – poor supply, quality and perhaps, out dated

*The patients:* are often, anemic, undernourished children of economic crises, war or natural disasters. Fear, superstition, interference by 'local healers', poor understanding of medical problems, poor education and poor access to medical care often results in delayed presentation.

*Spectrum and nature of the disease:* Often marasmic, anemic, undernourished, riddled with tuberculosis or HIV

*Personnel – staffing:* Anaesthesia is not perceived as an attractive career for many undergraduates who have little or no exposure to the subject during their studies Anaesthesia does not enjoy a high profile and lacks the voice to demand access to basic resources in developing countries. Anaesthesia providers are often too busy providing clinical services to find the time to approach the 'powers that be' for basic requirements. There is a critical shortage of manpower and this proves a barrier to progress. Anaesthesia is often delivered by nurses or non-technical people. Supervision is invariably inadequate In some countries surgery is performed without the 'luxury' of an anaesthetist Access to textbooks and journals are limited and internet access is non-existent. Most 'trained' anaesthetists are afraid to deal with children especially neonates and infants because of perceived difficulty or fear Invariably a 'paediatric anaesthetist is one who shows an interest in children, likes children or is just allocated to 'do' children on a particular day. A trained Paediatric Anaesthetist is, therefore, a luxury

## Facilities and Drugs

Operating Rooms are often poorly equipped, non-air conditioned, with poor facilities for sterilization of equipment. Water supply and electricity is erratic Supplies of anaesthetic gases and oxygen supplies unreliable and erratic Drugs are in short supply and are often outdated IV fluids- their choice and availability is limited. Halothane and Isoflurane are the most commonly used inhalational agents. Ketamine and paracetamol most often used analgesics. Narcotics like morphine are often unavailable or its use is restricted Choice of neuromuscular drugs is limited and often a 'reversal' drug like neostigmine is unavailable Regional anaesthesia has benefits like safety, cost savings and analgesia but is often not used in children for lack of training, fear of failure or non-availability of drugs and disposables etc.

## Blood availability and safety

Fewer than 30% of developing countries have nationally coordinated blood transfusion services. Screening of donors is often not done. Many do not perform even rudimentary tests for diseases such as hepatitis and HIV Storage of blood is difficult especially as electricity supply is often erratic.

## Equipment

Electricity is unreliable and reliable functional 'back up' generators are often unavailable Sterilization of re- use- able equipment is the norm but availability and performance of sterilizers is unreliable Recycling of disposable equipment such as endotracheal tubes is also often relied on General facilities for infection control such as running water, disinfectants and gloves is also unreliable Essential equipment to provide safe anaesthesia for neonates and

infants are in short supply from appropriately sized endotracheal tubes, small IV cannulae, appropriate airways, laryngoscopes and syringe pumps.

*Monitoring* is often basic – a precordial stethoscope and a finger on the pulse is often all that is available. The Global oximetry project has helped with providing reasonably priced pulse oximeters.

Anaesthesia machines are of 2 categories

1. Modern, sophisticated electronic machines. These are often donated by well meaning donors

- They require electricity,
- operating manuals that require to be understood (especially if in a foreign language),
- regular maintenance by individuals trained to do so.
- service contracts do not often hold good in remote rural locations.
- often discarded at the first sign of trouble

Poorly understood and poorly maintained equipment becomes hazardous and potentially life threatening

2. Simple, durable and safe

- versatile, easily understood and easy to use
- able to function even if there is no electricity and if there are no cylinders available
- robust,
- able to withstand extreme climate conditions,
- Inexpensive, economical and easily maintained by locally available skills

3. Oxygen concentrators

## Visiting Providers

Often come with no idea of the facilities or the needs of the local people or with preconceived ideas that 'they know best'. However some countries organize well staffed 'missions' to remote areas

## Solutions?

Knowing that there is a dearth of qualified paediatric anaesthesia providers especially in rural areas, I would look at what measures need to be taken to bridge the 'demand/supply' gap of qualified, committed anaesthesia providers in those areas

- Can we bring about quality improvement with education?
- Establish protocol driven clinical outcomes leading to standardization of safety protocols.

*But who is to ensure that these are followed?*

- Can we find a way to 'match' safety policies to implementation across vast and diverse countries or diverse re-



gions in the same country?

- How do we gauge whether these policies and protocols are working?

*What 'outcome measures' would be appropriate?*



# Room B



## **Session 1.**

# **Optimization of Intraoperative Ventilation in Children**

**Chair(s): Ekta Rai (India)**

**Chul-Ho Chang (Korea)**



# Optimal Target of O<sub>2</sub> and CO<sub>2</sub>

Sung-Ae Cho

Department of Anesthesiology and Pain Medicine, College of Medicine, Konyang University, Korea

## Declaration

- No conflicts of interest

The Korean Society Pediatric Anesthesia  
대한소아마취학회

## Oxygen and carbon dioxide



Cummins EP, Stroutzki MJ, Taylor CT. Physiol Rev. 2020 Jan 1;100(1):469-488.

## With anesthesia



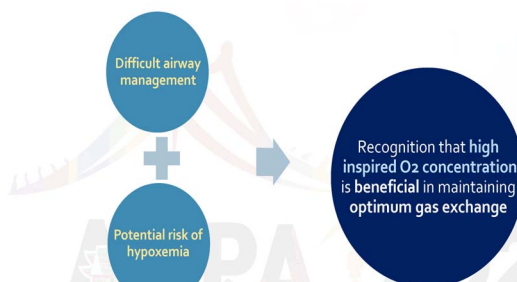
The Korean Society Pediatric Anesthesia  
대한소아마취학회

## With anesthesia



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## With anesthesia



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## Difficult airway

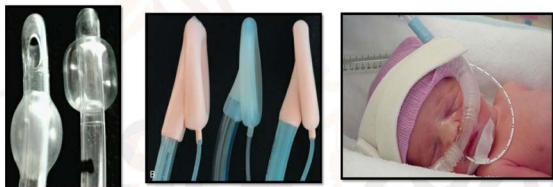


Basics of pediatric anesthesia, Ronald S. Litman

## With anesthesia

### • Several oxygen delivery method

- Invasive involuntary; Intubation, LMA, bronchoscopy.....
- noninvasive self breathing; CPAP, nasal cannular, oxygen mask....



A Practice of Anesthesia for Infants and Children, sixth edition; Cote, Lemman, Anderson  
Pediatric and neonatal mechanical ventilation; Rimensberger

## Optimal oxygen

### • The Optimal Arterial Oxygen Tension (Pao<sub>2</sub>)

at the **Lowest Inspired Oxygen Concentration (Fio<sub>2</sub>)**

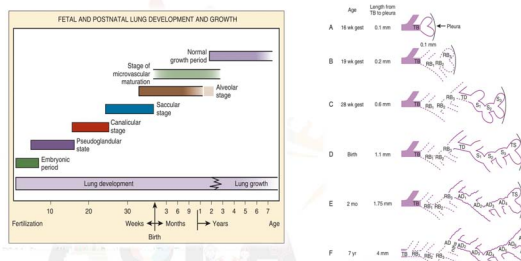
#### • With ABGA – direct method

- PaO<sub>2</sub>, Fio<sub>2</sub>, A-a gradient

#### • Without ABGA – indirect method; SpO<sub>2</sub>

- Measure arterial oxyhemoglobin saturation, not arterial oxygen partial pressure

## Prenatal Development of the Lungs



### BOX 3-1 Mechanism of Continuous Neonatal Breathing

- The onset of breathing activities occurs not at birth but in utero as a part of normal fetal development.
- The clamping of the umbilical cord initiates rhythmic breathing.
- Relative hypoxia with air breathing, compared with low fetal PaO<sub>2</sub>, augments and maintains continuous and rhythmic breathing.
- Continuous breathing is independent of the level of PaO<sub>2</sub>.
- Breathing is unaffected by carotid denervation.
- Hypoxia depresses or abolishes continuous breathing.

TABLE 3-1 Normal Blood-Gas Values

	PaO <sub>2</sub> (mm Hg)	PaO <sub>2</sub> (%)	Paco <sub>2</sub> (mm Hg)	pH
Pregnant woman at term	88*	96	32	7.40
Umbilical vein	31	72*	42	7.35
Umbilical artery	18	46*	61	7.28
1 hour of life (artery)	82	95	28	7.36
24 hours of life (artery)	68	94	29	7.37
Child and adult (artery)	99	97	41	7.40

\*Estimated values.

### the level of PO<sub>2</sub> at which SaO<sub>2</sub> is 50%, indicating the affinity of hemoglobin for oxygen

Age	P <sub>50</sub> (mm Hg)	Percent Saturation at Venous Oxygen Tension of 40 mm Hg	Hemoglobin (g/100 mL)	Oxygen Unloaded* (mL/100 mL)
1 day	19.4	87	17.2	1.84
3 wk	22.7	80	13.0	2.61
6-9 wk	24.4	77	11.0	2.85
3-4 mo	26.5	73	10.5	3.10
6 mo	27.8	69	11.3	3.94
8-11 mo	30.0	65	11.8	4.74
5-8 yr	29.8	67	12.6	4.73
9-12 yr	27.8	69	13.4	4.67
Adult	27.0	71	15.0	4.52

\* Assumes arterial oxygen saturation of 95%.

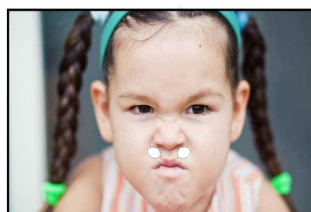
Data from Oski FA. Designation of anemia on a functional basis. J Pediatr. 1973;83:353.

TABLE 3-5 Hemoglobin Requirements for Equivalent Tissue Oxygen Delivery

P <sub>50</sub> (mm Hg)	Hemoglobin for Equivalent O <sub>2</sub> Delivery (g/dL)
Adult	27
Infant >6 mo	30
Neonate <2 mo	24

Data calculated from Motoyama EK, et al. Functional basis of childhood anemia [abstract]. Am Soc Anesthesiology. 1974;283.

## Hmmmm.....



## The purpose of O<sub>2</sub> supplement

### • In pediatrics

- Indication; for correction hypoxemia (low oxygen content in the blood)

### • In anesthesiology

- Indication; for adequate tissue oxygenation during perioperative period

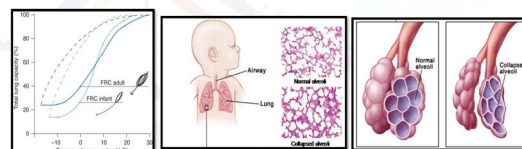
## Pediatric anesthesia

- Adequate tissue oxygenation during perioperative period

- Prevention and treatment for hypoxemia

- m/c hypoxemia during anesthesia : d/t V/Q mismatch

- In this case, high Fio<sub>2</sub> can seriously affect hypoxemia



Trachsel D, Svendsen J, Erb TO, von Ungern-Sternberg BS. Br J Anaesth. 2016 Aug;117(2):151-63.

## Normal Children



Duncan L, Correia M, Morgan P. Children. 2022;9(3):1416

## High inspired oxygen fraction impairs lung volume and ventilation heterogeneity in healthy children: a double-blind randomised controlled trial

Béatrice de la Grandville<sup>1,2,3,4</sup>, Ferenc Petak<sup>5</sup>, Gergely Abou<sup>6,7</sup>, Sam Bayat<sup>8,9</sup>, Isabelle Pichon<sup>10</sup> and Walid Habre<sup>1,2,3,4</sup>

<sup>1</sup>Department of Anaesthesiology, Hôpital Necker, Hôpital Saint-Antoine, Paris, France; <sup>2</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>3</sup>Department of Anaesthesiology, Hôpital de la Cochin, Paris, France; <sup>4</sup>Department of Anaesthesiology, Hôpital de la Saint-Jacques, Paris, France; <sup>5</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>6</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>7</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>8</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>9</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France; <sup>10</sup>Department of Anaesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France

- 6-16 years, elective non-abdominal and non-thoracic surgery <200 min, general anesthesia with tracheal intubation
- ASA 1 or 2, BMI <30 kg/m<sup>2</sup>
- Group
  - FiO<sub>2</sub> 0.8 vs. 0.35 group (FiO<sub>2</sub> 0.8 at induction/emergency; FiO<sub>2</sub> 0.35 intraoperative)
  - FiO<sub>2</sub> 0.8 group (FiO<sub>2</sub> 0.8 at induction/emergency; FiO<sub>2</sub> 0.8 intraoperative)
- FiO<sub>2</sub> 0.8 decreased lung volume in the immediate postoperative period

The effect of oxygen concentration on atelectasis formation during induction of general anesthesia in children: A prospective randomized controlled trial

Hyun H Kim<sup>1</sup>, J Young Kim<sup>2</sup>, J Young Kim<sup>3</sup>, Chul Kwon Lee<sup>4</sup>, Chul Kwon Lee<sup>5</sup>, Matthew R. Cho<sup>6</sup>, Hyeon Byun<sup>7</sup>

	60% oxygen	80% oxygen	100% oxygen	p value
After anesthetic induction	2.0 (1.0-2.5)	2.0 (1.0-2.8)	3.0 (2.0-3.0)	.003
At the end of operation	2.0 (1.3-3.8)	3.0 (1.8-3.0)	4.0 (2.0-4.0)	.205

Groups compared	p value
60% vs. 80%	.422
60% vs. 100%	.0151*
80% vs. 100%	.0744

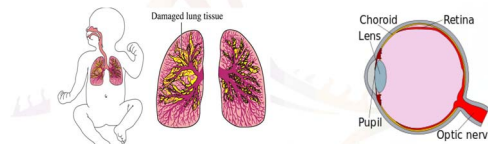
Lower FiO<sub>2</sub> : atelectasis ↓, keep lung volume

## Negative effect of oxygen

- **Absorption atelectasis**
  - High O<sub>2</sub> : inducing airway closure and alveolar collapse
    - ↑ gradient between intra-alveolar partial pressure of O<sub>2</sub> and mixed venous blood in the capillaries
    - rapid diffusion of O<sub>2</sub> across the alveolar-capillary barrier → alveolar collapse
- **Circulatory effect**
  - PVR ↓, pulmonary circulation ↑
  - Systemic artery constriction : SVR ↑
  - Cerebral vessel constriction : CBF ↓
  - significant deleterious consequences on the immature brain
- **Oxygen toxicity** ← Reactive oxygen metabolite (ROM)

## Oxygen toxicity

- **Bronchopulmonary dysplasia**
- **Retinopathy of prematurity**



Higano NS, Russo JL, Woods JC. J Perinatol. 2022 Apr;41(4):707-717.  
Habre W, Petak F, Br J Anaesth. 2014; Dec;113 Suppl 3:105-116.  
Seagard OD, Oei JL, Lakshminrusimha S, Vento M. Pediatr Res. 2019 Jan;85(1):20-29.

## Preterm

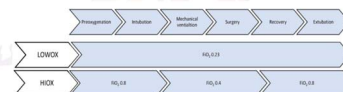
- **SUPPORT** (surfactant, positive pressure and pulse oximetry randomized trial), **COT** (Canadian oxygen trial), **Three BOOST 2** (benefits of oxygen saturation targeting)
- 5 large multicenter, masked, randomized control trials
- 5000 preterm infants less than 28 weeks postmenstrual age at birth
- **Low target spo2 (85-89%) vs high target spo2 (91-95%)**
- **Conclusion**
  - Maintaining an oxygen saturation **target of 85-89%**
    - leads to a **lower risk of retinopathy of prematurity (ROP)** but a **higher risk of mortality**

Lakshminrusimha S, Manja V, Mathew B, Suresh GK. J Perinatol. 2015 Jan;35(1):8-15.

## Neonatal anesthesia

Randomized controlled trial of low vs high oxygen during neonatal anesthesia: Oxygenation, feasibility, and oxidative stress

Victoria Karlsson<sup>1,2</sup>, Bengt Sporre<sup>3</sup>, Filip Fredén<sup>4</sup>, Johan Ågren<sup>1,2</sup>



- **↓ cerebral oximeter is independent of FiO<sub>2</sub>**
- reflects the pharmacological effects of anesthetic induction agent.

Lower in low oxygen group

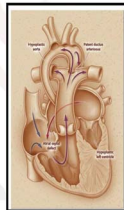
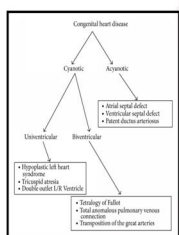


Lower in low oxygen group



No difference in regional cerebral oximetry

## Congenital heart disease

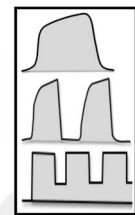


- **Acyanotic CHD**
  - O<sub>2</sub> supplement
  - SVR ↑
  - CO ↓, systemic O<sub>2</sub> transport ↓
- **Ductus dependent CHD**
  - pulmonary circulation ↑
  - relatively systemic circulation ↓
  - unstable d/t ductus arteriosus occlusion

Habre W, Petak F, Br J Anaesth. 2014; Dec;113 Suppl 3:105-116.

## Carbon dioxide

- Acceptable arterial carbon dioxide
- **Capnography**
  - **Most available bedside** surrogate for assessing PaCO<sub>2</sub> without ABGA
  - EtCO<sub>2</sub> : **cannot** be used as a reliable quantitative indicator
    - d/t Gradient between end-tidal and arterial CO<sub>2</sub>
    - **Magnitude of that gradient cannot be predicted**
      - In particular, in a situation like tidal volume ↓, dead space ↑
        - ↑ gradient between end-tidal and arterial CO<sub>2</sub>
        - significant hypercapnia with normal end tidal CO<sub>2</sub>



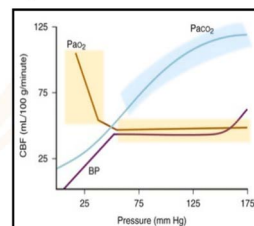
Lakshminrusimha S, Manja V, Mathew B, Suresh GK. J Perinatol. 2015 Jan;35(1):8-15.  
Feldman JM. Anesth Analg. 2015 Jan;120(1):155-175.  
Riley CM. Crit Care Nurs Clin North Am. 2017;29(2):251-258.



- **Lung-protective ventilation** in small patients
  - Risk of inadequate tidal volume or an unfavorable VD/Vt ratio, causing a **larger than normal difference between PaCO<sub>2</sub> and end tidal CO<sub>2</sub>**
- Caring for patients with **immature lungs**
  - **Difficult to assess ventilation** definitively based upon **EtCO<sub>2</sub> alone**.
  - Accepting hypercarbia can be part of the lung protective ventilation strategy.
- When **accurate control of PaCO<sub>2</sub> is required** (e.g., increased ICP)
  - **Arterial blood gas analysis** is necessary to document effective ventilation

Feldman JM. Anesth Analg. 2015;121(3):165-175

## Relationship with cerebral circulation



- The influence on the cerebral circulation : **PaCO<sub>2</sub> > PaO<sub>2</sub>**
- **↓ CBF d/t hyperoxia** in children is larger than in adults.

Habre W, Petak F. Br J Anaesth. 2014; Dec;113 Suppl 2:i26-36  
Anesthesia for congenital heart disease 3<sup>rd</sup> edition

## Neonate

- In healthy neonates,
  - the physiological CO<sub>2</sub> range is defined as **35-45.0 mmHg**.
- **Hyper- and hypocapnia** can both have **deleterious effects** for newborn infants.

Wong SK, Chim M, Allen J, Butler A, Tyrrell J, Hurley T, McGovern M, Omer M, Lagan N, Meehan J, Cummins EP, Molloy EJ. Carbon dioxide levels in neonates: what are safe parameters? Pediatr Res. 2015;77(5):505-510

## REVIEW ARTICLE OPEN Carbon dioxide levels in neonates: what are safe parameters?

Sie Kai Wong<sup>1</sup>, M. Chim<sup>1</sup>, J. Allen<sup>1,2</sup>, A. Butler<sup>1</sup>, J. Tyrrell<sup>1</sup>, T. Hurley<sup>1</sup>, M. McGovern<sup>1</sup>, M. Omer<sup>1,3</sup>, N. Lagan<sup>1,2</sup>, J. Meehan<sup>1,2</sup>, E. P. Cummins<sup>4</sup> and E. J. Molloy<sup>1,2,3,5</sup>

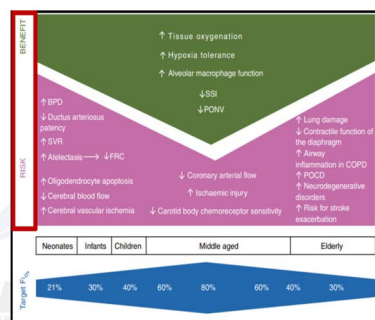
Pathology	Citation	Study type	Safe range	Comments
NE	Nadarem et al. <sup>11</sup> (2009)	Retrospective cohort study (Level 4)	pCO <sub>2</sub> 24-33 kPa (18-24.7 mmHg)	No significant association between moderate hypocapnia (2.6-3.3 kPa or 19.5-24.7 mmHg) and hypercapnia (>4.6 kPa or 45.5 mmHg) over the first 3 days after birth and adverse neurodevelopmental outcomes
PVL	Pappas et al. <sup>12</sup> (2011)	Secondary study RCT (Level 2)	pCO <sub>2</sub> > 2.6-3.3 kPa (>19.5-24.7 mmHg)	Association between poor neurodevelopmental outcomes at 18-22 months of age and both minimum pCO <sub>2</sub> and cumulative 2.6-3.3 kPa for 19.5-24.7 mmHg in infants with NE
Neurodis & CP	Klinger et al. <sup>13</sup> (2005)	Retrospective cohort study (Level 4)	pCO <sub>2</sub> > 2.6 kPa (>19.5 mmHg)	Severe hypocapnia (pCO <sub>2</sub> < 2.6 kPa or <19.5 mmHg) is associated with adverse neurological outcomes (severe CP, etc.) in term infants with post-asphyxial neonatal encephalopathy
CDH	Albasir et al. <sup>14</sup> (2015)	Retrospective cohort study (Level 4)	pCO <sub>2</sub> 5.24 kPa (39.0 mmHg)	Maintaining initial, best pCO <sub>2</sub> and PaCO <sub>2</sub> after resuscitation within physiological range (5.2 kPa or 39.0 mmHg) is associated with improved survival rate
	Bojancic et al. <sup>15</sup> (2015)	Retrospective cohort study (Level 4)	pCO <sub>2</sub> < 8.7 Pa (65.3 mmHg)	Permissive hypercapnia (pCO <sub>2</sub> < 8.7 Pa or <65.3 mmHg) is potentially protective

Table 2. Limits of CO<sub>2</sub> hypercapnic, hypocapnic and permissive hypercapnia parameters for term infants NE and CDH.

NE = neonatal encephalopathy; CP = cerebral palsy; PVL = periventricular leukomalacia; CDH = congenital diaphragmatic hernia; NE = neonatal encephalopathy; CP = cerebral palsy; PVL = periventricular leukomalacia; CDH = congenital diaphragmatic hernia.

- **Periventricular leukomalacia**: PaCO<sub>2</sub> > 35mmHg
- **Neurodevelopmental, cerebral palsy**: 35.3mmHg < PaCO<sub>2</sub> < 54.8mmHg
- **Neonatal enterocolitis**: PaCO<sub>2</sub> > 24.7mmHg
- **Bronchopulmonary dysplasia**: PaCO<sub>2</sub> < 50mmHg
- **Intraventricular hemorrhage**: PaCO<sub>2</sub> < 57.8-60mmHg
- **Congenital diaphragmatic hernia**: PaCO<sub>2</sub> < 39mmHg, PpCO<sub>2</sub> < 65.3mmHg

Wong SK, Chim M, Allen J, Butler A, Tyrrell J, Hurley T, McGovern M, Omer M, Lagan N, Meehan J, Cummins EP, Molloy EJ. Carbon dioxide levels in neonates: what are safe parameters? Pediatr Res. 2015;77(5):505-510



Habre W, Petak F. Br J Anaesth. 2014; Dec;113 Suppl 2:i26-36

## So, What is optimal O<sub>2</sub> and CO<sub>2</sub>?

- **Avoiding both hypocapnia/hypoxia and hypercapnia/hyperoxia is optimal**, but there is **not** a uniform range of optimal CO<sub>2</sub>/O<sub>2</sub>.

- It depends on **what you focus on most**
- Unless the patient's condition is bad, it is better to **avoid providing high oxygen**
- Consider **patient's condition**

# PEEP and Recruitment, Mode of Ventilation

Pichaya Waitayawinyu

Department of Anesthesiology, Siriraj Hospital, Mahidol University, Thailand

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Outline

- Children's lungs – what differ from adults'
- Atelectasis during general anesthesia
- PEEP and Lung recruitment – role and how to perform intraoperatively
- Lung protective ventilation
- Mode of intraoperative mechanical ventilation in pediatric patients

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Anatomical Differences

- Chest or thorax: shape, ribcage, mechanism of breathing

Infant Child/adult

Thoracic configuration

Thoracic cross section

Newborn  
Diaphragmatic fatigue → respiratory failure

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Anatomical Differences

- Breathing pattern – preferential nasal breathing, diaphragmatic breather, poor developed intercostal muscles and abdominal muscle, high RR due to limit chest expansion
- Diaphragm – angle of insertion more horizontal, infants have less high endurance muscle fibers
- Large internal organs
- Airway diameter – short trachea, small airway diameter, right bronchus less angled, airway swelling produces high resistance

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Anatomical Differences

- Bronchial walls – more cartilage & connective tissue, less muscle
- Surfactant – reduces surface tension, secreted from 23 week GA, surge at 30-34 week GA
- Alveoli – very few, small alveoli at birth (→ increases in numbers and sizes rapidly in 2 years), susceptible to collapse and atelectasis
- Collateral ventilation – poorly developed in children < 2-3 years → more susceptible to alveolar collapse

Obstructing Mucus  
Conal of Lumen  
Pores of Kohn

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Physiologic Differences

- Lung compliance – newborn & infant < adult's, child ~ adult's
  - Compliant chest wall
  - Need for adequate pressure to open up the alveoli with a risk of volutrauma and barotrauma
- Airway resistance - newborn ↑↑ and decreases to adult values at 8 years old

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

## Physiologic Differences

Neonate 3 kg Adult 70 kg

Trachea

Av

FRC

Av/FRC=0.1 Av/FRC=1.01

- FRC - proportionally less than in the adult and than the pulmonary capacity
- Normal glottic closure at end exhalation is prevented by ETT – a minimal PEEP maintain physiologic FRC in pediatric patients

Figure 1. Functional residual capacity. Av=alveolar ventilation; FRC=Functional residual capacity. Av/FRC=alveolar ventilation/Functional residual capacity.  
Source: Authors.

Rivera-Tocancipa D, Diaz-Sanchez E. How to ventilate the anesthetized child with the modern anesthesia machines? Rev Colomb Anestesiol 2018; 46:Supp

## Physiologic Differences

Figure 2. Closing volume. IRV=expiratory reserve volume; RV=residual volume; FRC=functional residual capacity; IRV=inspiratory reserve volume; TV=tidal volume.

Rivera-Tocancapa D, Diaz-Sanchez E. How to ventilate the anesthetized child with the modern anesthesia machines? Rev Colomb Anestesiol 2018; 46:Supp

## Physiology of Atelectasis

- Airway collapse begins quickly following induction of anesthesia
- Mostly affects the dependent areas of the lungs where the transpulmonary pressure is lowest
- Loss of muscle tone → FRC ↓ → small airway closure
- Compression of lung tissue by transmitting intra-abdominal pressure
- High FiO<sub>2</sub> use at induction promotes atelectasis
- Atelectasis → intra-pulmonary shunt ↑ → hypoxemia
- Atelectasis – also place the patient at risk of developing ventilator-associated lung injury

Trachsel D, Svendsen J, Erb TO, von Ungern-Sternberg. Effects of anaesthesia on paediatric lung function. Br J Anaesth 2016; 117(2):149-53

## Physiology of Atelectasis

- Anesthetic agent use – atelectasis occurs with both intravenous and inhalational general anesthesia
- Light sedation is associated with less atelectasis compared with general anesthesia
- Muscle relaxant reduces FRC and impair ventilation distribution in children (FRC decreases 45% in infants vs 10% in preschool-age children)
- Ketamine has less impact to muscle activity compared with propofol → FRC 20% higher in preschool-age children

Bruins S, Sommerfield D, Powers N, et al. Atelectasis and lung recruitment in pediatric anesthesia: an educational review. Ped Anesth 2022;32:321-329

## Recruitment maneuver and PEEP improve ventilation/perfusion mismatch

## Effects of Recruitment Maneuver on Atelectasis in Anesthetized Children

Gerardo Torres, M.D.,<sup>1</sup> Stephen H. Bohn, M.D.,<sup>1</sup> Alejandro Torres, M.D.,<sup>1</sup> Fernando Melian, M.D.,<sup>2</sup> Eduardo Garcia, M.D.,<sup>1</sup> Elvio Turchetto, M.D.,<sup>3</sup> Paul G. H. Mulder, M.S., Ph.D.,<sup>1</sup> Burkhard Lachmann, M.D., Ph.D.<sup>1</sup>

CPAP 5 → 10 → 15 every 4 breaths  
Then bring PIP up to 40 cmH<sub>2</sub>O  
RR 30 /min for 10 breaths

24 children (6 mo-6 y) for cranial MRI  
Use MRI imaging for measuring atelectasis volume during anesthesia  
Randomized to ZEEP, CPAP 5, ARS group  
ARS: Alveolar recruitment performed after induction of GA then keep PEEP at 5 throughout

Fig. 1. Study protocol. The study protocol, lung ultrasound method by Aerts and colleagues,<sup>24</sup> and the degree of consolidation and B-lines by lung ultrasound (B0) described by Song and colleagues.<sup>25</sup> C0, no consolidation; C1, minimal juxtacardiac consolidations; C2, small-sized consolidations; and C3, large-sized consolidations. B0, fewer than three isolated B-lines; B1, multiple well-defined B-lines; B2, multiple confluent B-lines; and B3, white lung. ARS, alveolar recruitment maneuver; TV, tidal volume.

Jang YE, Ji SH, Kim EH, et al. Effect of regular alveolar recruitment on intraoperative atelectasis in paediatric patients ventilated in the prone position: a randomized control trial. Br J Anaesth 2020; 124(5): 648-55.

## Recruitment maneuver and PEEP improve ventilation/perfusion mismatch

Fig. 3. Nuclear magnetic resonance images of representative patients for each of the three treatment groups. (Left) ZEEP = zero end-expiratory pressure; (middle) PEEP = positive end-expiratory pressure of 5 cm H<sub>2</sub>O; (right) ARS = alveolar recruitment maneuver with lung pressure of 5 cm H<sub>2</sub>O. The top of each volume shows a coronal view, followed by an upper, a middle, and a lower axial cut through the thorax (for details, see text). In children of the ZEEP group, atelectasis volume was 18 ml in the right lung and 16 ml in the left lung. In children of the CPAP group, atelectasis volume was 18 ml in the right lung and 33 ml in the left lung. The ARS group showed no atelectasis.

## Effects of Recruitment Maneuver on Atelectasis in Anesthetized Children

Gerardo Torres, M.D.,<sup>1</sup> Stephen H. Bohn, M.D.,<sup>1</sup> Alejandro Torres, M.D.,<sup>1</sup> Fernando Melian, M.D.,<sup>2</sup> Eduardo Garcia, M.D.,<sup>1</sup> Elvio Turchetto, M.D.,<sup>3</sup> Paul G. H. Mulder, M.S., Ph.D.,<sup>1</sup> Burkhard Lachmann, M.D., Ph.D.<sup>1</sup>

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Randomized to ZEEP, CPAP 5, ARS group  
ARS: Alveolar recruitment performed after induction of GA then keep PEEP at 5 throughout

Fig. 1. Study protocol. The study protocol, lung ultrasound method by Aerts and colleagues,<sup>24</sup> and the degree of consolidation and B-lines by lung ultrasound (B0) described by Song and colleagues.<sup>25</sup> C0, no consolidation; C1, minimal juxtacardiac consolidations; C2, small-sized consolidations; and C3, large-sized consolidations. B0, fewer than three isolated B-lines; B1, multiple well-defined B-lines; B2, multiple confluent B-lines; and B3, white lung. ARS, alveolar recruitment maneuver; TV, tidal volume.

Jang YE, Ji SH, Kim EH, et al. Effect of regular alveolar recruitment on intraoperative atelectasis in paediatric patients ventilated in the prone position: a randomized control trial. Br J Anaesth 2020; 124(5): 648-55.

## ORIGINAL ARTICLE

### Lung recruitment prevents collapse during laparoscopy in children

A randomised controlled trial

Onelia M. Acosta, Tomas Sans, Martin Caprinella, Giovanni Volpicelli, Lila Ricci, Sergio Polito, Diego Abrigo, Sergio Goncalves, Stephen H. Bohn and Gerardo Torres

Lung ultrasound images of one representative patient per group during the protocol. C-group, control group; CP, capnoperitoneum; RM-group, lung recruitment manoeuvre group.



**Recruitment maneuver regimens**

- Sustained application of positive airway pressure up to a set of minimum of 40 cmH<sub>2</sub>O for 10-30 sec before returning to baseline
- Varying airway pressures during the respiratory cycle by gradually and stepwise increasing PEEP (to approximately 15-20 cmH<sub>2</sub>O) → increase in tidal volume to a maximum PIP 40 cmH<sub>2</sub>O → gradual lowering of PEEP to level required to prevent de-recruitment

Bruins S, Sommerfield D, Powers N, et al. Atelectasis and lung recruitment in pediatric anesthesia: an educational review. *Ped Anesth* 2022;32:321-329

**TABLE 2 Strategies to reduce atelectasis in anesthetized children**

**Strategies to reduce atelectasis**

- Continuous positive airway pressure (30-40 cmH<sub>2</sub>O) for 5-10 s
- Multiple prolonged breaths of 30-40 cmH<sub>2</sub>O of continuous pressure over PEEP
- Stepwise increase in airway pressure to max 40 cmH<sub>2</sub>O under LUS guidance
- PCM with constant driving pressure of 15 cmH<sub>2</sub>O and stepwise increase by 5 cmH<sub>2</sub>O until 30-40 cmH<sub>2</sub>O
- PEEP > 4 cmH<sub>2</sub>O
- Postural RM, particularly following thoracotomy
- Avoiding high FiO<sub>2</sub>
- RM with cuffed ETT superior to SGA/face-mask
- Avoidance of neuromuscular blockade

Abbreviations: LUS, lung ultrasound; PCM, Pressure Controlled Mode; PEEP, positive end-expiratory pressure; RM, recruitment maneuver; SGA, supraglottic airway; ETT endotracheal tube.

Bruins S, Sommerfield D, Powers N, et al. Atelectasis and lung recruitment in pediatric anesthesia: an educational review. *Ped Anesth* 2022;32:321-329

**What is Lung Protective Ventilation? and Why Should We Care?**

- Mechanical ventilation strategies aimed at minimizing lung injury
- Avoidance of volutrauma and atelectrauma
- Most data from adults' studies
- Lower mortality rates in adult patients ventilated with a tidal volume (Vt) of 6mL/kg ideal body weight (IBW) and plateau pressures (Pplat) <30cmH<sub>2</sub>O compared to Vt of 12mL/kg IBW and Pplat <50 cmH<sub>2</sub>O (ARDSNet)
- In nonobese adult patients undergoing open abdominal surgery, ventilation of Vt 8 mL/kg with PEEP of 12 cmH<sub>2</sub>O combined with recruitment maneuvers was compared with PEEP of 2 cmH<sub>2</sub>O without recruitment maneuvers. No difference in postoperative pulmonary complication

Kilpatrick B, Slinger P. Lung protective strategies in anaesthesia. *Br J Anaesth* 2010; 105(5):1108-16  
ARDSNet trial, PALIVE study, PROPHILO study  
Heath C, Hauser N. Is there a role for lung-protective ventilation in healthy children?. *Ped Anesth* 2022; 32(2):278-85

**What is Lung Protective Ventilation? and Why Should We Care?**

- Concerns with the use of low Vt - increased risk of atelectasis, development of hypercapnia, reduction in respiratory compliance.
- Specifically, in the pediatric context, lowering Vt is associated with concerns about increased dead space and hypercapnia.
- In simulated models of pediatric acute respiratory distress (PARDS) patients ventilated with Vt of 10 mL/kg, no compromise in gas exchange was demonstrated

**Recommendations for Lung Protective Strategies in Healthy Pediatric Patients**

- Target Vt 6-10 mL/kg IBW, avoiding Vt > 10 mL/kg
- Limit PIP < 30 cmH<sub>2</sub>O and delta pressure < 10 cmH<sub>2</sub>O. Monitor variations in Vt carefully to avoid volutrauma
- PEEP remains an important component of LPV but the optimal level of PEEP for pediatric patients is unknown. Suggest PEEP range of 4-8 cmH<sub>2</sub>O
- Recruitment maneuver

Heath C, Hauser N. Is there a role for lung-protective ventilation in healthy children?. *Ped Anesth* 2022; 32(2):278-85.

**Recommendations for Lung Protective Strategies in Healthy Pediatric Patients (cont)**

- Avoid FiO<sub>2</sub> of 1.0 unless a clinical emergency occurs
- Recruitment advised to maintain FRC – suggest either sustained inflation of 30 cmH<sub>2</sub>O for 10-30 sec or an incremental increase in PEEP based on individual patient needs

Heath C, Hauser N. Is there a role for lung-protective ventilation in healthy children?. *Ped Anesth* 2022; 32(2):278-85.

**Mode of Ventilation**

**Pressure-controlled Ventilation**

- Square wave pressure waveform provides the maximum inspiratory pressure for the entire i-time favoring lung recruitment
- Maximum volume of ventilator is available to develop the rest pressure → the desired tidal volume can be delivered even small leak presents
- Provide rapid rate, high inflating pressure – suitable for patients with severe lung pathology
- Maximum PIP is limited → prevent barotrauma

Flow, Pressure, Lung Volume, Set – inspire pressure, i-time, RR

**Initial settings for pressure-controlled mechanical ventilator in children**

	Infant (<1 year of age)	Toddler/Child (1-12 year)	Adolescent (>12 year)
PIP (cmH <sub>2</sub> O)	16-25		
PEEP (cmH <sub>2</sub> O)	3-7		
Rate (breaths/min)	20-30	15-25	12-20
Pressure support (cmH <sub>2</sub> O)	Minimum 6-10		
Peak inspiratory flow (L/min)	Adjust to desired inspiratory time		
Inspiratory time (sec)	0.4-0.6	0.7-0.9	0.9-1.2
Targeted, based upon changes to inspiratory flow			
FiO <sub>2</sub>	Start with 1.0 rapidly wean to ≤ 0.6		
Flow trigger (L/min)	0.25-0.5	0.8-2	0.8-2
Pressure support cycle	10-25% of peak flow rate		

**Volume- controlled Ventilation**

Set – tidal volume, i-time or I:E ratio, RR

- Square wave flow waveform, with flow rate determined by the ration of the set tidal volume to the i-time
- Ensure tidal volume to be delivered by the ventilator
- Tidal volume is delivered regardless of PIP -> risk of barotrauma (stop when maximum pressure limit is reached)
- Risk of losses from the ETT leak

**Initial settings for volume-controlled mechanical ventilator in children**

	Infant (<1 year of age)	Toddler/Child (1-12 year)	Adolescent (>12 year)
Tidal volume (mL)	5-8 mL/kg		
Rate (breaths/min)	20-30	15-25	12-20
PEEP (cmH <sub>2</sub> O)	3-7		
Pressure support (cmH <sub>2</sub> O)	Minimum 6-10		
Peak inspiratory flow (L/min)	Adjust to desired inspiratory time		
Inspiratory time (sec)	0.4-0.6	0.7-0.9	0.9-1.2
Targeted, based upon changes to inspiratory flow			
FiO <sub>2</sub>	Start with 1.0 rapidly wean to ≤ 0.6		
Flow trigger (L/min)	0.25-0.5	0.8-2	0.8-2
Pressure support cycle	10-25% of peak flow rate		

**Dual Ventilation**

- Ensure accurate tidal volume, cycle after cycle, with a limited maximum pressure
- PCV with volume guaranteed (PVC-PG)
- Convenient for frequent and broad airway pressure changes occur; laparoscopic, thoracoscopic surgeries

**Pressure Support Ventilation**

- Patient initiates spontaneous breathe
- Reduce work of breathing imposed by endotracheal tube or LMA
- Need to keep PCO<sub>2</sub> level to maintain spontaneous breathing
- Combined SIMV and PSV to insure minute ventilation
- Potential advantages:
  - Facilitating emergence of anaesthesia
  - Improved hemodynamics due to less positive pressure needed
  - Assessing depth of anaesthesia
  - Titration of opioid analgesia

**Synchronized Intermittent Mandatory Ventilation**

- Improve the patient-ventilator relationship
- SIMV-Pressure Control (PC) or SIMV-Volume Control (VC)
- Determine patient's 'trigger flow' in order for the ventilator to allow and assist spontaneous ventilation

**To Protect the Lungs: keep an eye on**

- Impact of breathing systems used for manual ventilation – use modified Jackson Rees T-piece with caution (inexperienced use)
- Impact of extubation – FRC loss, consider put non-invasive ventilation immediately in high risk patient
- Impact of CPB and cardiothoracic surgery – FRC reduction during open chest and CPB

Trachsel D, Svendsen J, Erb TO, von Ungern-Sternberg. Effects of anaesthesia on paediatric lung function. Br J Anaes 2016; 117(2):151-63

**Dead Space and the Pediatric Patient**

Dead space = any portion of the breathing circuits or lungs in which there is bidirectional gas flow without gas exchange (include device that provide gas sampling)

$V_D/V_T$  ratio increases -> exponential increases in PaCO<sub>2</sub> level




Figure 4. Typical apparatus added to the breathing circuit with internal volume noted. Dead space volume added to the circuit can range from 9 mL for the smallest heat and moisture exchanger (HME) pictured to 55 mL for the combination of elbow, large HME, and expanded flexible extension. (from Trachsel M, Feldman JM. When does apparatus dead space matter for the pediatric patient? Anesth Analg 2014;118:776-80.)

### Ventilation Monitoring



Clinical signs:

- Respiratory rate
- Physical examination – chest movement, synchrony, percussion, breath sounds
- Movement of reservoir bag

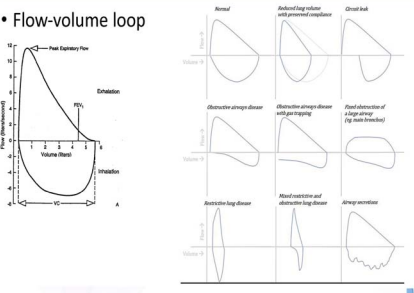
### Monitoring to Achieve Optimal Ventilation

- Gold standard – Arterial blood gas analysis
- Standard
  - Oxygenation: pulse oximeters
  - Ventilation:  $\text{ETCO}_2$
  - Respiratory mechanics: loops and scalars

Continuous vigilance of trained anesthesia personnel

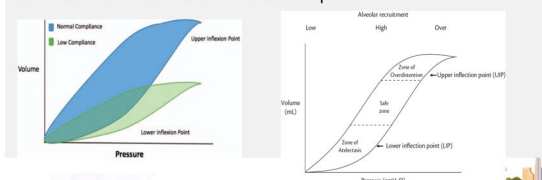
### Ventilation Monitoring in the Modern Machines Spirometry:

- Flow-volume loop



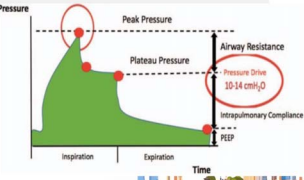
### Ventilation Monitoring in the Modern Machines Spirometry:

- Pressure-volume loop
- Identify the pulmonary compliance – flattened curve -> decrease pulmonary compliance
- Determine ideal PEEP at lower inflexion point



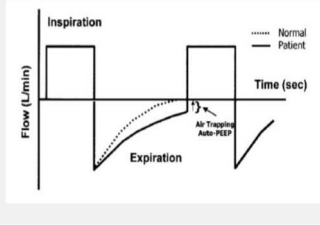
### Ventilation Monitoring in the Modern Machines Pressure-time curve:

- Airway resistance – approximately  $5 \text{ cmH}_2\text{O}$ , if  $> 8-10 \text{ cmH}_2\text{O}$  = high endotracheal resistance (tube kink, partial airway obstruction from secretion, very small tube)
- High PIP with normal airway resistance = high Pplat -> changes in pulmonary compliance
- Pressure drive (driving pressure) ideally  $< 10 \text{ cmH}_2\text{O}$ , should not  $> 14$  → raise PEEP level



### Ventilation Monitoring in the Modern Machines Flow-time curve:

- Determine I:E ratio



### Goals for an Optimal Ventilation

- Optimal  $\text{PaO}_2$  at the lowest inspired oxygen concentration
  - Recruitment maneuver in case of using  $\text{FiO}_2 < 0.25$
- An acceptable  $\text{PaCO}_2$ 
  - $\text{ETCO}_2$  less predictable in small tidal volume or increased dead space
- The desired tidal volume at the least inspiratory pressure
  - Interpret expired tidal volume with caution
  - Use pressure-volume (PV) loop as a guide
  - Add PEEP or recruitment maneuver

Be acquainted with your anesthesia machine

### Summary



- Atelectasis develop easily in children especially during general anesthesia
- PEEP and lung recruitment should be performed to prevent atelectasis
- Lung protective ventilation is suggested
- The ideal mode of intraoperative mechanical ventilation in pediatric patients is not definite.



# Inhale the Future Exhale the Past Smart Choice of Ventilation Equipment




Joy E. Luat-Inciong

St. Luke's Medical Center, Philippines

## OBJECTIVES




- Identify novel pediatric ventilation related equipment
- Discuss perioperative applicability of novel equipment
- Cite pros and cons of equipment innovations

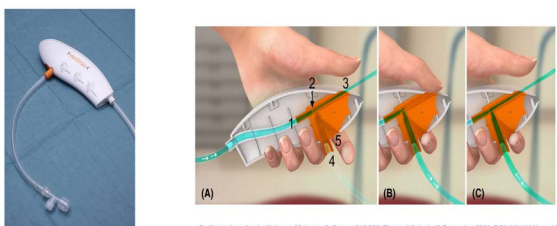
## Optimal Ventilation Strategy Goals

1. Optimal arterial oxygen tension ( $P_{aO_2}$ ) at the lowest inspired oxygen concentration ( $F_{iO_2}$ )
2. An acceptable arterial carbon dioxide tension ( $P_{aCO_2}$ )
3. The desired tidal volume at the least inspiratory pressure




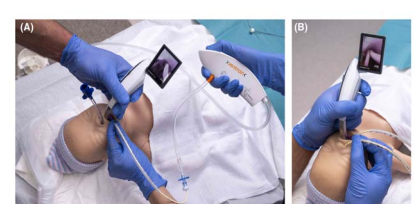
Optimal Ventilation of the Anesthetized Pediatric Patient by Jeffrey M. Feldman, MD, MSE  
Anesthesia & Analgesia January 2015 • Volume 120 • Number 1




## Ventrain®



Pediatric Anesthesia, Volume: 32, Issue: 2, Pages: 312-320, First published: 13 December 2021, DOI: 10.1111/pan.14379









## Ventrain®


## Advantages

- It does not require high pressures ; requires only a stable flow
- The shorter (and active) expiratory time permits higher minute volume and prevents pressure build up, barotrauma and air trapping.
- Capability for expiratory ventilation assistance to counteract the expiratory flow limitation that arises from narrow tracheal tubes.
- It facilitates both oxygenation and  $CO_2$  removal when ventilating through small lumen tubes.

## Disadvantages

- Requires manual operation
- Lacks continuous pressure monitoring




ASPA 2023 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting 대한소아마취학회

## Flow Controlled Ventilation

- energy dissipation that occurs during intermittent positive-pressure ventilation is one of the contributors to ventilator induced lung injury (VILI)
- to reduce energy dissipation, the flow must be held constant with an inspiratory to expiratory ratio (I:E) close to 1:1.

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## Evone® Flow Controlled Ventilator using Tritube®




ASPA 2023 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting 대한소아마취학회

## Pros & Cons

- The use of relatively low flow rates leads to improved distribution of lung aeration and improved gas exchange compared to conventional ventilation.
- Possibility to ventilate through very narrow endotracheal tubes
- Can only be used with total intravenous anesthesia since vaporizers cannot be included in the breathing circuit.
- Lacks adaptive ventilation modes and the possibility to be triggered by the patient
- Only recommended for use with an ideal body weight of over 40 kg

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## Negative Pressure Ventilation



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## Negative Pressure Ventilation

- benefits cardiac patients by improving hemodynamics
- wean from positive-pressure ventilation or combined with it
- bridge therapy until intubation or lung transplantation is available
- used to avoid intubation in selected patients
- could be involved in physiotherapy, home care, or palliative care with better quality of end-life
- need to develop standardized ventilation strategies and protocols based on prospective and controlled studies
- determine indications and contraindications, and specific target populations

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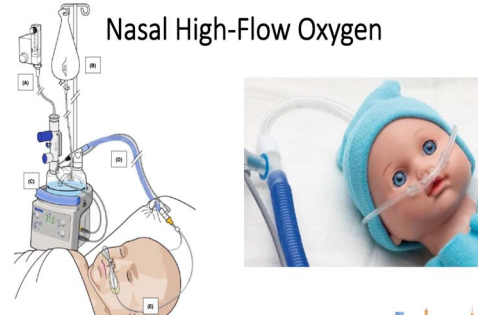
## PeDi R



Difficult Airway Bundle Checklist  
PEdiatric DIfficult Intubation Registry Group

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## Nasal High-Flow Oxygen

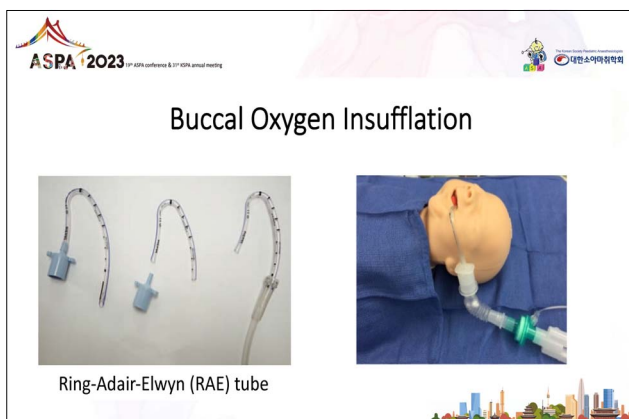


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## Modified Nasal Trumpet



Naso-Flo®





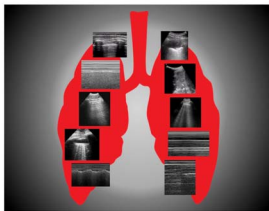
# How to Optimize Our Children's Intraoperative Ventilation Care with POCUS

Ayşe Cigdem Tutuncu

IU-Cerrahpasa University, Medicine School of Cerrahpasa, Türkiye

## Learning objectives

- Intraoperative ultrasound assesment and normal ultrasound findings
- The use of ultrasound as a tool for PEEP titration intraoperatively
- Ultrasound guided recruitment maneuver and detection of alveolar overdistension

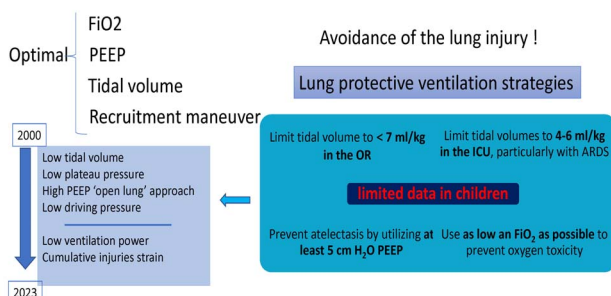


## Q1; How to optimize our children's intraoperative ventilation care?

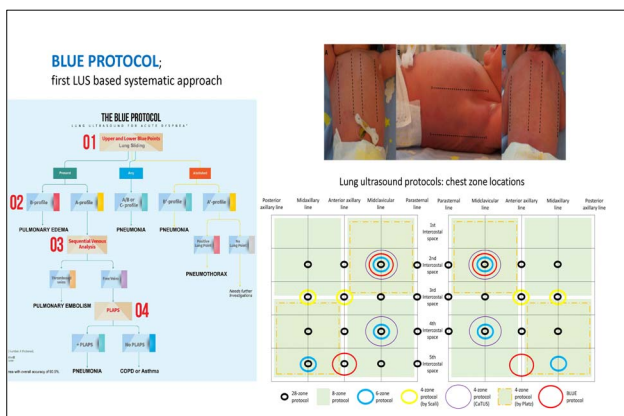
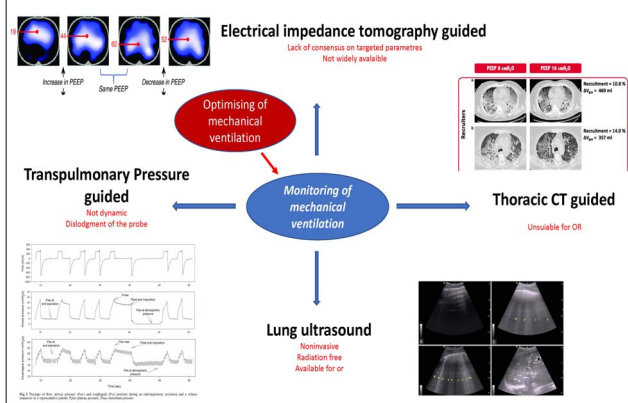
The ultimate goal of MV:

- Maintain adequate gas exchange in the alveoli.
- Prevent alveolar collapse
- To induce alveolar opening,
- To avoid lung injury

## Q 2; How do we reach this goal ?



Best Practice & Research Clinical Anaesthesiology 2015



Study	Clinical Condition/Setting	Diagnostic Accuracy	Comments
Jung et al <sup>1</sup>	Initial intraoperative assessment of pneumothorax	Care reported: elective laparoscopic procedure/traumatic thoracic dissection. Both cases of lung ultrasound provided timely diagnosis	Not mentioned CT as gold standard for diagnostic accuracy. Lung ultrasound can be an important part of high-quality anesthesia care
Jung et al <sup>2</sup>	Intraoperative radiological assessment of pleural effusion	Two cases of massive pleural effusion that were only recognized after induction of anesthesia in long prone thoracic transplantation	Lack of utilization of lung ultrasound having higher diagnostic accuracy and availability in the operating room setting
Choi et al <sup>3</sup>	Detection of esophageal intubation. Twelve eligible studies involving adult patients and cadaveric models were identified from 1488 references	Ultrasoundography had pooled sensitivity of 93% (95% CI, 85-95) and a specificity of 97% (95% CI, 93-99). The area under the summary ROC curve was 0.97 (95% CI, 0.95-0.98)	Summary of evidence for high diagnostic value of ultrasoundography for esophageal intubation
Arango et al <sup>4</sup>	Systematic review of 602 articles with the inclusion of 13 articles for meta-analysis review. The aim is to evaluate the diagnostic accuracy of pleural ultrasoundography in comparison with CXR for the diagnosis of pneumothorax	Lung US had a sensitivity of 78.8% (95% CI, 65.4-88.2) and a specificity of 98.4% (95% CI, 97.3-99.5). CXR had a pooled sensitivity of 59.8% (95% CI, 50.4-69.3) and a specificity of 99.2% (95% CI, 98.4-100.0)	Lung US is more accurate than CXR for detection of pneumothorax
Al-Dabb et al <sup>5</sup>	Systematic review of 158 articles with the inclusion of 7 articles for a meta-analysis review. The aim is to determine the accuracy of US using B lines in diagnosing ARDS	The sensitivity of US using B lines to diagnose ARDS was 94.1% (95% CI, 81.3-98.3) and the specificity was 92.4% (95% CI, 84.2-96.4)	The results of this meta-analysis suggest that POCUS using B lines may aid clinicians in the diagnosis of ARDS

<p>LUSA-empowered evaluation of intraoperative/peroperative hypoxemia (Spo<sub>2</sub> &lt; 94%)</p> <p>LUSA</p> <p>Pulmonary edema: bilateral diffuse, homogeneous "B" pattern</p> <p>Pneumothorax: absent lung sliding, presence of "lung point", absent "B" pattern</p> <p>Pleural effusion: anechoic lung base-diaphragmatic interface</p> <p>Consolidation: heterogeneous hypoechoic visible lung/ "focal" "B" pattern—(atelectasis or pneumonia)</p> <p>Impending major atelectasis: absent lung sliding, presence of "lung pulse"</p> <p>Demarcated dorsal areas: LUSA, dorsal "B" pattern"</p>	<p>LUSA use in "Preinduction Evaluation in Unplanned Anesthesia" is consistent with:</p> <p>Pulmonary edema</p> <p>Pneumothorax</p> <p>Pleural effusion</p> <p>Consolidation</p> <p>Impending major atelectasis/endobronchial intubation: absent lung sliding, presence of "lung pulse"</p> <p>Demarcated dorsal areas</p> <p>Aspiration, pneumonitis: unilateral or bilateral, heterogeneous "B" pattern"</p>
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## LUNG POCUS;

Consolidation

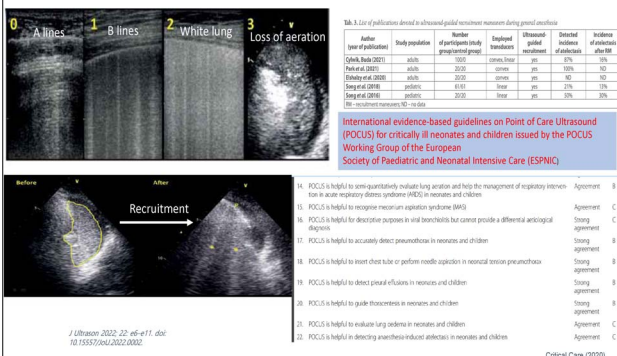
Pneumothorax

Pleural effusion

Pulmonary edema

Atelectasis; USG guided RM

## Is it possible to detect re-aeration of the lung with ultrasound after recruitment manoeuvre and PEEP setting ?



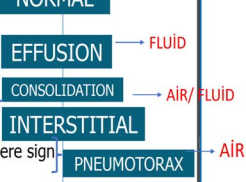
## Sensitivity specificity of lung POCUS ?

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Pleural Effusion	94	97	95	90
Alveolar Consolidation (Pneumonia)	90	98	88	95
Interstitial Syndrome (CHF, ARDS)	93	93	87	99
Complete Pneumothorax	100	96	100	98
Occult Pneumothorax	79	100	89	99
AECOPD	89	97	93	95
Pulmonary Embolism	81	99	94	98

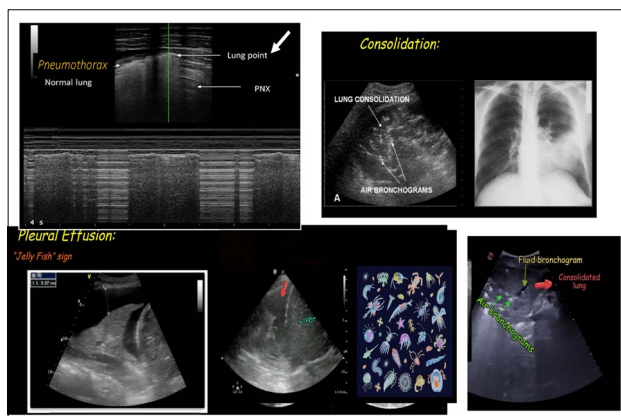
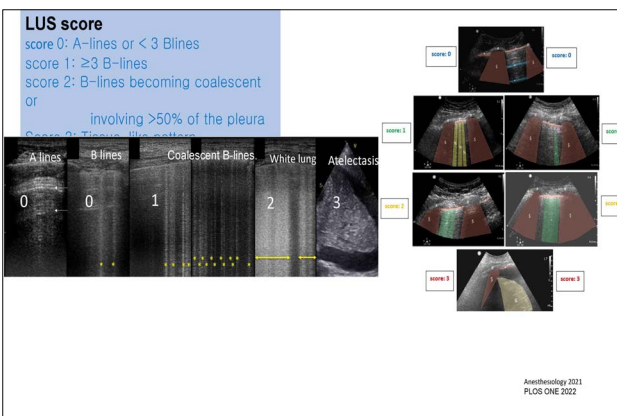
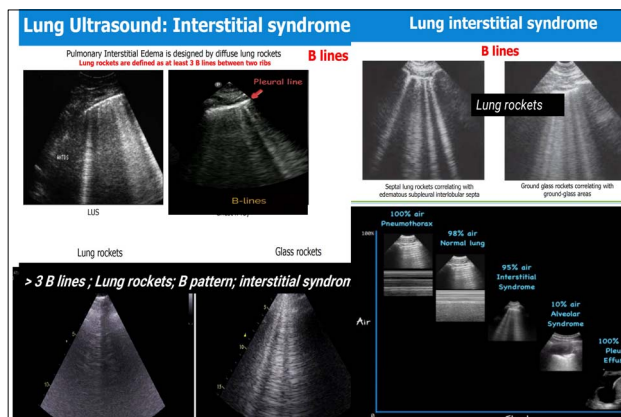
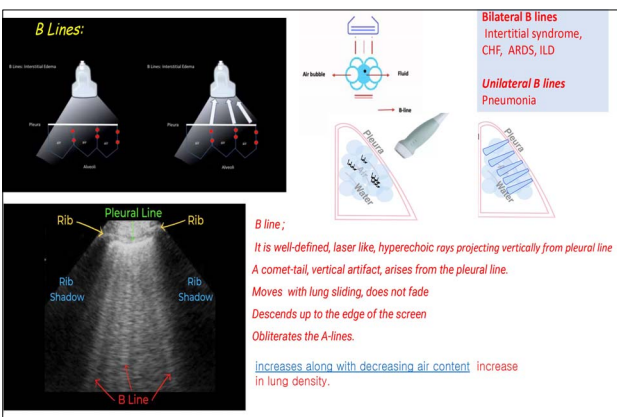
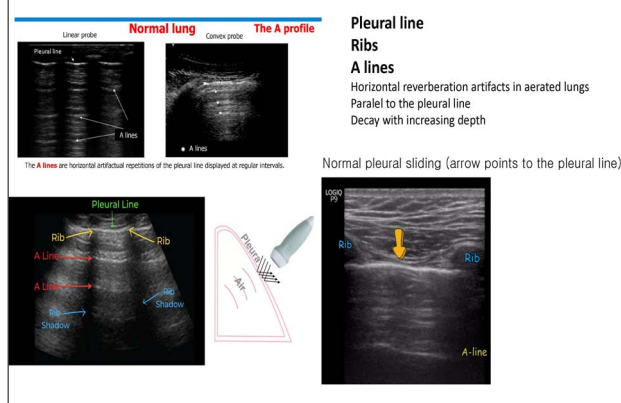
Anesth Analg 2017;124:494-504  
Ann int care 2004

## Lung findings of ultrasound

1. Bat sign (pleural line)
2. Lung sliding
3. A-line (horizontal artifact)
4. Quoad sign
5. Sinusoid sign
6. Fractal and Tissue-like sign
7. B-line (vertical artifact)
8. Lung rockets
9. Abolished lung sliding with Stratosphere sign
10. Lung point

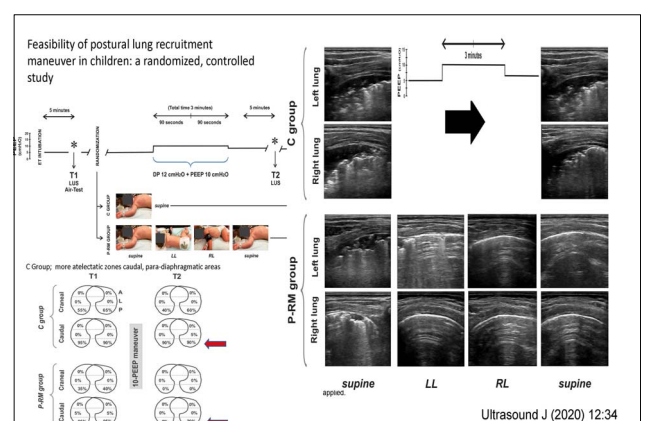
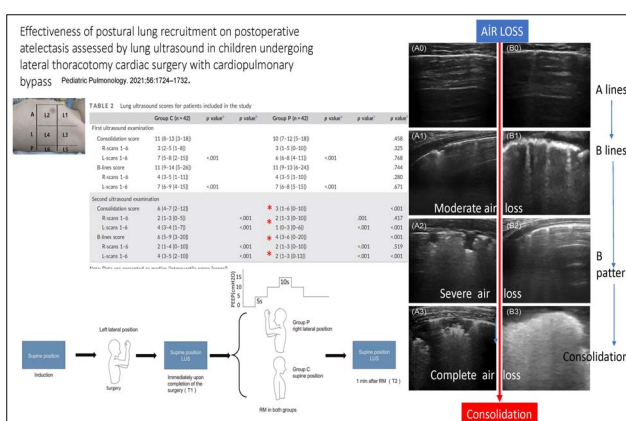
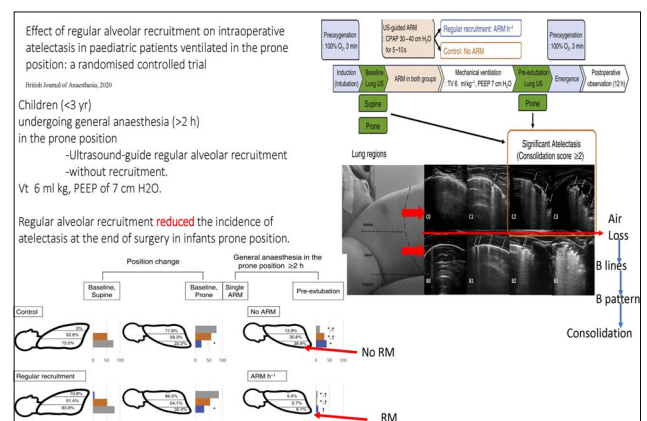
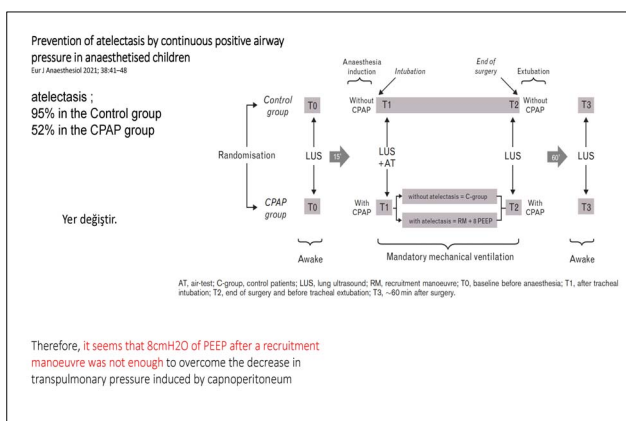
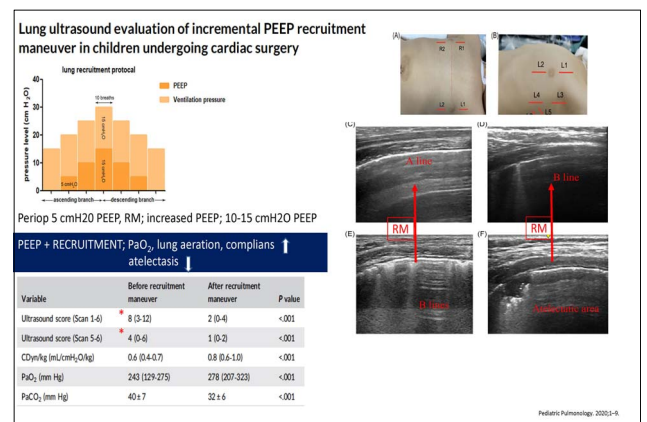
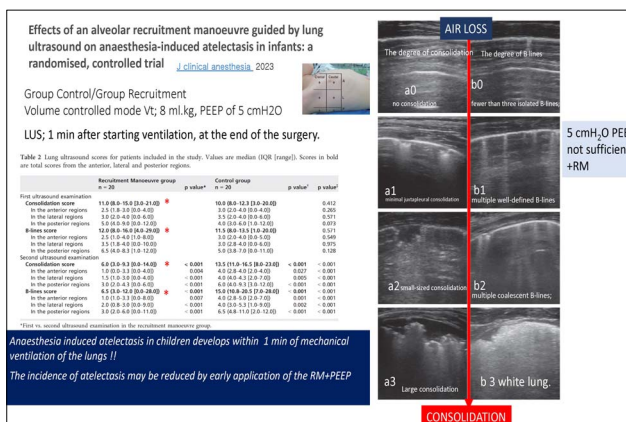
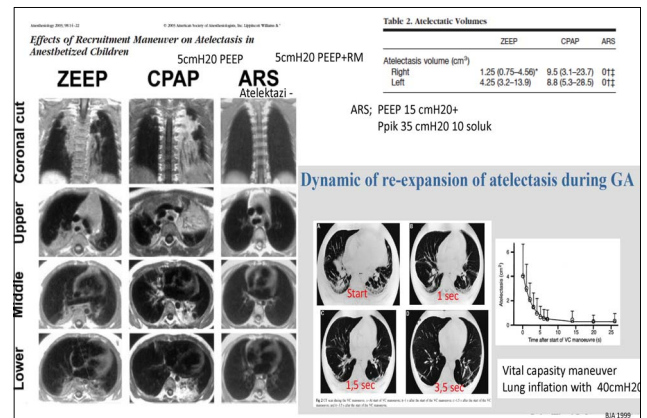
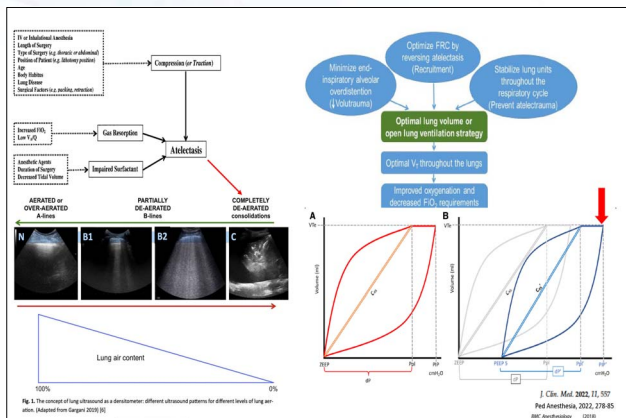


We can detect;  
pleura movement  
air loss  
air/fluid space  
no air; hepatization

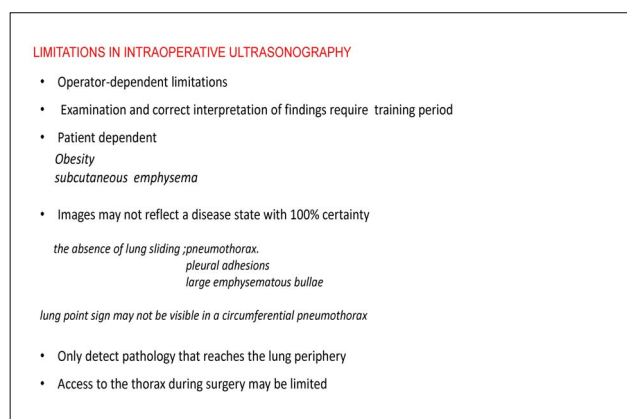
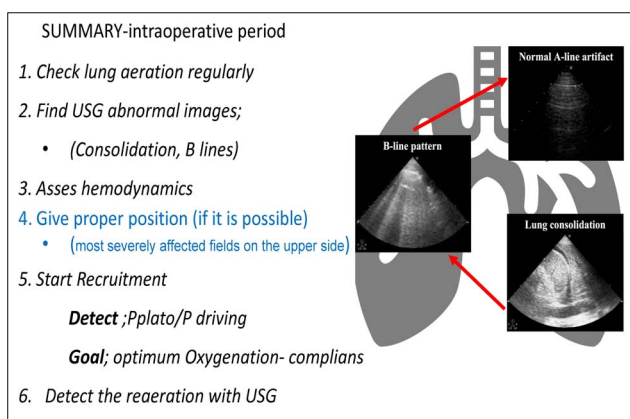
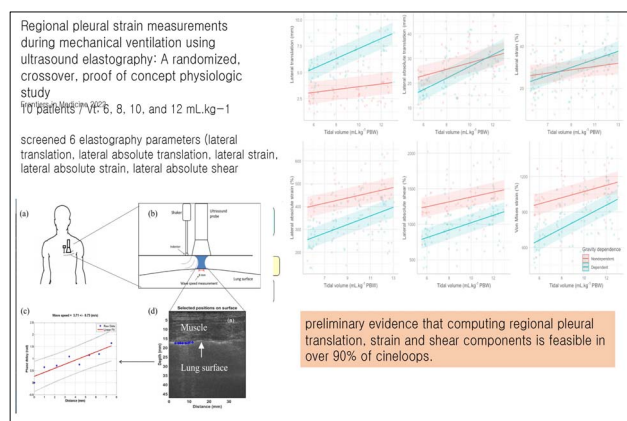
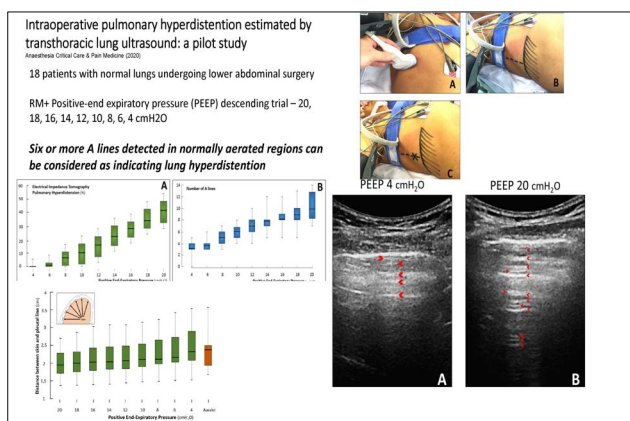
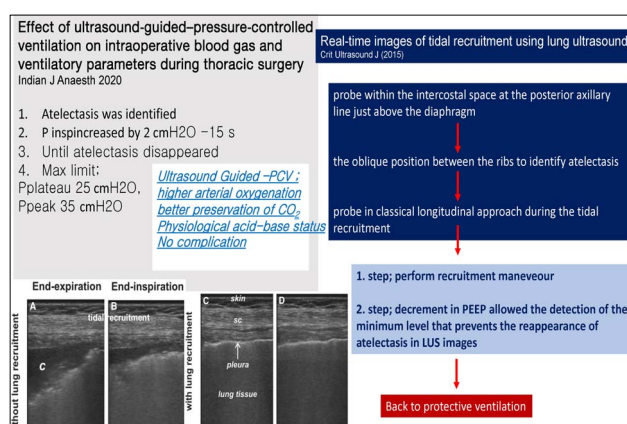
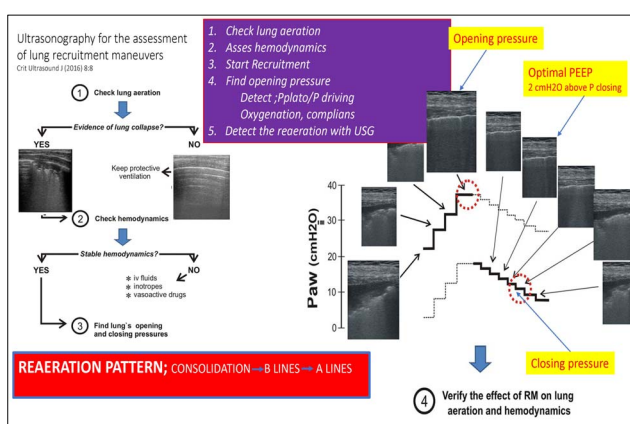
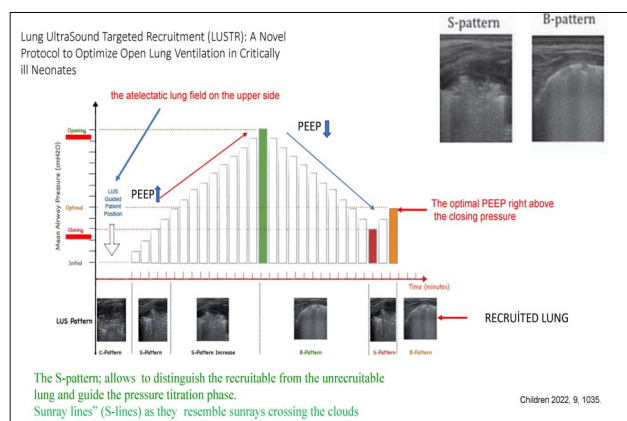
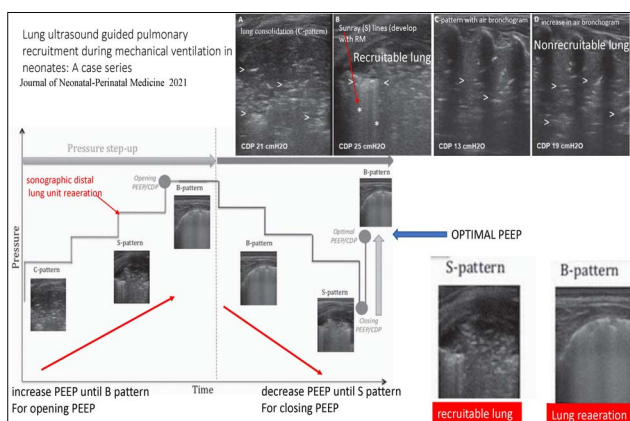




## Ayse Cigdem Tutuncu: How to Optimize Our Children's Intraoperative Ventilation Care with POCUS









## **Session 2.**

# **Experts' Advice of Monitoring for Better Anesthesia Care**

**Chair(s): Joy Luat-Inciong (Philippines)  
Hyo-Jin Byon (Korea)**

# Blood Pressure Considerations in Pediatric Anesthesia: Challenges & Implications

Stephen J. Gleich

Mayo Clinic, USA

## DISCLOSURES

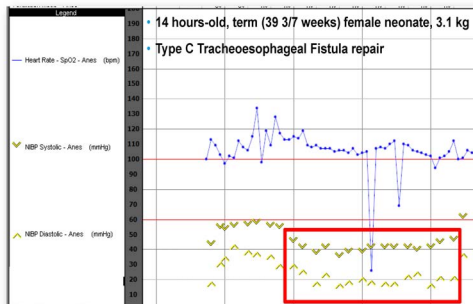
- No Conflicts of Interest

## LEARNING OBJECTIVES

- Describe challenges in noninvasive automated blood pressure monitoring in anesthetized children.
- Identify complications of intraoperative hypotension.
- Discuss individualized blood pressure management strategies in anesthetized children.

## PEDS INTRAOP BP

Case



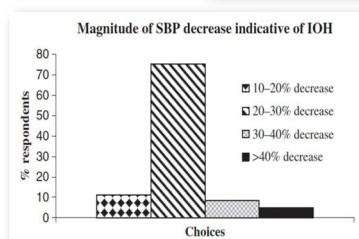
## 1 How is hypotension defined in children under anesthesia?

## PEDS INTRAOP BP

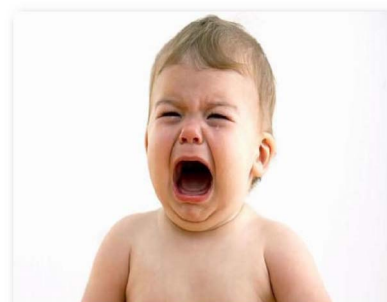
Hypotension Definition

### Pediatric Anesthesia

How do pediatric anesthesiologists define intraoperative hypotension?



Nafu OO et al. PediatrAnes 2009



"Baseline" BP

Sottas, CE et al. PediatrAnes 2016



**PEDS INTRAOP BP**

Hypotension Definition – Regional Differences

**Pediatric Anesthesia**

How do pediatric anesthesiologists define intraoperative hypotension?

## • SPA members (U.S.):

- Thresholds for hypotension were 5–7% lower across all pediatric age groups

Values and methods used to define IOH by societal affiliation

Age group	SPA members (n = 337)	APA members (n = 115)	P value
SBP threshold values mean (SD) mmHg for IOH			
Neonates	45.5 (8.5)	49.6 (8.4)	0.001
Infant-2 year	54.8 (8.3)	59.6 (9.1)	0.001
Children 2–12 years	66.9 (8.9)	70.1 (6.8)	0.001
Adolescents	78.4 (10.0)	84.5 (5.3)	0.001

Nafiu OQ et al. *PediatrAnes* 2009

Mayo Clinic Children's Center

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**PEDS INTRAOP BP**

Intraoperative Data – Reference Values

**ANESTHESIOLOGY**

Reference Values for Noninvasive Blood Pressure in Children during Anesthesia

A Multicentered Retrospective Observational Cohort Study

## • Multicenter Perioperative Outcomes Group data set

- 9 U.S. centers + 1 center in the Netherlands

## • 0–18 years, ASA I–II, non-Cardiac procedures

## • Developed sex-specific percentiles of NIBP values for age

## • 2 artifact-free measurements in each phase

116,362 cases analyzed

- Preparation Phase: 108,179
- Initial Surgical Phase: 94,283

deGraaff JC et al. *Anesthesiology* 2016

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**PEDS INTRAOP BP**

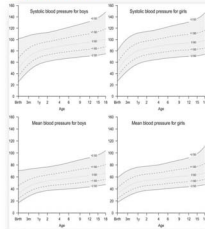
Intraoperative Data – Reference Values

**ANESTHESIOLOGY**

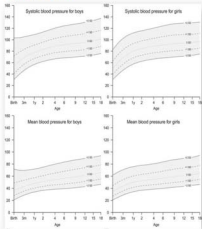
Reference Values for Noninvasive Blood Pressure in Children during Anesthesia

A Multicentered Retrospective Observational Cohort Study

## Preparation Phase



## Surgical Phase

deGraaff JC et al. *Anesthesiology* 2016

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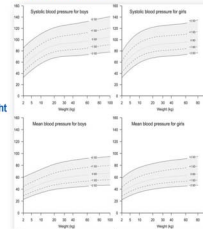
Intraoperative Data – Reference Values

**ANESTHESIOLOGY**

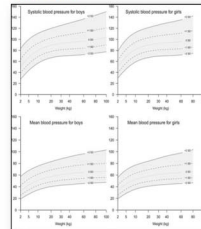
Reference Values for Noninvasive Blood Pressure in Children during Anesthesia

A Multicentered Retrospective Observational Cohort Study

## Preparation Phase



## Surgical Phase

deGraaff JC et al. *Anesthesiology* 2016

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**PEDS INTRAOP BP**

Intraoperative Data – Reference Values

**ANESTHESIOLOGY**

Reference Values for Noninvasive Blood Pressure in Children during Anesthesia

A Multicentered Retrospective Observational Cohort Study

## MBP – Preparation Phase

Table 2 Mean non-invasive blood pressure during preparation phase by relation to age

Preparation	Male					Female					
	Age	Mean	Mean ± standard error	95% CI	95% CI	Age	Mean	Mean ± standard error	95% CI	95% CI	
1 month	1	37	34	33	44	71	38	34	33	42	70
	2	35	33	40	52	72	34	33	39	50	66
	3	34	33	42	54	72	34	34	42	51	69
	4	34	33	44	55	73	34	35	44	51	69
	5	34	33	45	56	73	34	37	46	57	72
	6	34	34	46	57	74	34	38	47	58	73
	7	34	34	47	58	74	34	39	48	59	74
	8	34	34	48	59	75	34	40	50	61	75
	9	34	34	49	60	75	34	41	52	62	76
	10	37	45	53	63	77	37	45	54	65	78
	11	38	46	55	65	78	38	47	55	66	79
	12	39	47	56	66	80	39	47	56	67	80
2 years	1	40	48	57	68	82	40	48	57	68	82
	2	40	48	58	69	84	41	49	58	69	84
	3	41	50	60	72	87	42	50	60	72	87
	4	42	51	61	74	90	43	51	62	73	89
	5	43	52	62	75	92	44	52	63	75	91
	6	43	53	63	76	95	44	53	63	76	94
	7	44	54	64	78	99	45	54	65	79	98
	8	45	55	65	81	104	47	56	67	82	103
	9	46	56	66	84	109	48	57	68	85	108
	10	47	57	67	87	114	49	58	69	88	113
	11	48	58	68	90	119	50	59	70	91	118
	12	49	59	69	93	124	51	60	71	94	123

van Zadelhoff AC et al. *Anesthesiology* 2016

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**PEDS INTRAOP BP**

Neonatal Data – Reference Values

**BJA**

PEDIATRIC ANAESTHESIA

Age-dependent changes in arterial blood pressure in neonates during the first week of life: reference values and development of a model

## • Single center retrospective cohort

## • Noninvasive blood pressures of neonates, excluded severe comorbidities

## • Defined median +/- 2 standard deviations of reference BP

607 neonates  
5885 measurementsvan Zadelhoff AC et al. *BJA* 2023

Mayo Clinic Children's Center

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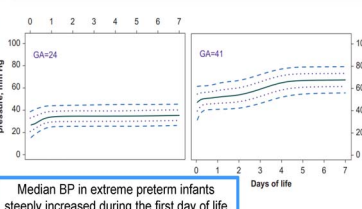
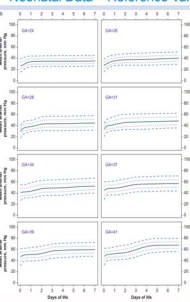
**PEDS INTRAOP BP**

Neonatal Data – Reference Values

**BJA**

PEDIATRIC ANAESTHESIA

Age-dependent changes in arterial blood pressure in neonates during the first week of life: reference values and development of a model



Median BP in extreme preterm infants steeply increased during the first day of life

van Zadelhoff AC et al. *BJA* 2023

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**PEDS INTRAOP BP**

Reference Values

bloodpressure-neonate.com

## Blood pressure reference values

Course of blood pressures during neonates' first week of life in the NICU

## Instructions

We have estimated reference ranges for the blood pressure of neonates. To find the appropriate range of blood pressure values for a child, please enter his / her gestational age and postnatal age. These reference values are only applicable to neonates admitted to NICU

Gestational Age at Birth:

37 weeks

0 days

Postnatal Age:

5 days

0 hours

Type

P02.3

P16

Median

P84

P97.7

Mean BP

43.14

49.76

56.47

63.24

69.95

Systolic BP

59.66

66.92

74.40

82.15

89.99

Diastolic BP

29.22

36.61

44.02

51.41

58.80

https://bloodpressure-neonate.com/

Mayo Clinic Children's Center

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## PEDS INTRAOP BP

### Intraoperative Data – Limitations

- No outcome data
- No "end-organ perfusion" data
- No correlation to:
  - Cerebral encephalopathy
  - Renal failure
  - Hospital LOS
  - Mortality
  - Long-term neurodevelopmental outcomes

**ANESTHESIOLOGY**  
Reference Values for Noninvasive Blood Pressure in Children during Anesthesia  
A Multicenter Retrospective Observational Cohort Study



deGraaff JC et al. Anesthesiology 2016

## 2 Challenges of intraoperative measurement of BP in children

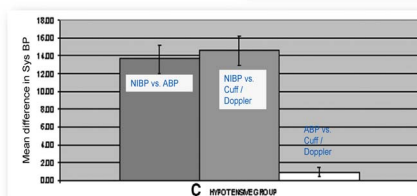
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## PEDS INTRAOP BP

### BP Measurement – Method

Which pressure to believe? A comparison of direct arterial with indirect blood pressure measurement techniques in the pediatric intensive care unit



Automated BP cuff readings were falsely elevated during hypotension

Holt TR et al. Pediatr Crit Care Med 2011

## PEDS INTRAOP BP

### BP Measurement – Anatomical Site

- Adults:
  - Higher BP measured in leg vs. arm

Moore C et al. Anesthesiology 2008

- Children (up to 8 years-old):
  - LOWER BP measured in leg vs. arm
  - Mean 10 mmHg lower 0-4 years

Short JA. Paediatr Anaesth 2000

Kardam I et al. JCA 2014

## 3 Complications of hypotension



## PEDS INTRAOP BP

### Complications of Hypotension

- 6 infants – undergoing elective procedures
- Developed postop encephalopathy
- Supratentorial watershed infarcts
- Outcomes:
  - 1 died, 2 had developmental delays, 2 normal
- Presumed cause: cerebral hypoperfusion

Infantile Postoperative Encephalopathy: Perioperative Factors as a Cause for Concern

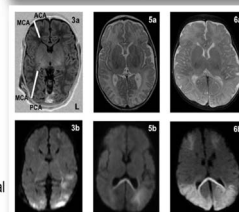
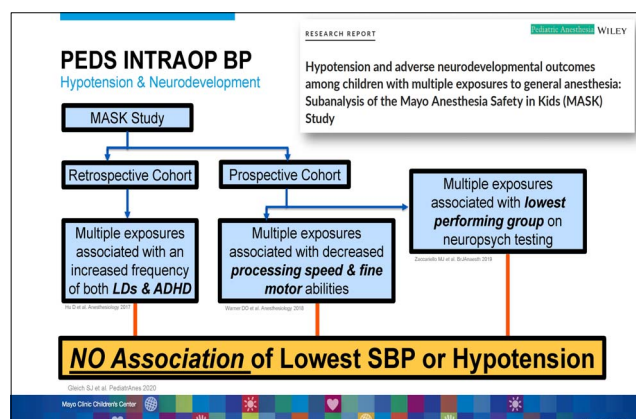
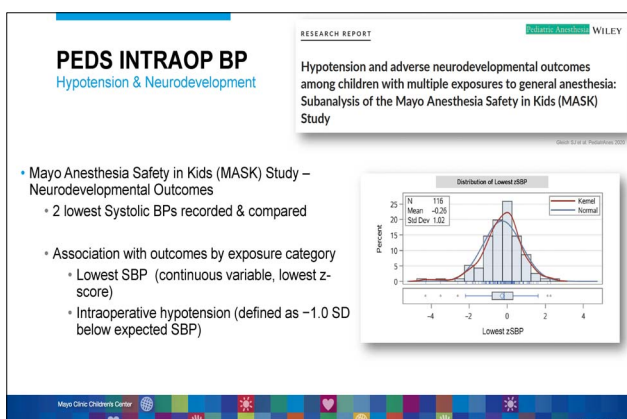
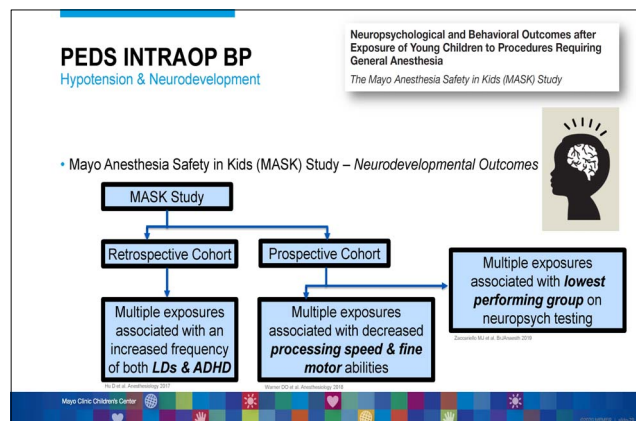
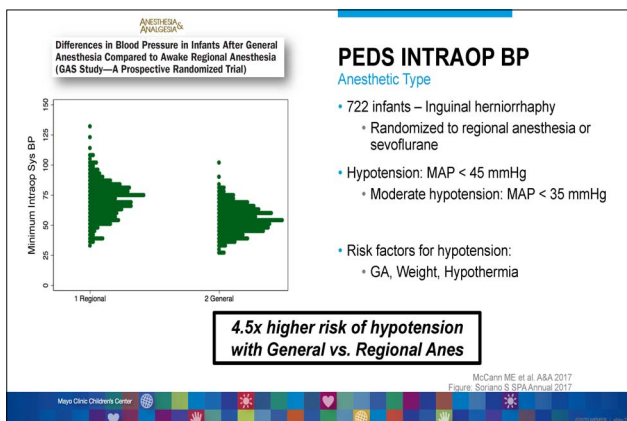
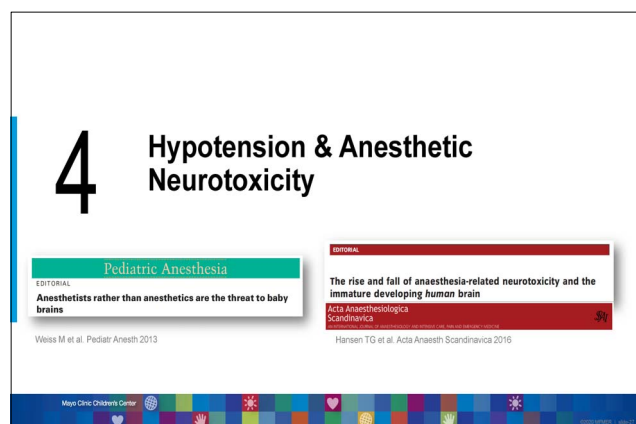
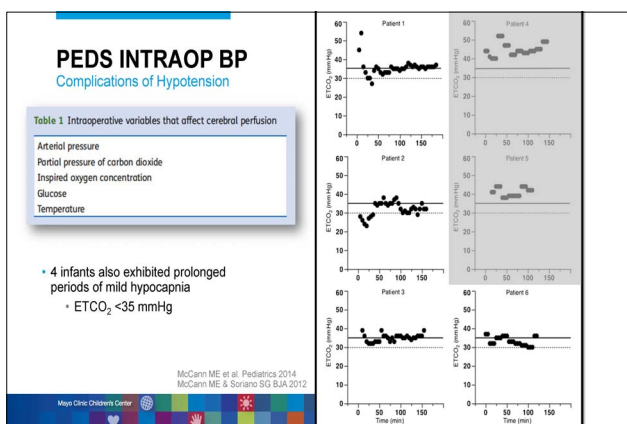
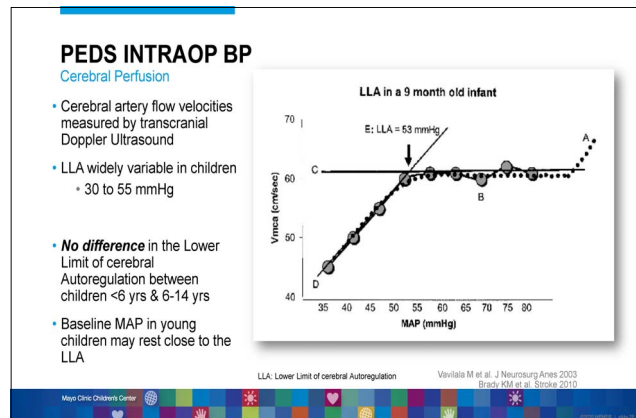
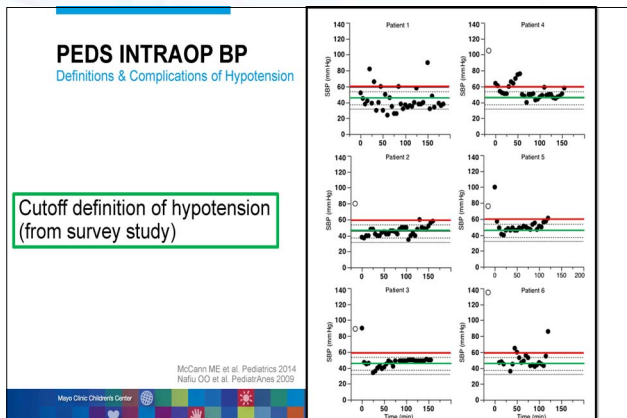


FIGURE 3. Axial MRIs in cases 3, 4, and 6. The upper panels show the findings in the T2-weighted images (T2) and the lower panels show the findings in the T1-weighted images (T1). The upper panels show the findings in the T2-weighted images (T2) and the lower panels show the findings in the T1-weighted images (T1). The upper panels show the findings in the T2-weighted images (T2) and the lower panels show the findings in the T1-weighted images (T1).

McGinn ME et al. Pediatrics 2014

## Stephen J. Gleich: Blood Pressure Considerations in Pediatric Anesthesia: Challenges &amp; Implications





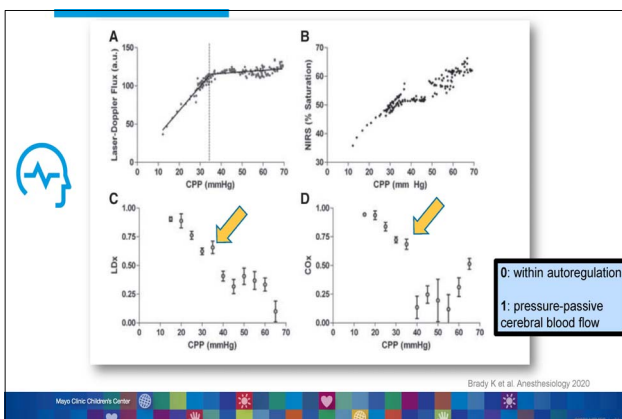
## FUTURE

### ANESTHESIOLOGY® Personalizing the Definition of Hypotension to Protect the Brain

Kenneth M. Brady, M.D., Aaron Hudson, M.D., Ryan Hood, M.D., Bruce DeCarle, M.D., Clay Lewis, M.D., Charles W. Hooper, M.D.

- Accurate and affordable non-invasive monitors to detect decrease in cerebral blood flow
  - Correlation to standard BP measurements
- Prompt treatments to maintain adequate blood pressure and cerebral perfusion

Brady K et al. Anesthesiology 2020



## PEDS INTRAOP BP

### Conclusions

- BP measurement & evaluation in children under anesthesia – should be individualized
- Hampered by inaccurate measurements of automated NIBP
- Reference ranges – not linked to clinical outcomes
- BP is 1 component of multifactorial cerebral perfusion
  - Inadequate cerebral perfusion → devastating neurologic consequences
- Future: outcome-based studies & monitors



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# Neuromonitoring in Neonatal Pain Assessment

Ian Yuan

Children's Hospital of Philadelphia, USA



## Oldest Children's Hospital in USA



### Childrens Hospital of Philadelphia (CHOP)

33,000 cases / year

75 Pediatric Anesthesiologist (9 Cardiac)

30 Nurse Anesthetists

11 Fellows

10 Residents



???

1- Hungry

2- Tired

3- In pain from surgery

## Neuromonitoring in Neonatal Pain Assessment

Consequences of untreated neonatal pain

Neuromonitoring to assess neonatal pain

Near-infrared spectroscopy pain assessment

### Misconceptions in Neonatal Pain

- Immature pain pathways and cannot transmit painful stimulus to brain.
- Lack context to identify experiences as painful.
- Analgesic or sedative agents cause adverse effects to the developing brain

### Neonatal Pain -> Worse Postop Outcomes

#### THE LANCET

Volume 395, Issue 10207, 31 January 2021, Pages 243-248

RANDOMISED TRIAL OF FENTANYL ANAESTHESIA IN PRETERM BABIES UNDERGOING SURGERY: EFFECTS ON THE STRESS RESPONSE

K.I.S. Anand<sup>1,2</sup>, W.G. Siqin<sup>3</sup>, A. Ajmal Green<sup>4</sup>

PDA ligation in babies without vs with fentanyl

↑ **stress response**  
(adrenaline, noradrenaline, glucagon, corticosterone, lactate)

↑ **protein catabolism** at POD#3

**Worse outcomes:** ↑ ventilation requirement, bradycardia, hypotension, metabolic acidosis, intraventricular hemorrhage.

### Neonatal Pain -> Increased Pain Sensitivity

#### THE LANCET

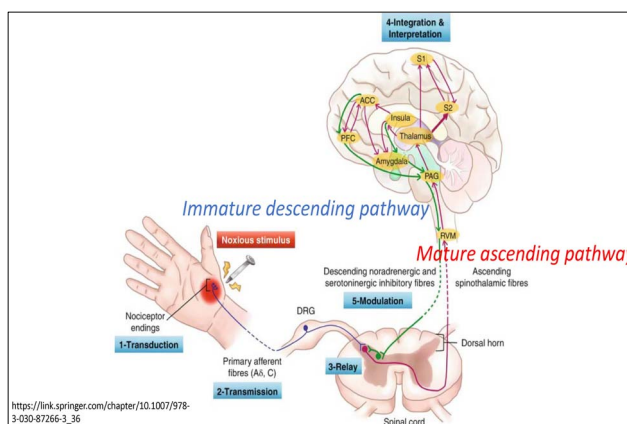
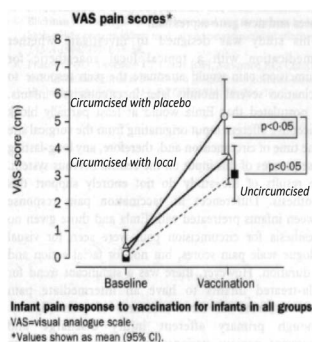
Volume 349, Issue 9052, 1 March 1997, Pages 599-603

Articles

Effect of neonatal circumcision on pain response during subsequent routine vaccination

Anna Taddio MSc<sup>1,2</sup>, Joel Katz PhD<sup>3,4,5</sup>, A. Lane Hersch MSc<sup>6</sup>, Prof Gideon Koren<sup>7</sup>

Pain response at 4 or 6mo vaccinations in babies circumcised with local vs with placebo vs uncircumcised.



### Neuromonitoring in Neonatal Pain Assessment

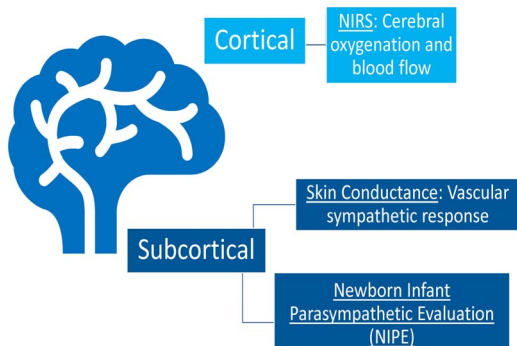
Consequences of untreated neonatal pain

Neuromonitoring to assess neonatal pain

### Neuromonitoring Neonatal Nociception

- Skin conductance test
- Newborn Infant Parasympathetic Evaluation (NIPE)
- Near infrared spectroscopy
- Surgical Pleth Index
- ANI (Analgesia nociception index)
- Pupillometer

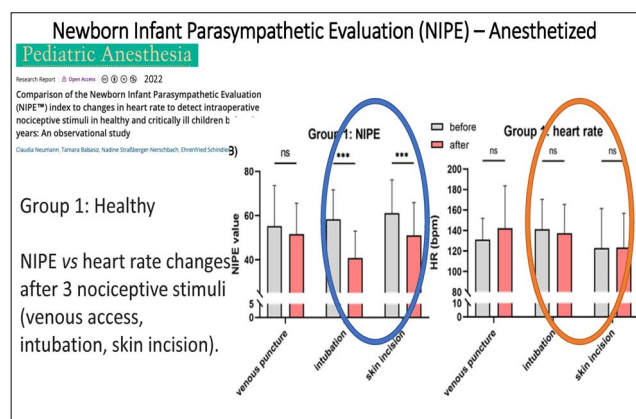
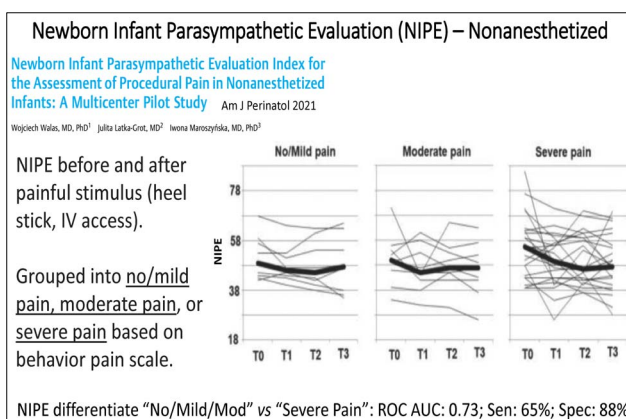
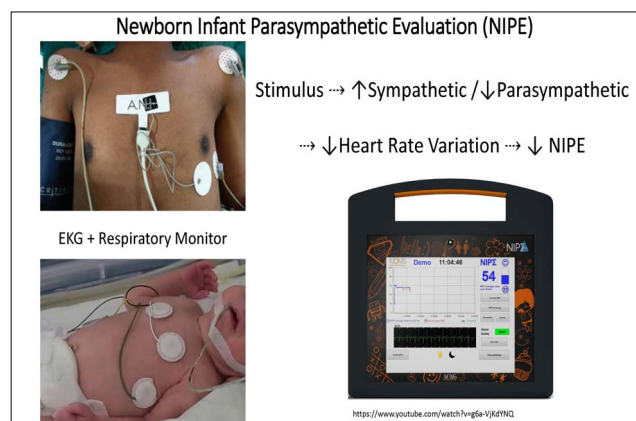
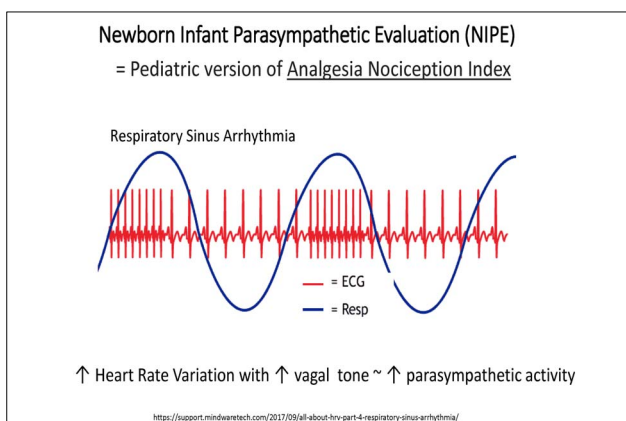
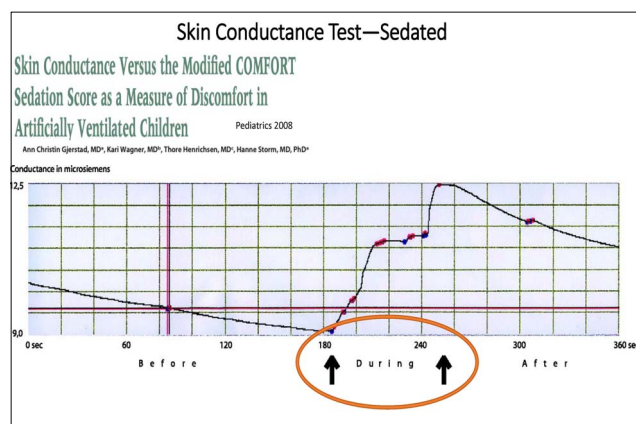
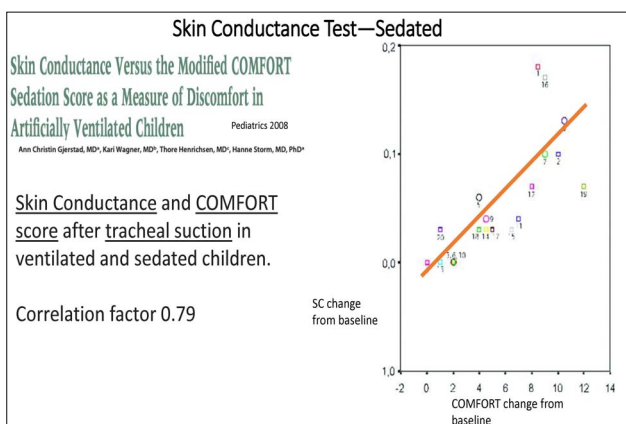
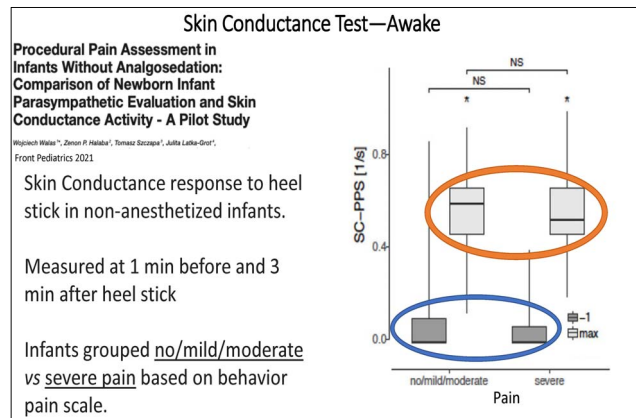
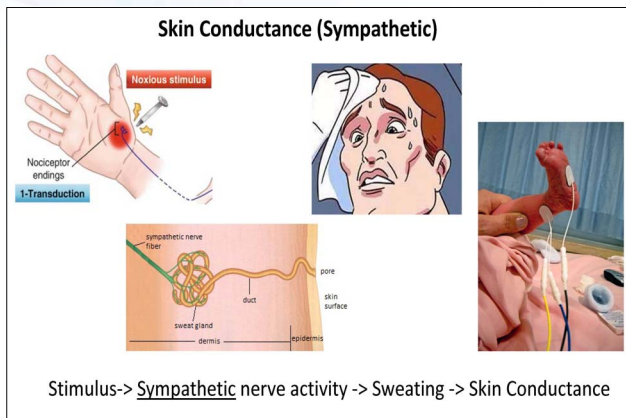
Sabourdin N. Current Opinion in Anaesthesiology, 2022

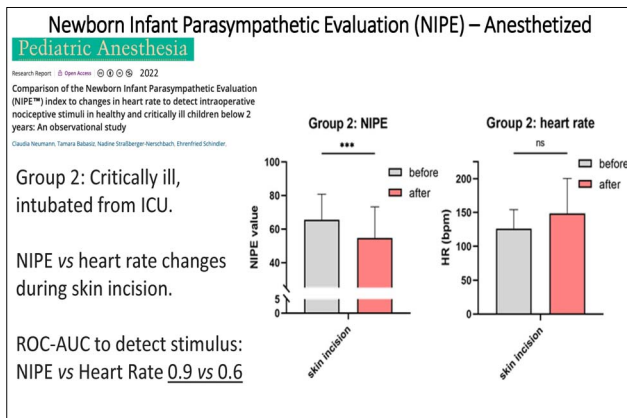


Summary of neonatal pain assessment tools						
Pain Assessment Tool	Gestational Age	Physiologic Components	Behavioral Components	Type of Pain	Adjusts for Prematurity	Scale Metric
Premature Infant Pain Profile-Revised (PIPP-R) <sup>10,18</sup>	26 wk to term	Heart rate, oxygen saturation	Alertness, brow bulge, eye squeeze, nasolabial furrow	Procedural and postoperative	Yes	0-21
Cries, Requires Oxygen, Increased Vital Signs, Expression, Sleeplessness (CRIES) <sup>19</sup>	32-56 wk	Blood pressure, heart rate, oxygen saturation	Cry, expression, sleeplessness	Postoperative	No	0-10
Neonatal Infant Pain Scale (NIPS) <sup>20</sup>	28-38 wk	Breathing pattern	Facial expression, cry, arms, legs, alertness	Procedural	No	0-7
COMFORT (and COMFORTneo) <sup>22,21</sup>	0-3 y (COMFORTneo: 24-42 wk)	Respiratory response, blood pressure, heart rate	Alertness, agitation, physical movements, muscle tone, facial tension	Postoperative (COMFORTneo: prolonged)	No	8-40
Neonatal Facial Coding System (NFCs) <sup>22</sup>	25 wk to term	None	Brow bulge, eye squeeze, nasolabial furrow, open lips, stretch mouth (vertical and horizontal), lip purse, taut tongue, chin quiver	Procedural	No	0-10
Neonatal Pain, Agitation, and Sedation Scale (N-PASS) <sup>23</sup>	0-100 d	Heart rate, respiratory rate, blood pressure, oxygen saturation	Crying or irritability, behavior state, facial expression, extremities or tone	Acute and prolonged pain. Also assesses sedation	Yes	Pain: 0-10 Sedation: 10-0
Échelle de la Douleur Inconfort Nouveau-Né (EDIN: Neonatal Pain and Discomfort) Scale <sup>18</sup>	25-36 wk	None	Facial activity, body movements, quality of sleep, quality of contact with nurses, consolability	Prolonged	No	0-15
Bernese Pain Scale for Neonates (BPSN) <sup>24</sup>	27-41 wk	Respiratory pattern, heart rate, oxygen saturation	Alertness, duration of cry, time to calm, skin color, brow bulge with eye squeeze, posture	Procedural	No	0-27

Maxwell LG et al. Assessment of pain in the newborn: an update. Clinics in perinatology, 2019





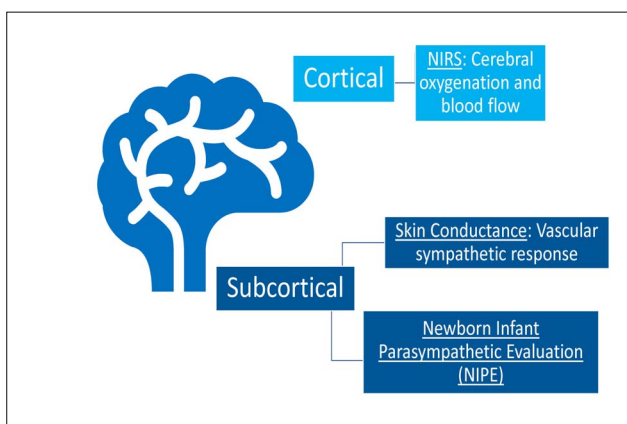


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Consequences of untreated neonatal pain

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Near-infrared spectroscopy pain assessment



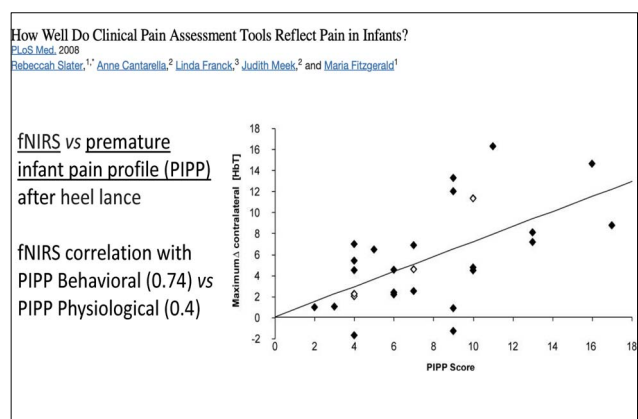
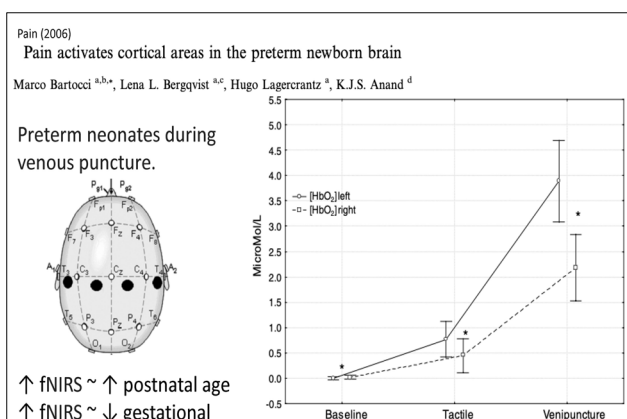
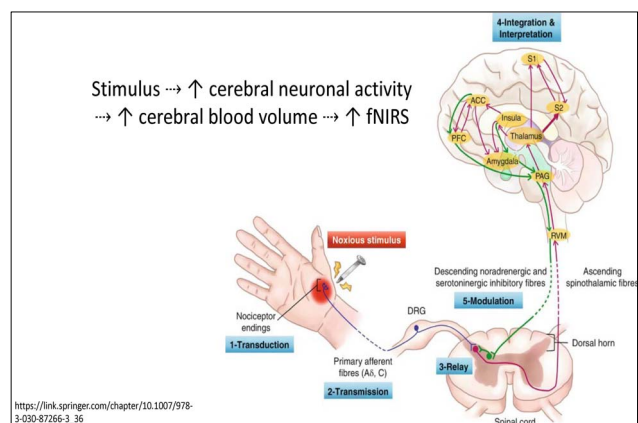
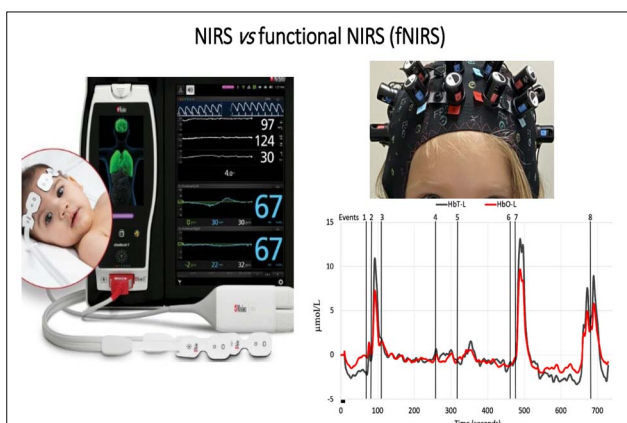
### Similar

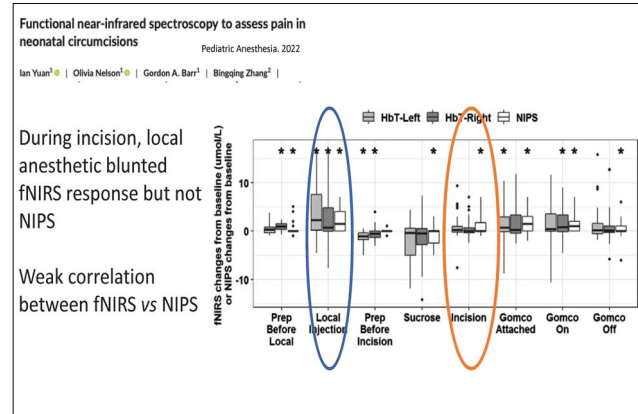
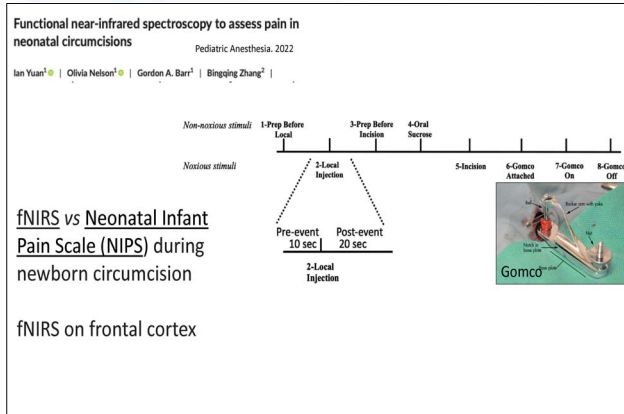
- Measure light absorption ratio of HbO/Hb.
- Subject to motion and light artifact.
- Depends on manufacturer algorithm.

### Different

- **PulseOx:**  
Arterial saturation and O<sub>2</sub> supply.
- **NIRS:**  
Venous saturation (~75%), O<sub>2</sub> supply and demand.  
Not dependent on pulsatile flow.

**NIRS vs PulseOx**





### Summary

- No "gold standard" for pain assessment
- Many devices still in research stage.
- Much research still needed in neonates... (especially under anesthesia)



# Accurate and Reliable Neuromuscular Monitoring in Children

Z Serpil Ustalar Ozgen

University of Mehmet Ali Aydınlar University, Türkiye



## No Disclosures

Except for My ASPA Family and my tiny patients



## Lecture Outlines

Importance of Neuromuscular Monitoring in Children

Key parameters to monitor NMB

Techniques for monitoring NMB in Children



Do we need to monitor NMB?

Sufficient blockade  
Adequate reversal

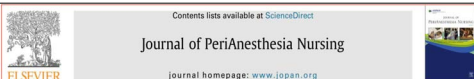
*Waiting to be used in the bottom drawer of the anesthesia machine forgotten within months of its purchase*



## How do we monitor NMB?

- Clinical signs
- Nerve stimulators

Head lift 5 s  
Leg lift 5 s  
Biting  
Maximum inspiratory pressure >50 cmH<sub>2</sub>O



### Research

Application of Neuromuscular Monitoring in Pediatric Anesthesia: A Survey in China

Lei Yang, MD<sup>1</sup>, Di Yang, MD<sup>2</sup>, Chunyan Liu, MD<sup>3</sup>, Yunxia Zuo, MD<sup>4,\*</sup>

<sup>1</sup> Department of Anesthesiology, West China Hospital, Sichuan University and The Research Unit of West China, Chinese Academy of Medical Sciences, Chengdu, China  
<sup>2</sup> Department of Anesthesiology, Sichuan Provincial Academy of Medical Sciences and Sichuan Provincial People's Hospital, Chengdu, China  
<sup>3</sup> Department of Anesthesiology, Jiangning District People's Hospital, Jiangning, China

**Keywords:**  
national survey  
neuromuscular monitoring  
pediatric anesthesia

### ABSTRACT

**Purpose:** To determine the popularity of neuromuscular monitoring in pediatric anesthesia.  
**Design:** Self-filled electronic questionnaire survey.  
**Methods:** Anesthesiologists were notified through a professional network platform of anesthesiology by mobile phone. The survey deadline was December 23, 2019.

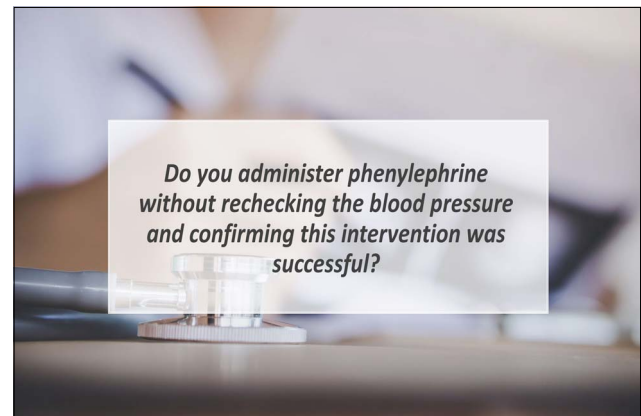
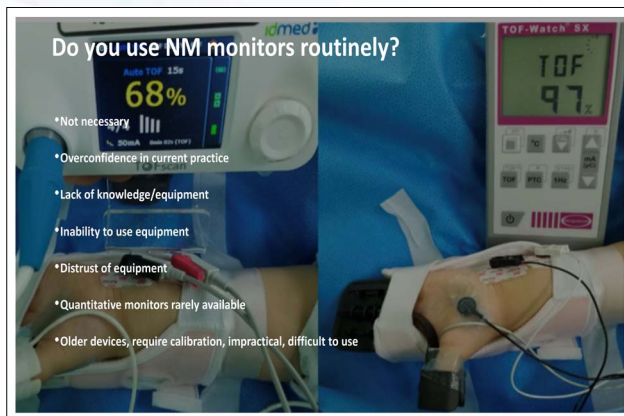
**Findings:** A total of 883 valid questionnaires were collected. A total of 738 (83%) anesthesiologists stated that they had never used neuromuscular monitoring in pediatric anesthesia, and 638 (72%) anesthesiologists stated that they were not equipped with neuromuscular monitors. A total of 869 (98.75%) anesthesiologists had used neostigmine, but only 291 (33%) anesthesiologists reported routine postoperative administration for the reversal of neuromuscular block.

**Conclusions:** Neuromuscular monitoring in pediatric anesthesia needs to be further popularized. However, how to effectively and safely use neuromuscular antagonists are also important issues that require attention from anesthesiologists.

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20% European anes  
10% US  
0% New Zealand and  
Australia anes use NMT

83% never  
72% no equipment  
33% routine reversal



## WHY?

Clinical assessment is challenging in children

- Difficulties in communication
- Non-compliance to instructions

10-28% of children experience postoperative residual block

Complications due to residual block can be detrimental

- smaller oxygen reserves
- more vulnerable to airway collapse

## Limitations of NM Monitoring in Neonates

- Variability in response- gestational age, postnatal age, weight, coexisting medical conditions
- Lack of standardized guidelines
- Technical difficulties
- Influence of temperature
- Influence of coexisting conditions – prematurity, congenital anomalies, NM diseases
- Limited pharmacokinetic data- organ immaturity, altered protein binding, different rates of drug metabolism and elimination
- Relevance of monitoring data- ongoing research and debate

## Why do we want to monitor NMB?

Stimulation pattern	Onset of block	Deep block (TOF=0)	Moderate block (TOF>0)	Recovery
Train-of-four (TOF)	Adequate	Not adequate	Adequate	Intermediate(a) Adequate(b)
Double burst stimulation (DBS)	Intermediate	Not adequate	Not adequate	Intermediate
Post-tetanic count (PTC)	Not adequate	Adequate	Not adequate	Not adequate
Tetanus (50/100Hz)	Not adequate	Not adequate	Not adequate	Intermediate

## Single twitch

- Supramaximal stimulus frequency 0.1-1.0 Hz
- Limited value in clinical setting
- Useful for baseline assessment of NM function before the administration of NMBA's

## Train-of-four (TOF)

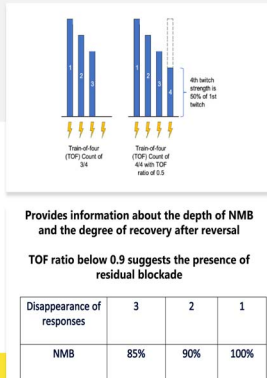
\* Stimulation pattern 4 twitches at 2 Hz

\* Loss of fourth response 75-80% NMB

\* Sufficient NMB for surgical procedure: until reappearance of 2-4 responses

\* TOF Ratio 0.7 = adequate diaphragmatic recovery

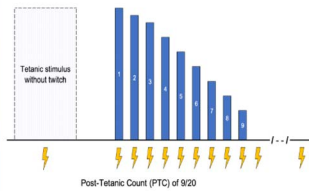
\* TOF Ratio >0.9 = adequate Pharyngeal muscle function



## Tetanic Stimulation

- High frequency (50-200) Hz stimulation applied for 5 s
- Fade effect in incomplete NMB recovery
- Sensitivity of using TS in detecting residual curarisation 70%, specificity 50%

## Post-tetanic count (PTC)



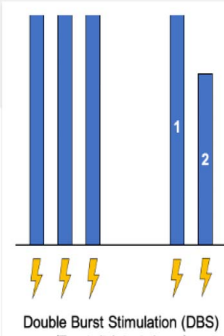
\*Tactile or visual evaluation of a deep non-depolarising NMB that does not respond to TOF

\*50 Hz tetanic stimulation for 5 s followed by 1 Hz supramaximal after a gap of 3 s

\*Ideally 0 if a very deep NMB is desired

\*5-7 responses are detectable = return of TOF imminent

## Double burst stimulation (DBS)



\*Greater tactile evaluation of minor NMB than tactile evaluation of TOF ratio

\*2 bursts stimuli at 50 Hz with an interval of 750ms

\*Burst consists of 2-3 impulses, combined 3/3,3/2

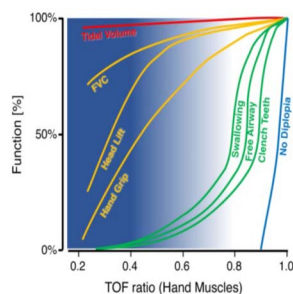
\*3/2 usually used at clinic

\*Fading of 2 impulse series compared to first= incomplete NM recovery, comparable TOF ratio <0.6

\*More sensitive for tactile evaluation of residual blockade

## Deep and Moderate block

- Train of four TOF
- Post tetanic count (PTC)



Level of Block	Depth of Block	Objective Measurement	Subjective Evaluation
Level 5	Complete		PTC = 0
Level 4	Deep		PTC ≥ 1, TOFC = 0
Level 3	Moderate		TOFC = 1-3
Level 2b	Shallow	TOFR < 0.4	TOFC = 4 & fade detected
Level 2a	Minimal	TOFR = 0.4-0.89	TOFC = 4 & fade not detectable
Level 1	Adequate recovery	TOFR ≥ 0.9	Cannot be determined

*Do you palpate the carotid artery during volume administration to assess the efficiency of your treatment?*

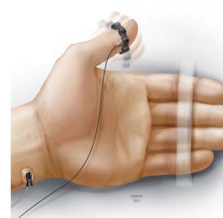
## NMT monitors



## Quantitative neuromuscular monitoring NMB Monitoring

- \*Mechanomyography
- \*Acceleromyography
- \*Electromyographic monitoring

## Acceleromyography (AMG)

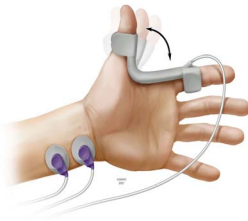


- Most widely used
- De facto standard of clinical care
- Easy to handle
- Suitable for any free moving muscle
- TOFR overestimation by at least 0.15
- Baseline TOFR >1.0
- Classic AMG TOF-Watch, Infinity Trident NMT Pod
- 3D TOFScan, Stimpod NMS 450 Mindray NM transmission transducer

• Use 3 perpendicular piezoelectric probes to thoroughly measure freely moving target muscles



## Kinemyography



- Easy to use
- Available only for the ulnar nerve-APM group
- Free thumb movement required
- Good strip placement between the fingers required
- Datex Ohmeda
- NMT
- MechanoSensor

• Measurement of the electrical signal generated by the bending of a piezoelectric sensor strip placed between the thumb and the index

## Electromyography



- Best indicator of pure NM function
- Free muscle movement not required
- Influenced by other electronic devices in OR (diathermy) or local temperature

• Measurement of the muscle action potential following nerve stimulation

## Cuff-based Monitoring Compressomyography (CMG)

- No need for free arm movement
- Modified non-invasive BP cuff measuring the block depth by brachial plexus stimulation through electrodes attached on its inner surface

• TOF-Cuff

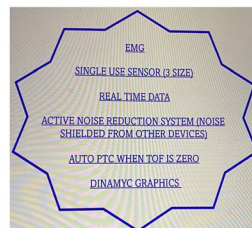
- No need for free arm movement
- Modified non-invasive BP cuff measuring the block depth by brachial plexus stimulation through electrodes attached on its inner surface



Monitor	Advantages	Disadvantages
MMG	Considered the "gold standard", as results are precise and reliable.	Inconvenient set-up process. Not manufactured for clinical use. (Research uses only.)
KMG	Simple setup that does not require an external display or calibration.	Can only be deployed at the APM.
AMG	Can be deployed on any free-moving muscle, including locations on the hand, foot, or face.	Cannot be deployed on immobilized muscles. Greatest accuracy requires device calibration prior to NMBA and normalization of baseline readings.
EMG	Considered as accurate and reliable as MMG. Can be deployed in a wide variety of locations, including immobilized muscles.	Subject to electrical interference. Accuracy reduced by low muscle temperature. Greatest accuracy requires device calibration prior to NMBA.

## Quantitative Monitors

- Tetragraph
- TwitchView
- TOFScan
- Be able to display PTC and TOF<sub>r</sub> in real time



Received: 29 May 2022 | Revised: 9 August 2022 | Accepted: 21 September 2022  
DOI: 10.1111/ven.13429

### ARTICLE

## Reversal of rocuronium-induced intense neuromuscular blockade by sugammadex in Korean children: A pharmacokinetic and pharmacodynamic analysis

Sang-Hwan Ji<sup>1,2</sup> | Ki Young Huh<sup>1,3</sup> | Jaeseong Oh<sup>1,3</sup> | Hee-Jeong Jeong<sup>1,2</sup> | Young-Eun Jang<sup>1,2</sup> | Eun-Hee Kim<sup>1,2</sup> | Ji-Hyun Lee<sup>1,2</sup> | Jin-Tae Kim<sup>1,2</sup> | Hee-Soo Kim<sup>1,2</sup>

10-28% postoperative residual blockade (TOF<0.9)  
6.5% severe block (TOF<0.7)

TOF-Watch SX accurate when calibrated, otherwise overestimate TOF ratio

TOFscan, 3D, no calibration

Wien et al. Perioperative Medicine. 2021;10(4):1-10.  
https://doi.org/10.1002/pm.1402

Perioperative Medicine

RESEARCH Open Access

Comparison of the TOFscan and the TOF-Watch SX during pediatric neuromuscular function recovery: a prospective observational study

Hyung Beom Yoon<sup>1</sup>, Young Eun Jang<sup>2</sup>, Ji-Hyun Lee<sup>3</sup>, Eun-Hee Kim<sup>4</sup>, Jin-Tae Kim<sup>5</sup> and Hee-Soo Kim<sup>1,2</sup>

- When using neuromuscular blocking agents (NMBA), quantitative NM monitoring is mandatory to optimize intubation time, monitor intraoperative muscle relaxation, determine adequate pharmacologic reversal agents, and reduce postoperative residual paralysis

Supinated palm, passively extended  
Fixed to an arm board to ensure sole movement of adductor pollicis brevis  
Clean with an alcohol swab  
Skin surface allowed to dry  
Two electrodes placed along the ulnar nerve  
The negative (black) electrode at distal near the styloid process of radius  
Positive electrode 3 cm proximally  
Pediatric hand sensor  
"to expand TOFscan's validity to infants and neonates, a smaller sensor is required"



Wien et al. Perioperative Medicine. 2021;10(4):1-10.  
https://doi.org/10.1002/pm.1402

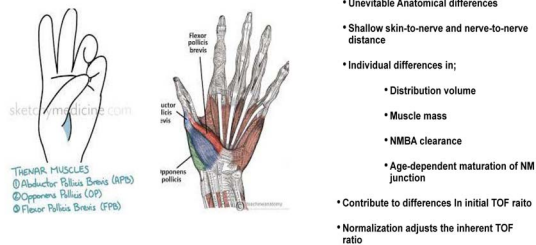
Perioperative Medicine

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Comparison of the TOFscan and the TOF-Watch SX during pediatric neuromuscular function recovery: a prospective observational study

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## Assessing 3D acceleration in children



- Unavoidable Anatomical differences
- Shallow skin-to-nerve and nerve-to-nerve distance
- Individual differences in;
  - Distribution volume
  - Muscle mass
  - NMBA clearance
  - Age-dependent maturation of NM junction
- Contribute to differences in initial TOF ratio
- Normalization adjusts the inherent TOF ratio

## Pediatric Anesthesia

Pediatric Anesthesia 2023 28: 391-404 doi:10.1111/1365-2025.15572

### Neuromuscular block and current treatment strategies for its reversal in children

OLLI A. MEHTOLA MD, PhD  
 Department of Anaesthesiology, Hospital for Children and Adolescents, University of Helsinki, Finland  
 Section Editor: Prof. Steve Anderson

• Use of neostigmin to reverse deep NMB will not be effective and will not result in adequate recovery, may result in recurarization

• Inadequate antagonism, subsequent fatigue rather than recurrence of block

• Recurarization may be seen clinically after using inadequate doses of sugammadex

## Keep it Simple

- Easy -to understand interface
- Greater acceptance among clinicians
- Learning curve not steep



EDITORIAL

### Neuromuscular Monitoring: Keep It Simple!

Mohamed Naguib, MD, MSc, FCARCSI,\* and Aaron F. Koopman, MD†

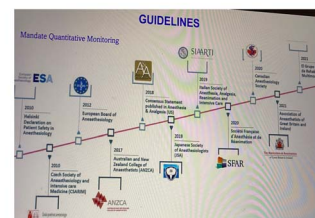
Acquiring the latest and most expensive quantitative monitor is not likely to solve the problem of undetected postoperative residual NMB

## Postoperative Residual Weakness

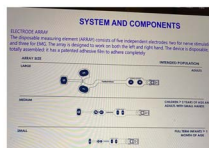
- Observing an unacceptable number of patients encountering respiratory distress in the recovery- 20-40% even reversed
- Pharyngeal dysfunction, increased risk for aspiration and pneumonia, acute respiratory events (hypoxemia, airway obstruction), need of tracheal intubation, discomfort for patients and surgeons, increased stay in PACU
- Using quantitative NMB Monitoring whenever a non-depolarizing muscle relaxant is used and documenting train of four in the anesthetic record

### NM MONITORING IS MANDATORY TO

- Optimize intubation time
- Monitor intraoperative muscle relaxation
- Determine adequate pharmacologic reversal agents
- WFSA, SFAR recommend incorporating objective NM monitoring into daily practice



## Tips and Tricks



- Choose the appropriate monitoring device
- Familiarize yourself with the equipment
- Proper electrode placement
- Optimize skin preparation
- Monitor baseline values
- Individualize monitoring approach
- Consider the effect of temperature
- Avoid electrode movement
- Interpret the data carefully
- Monitor throughout the procedure
- Maintain communication
- Stay updated with guidelines and best practices

## Take home

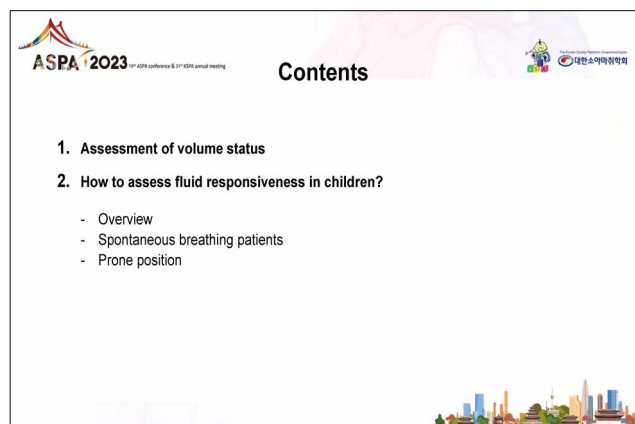
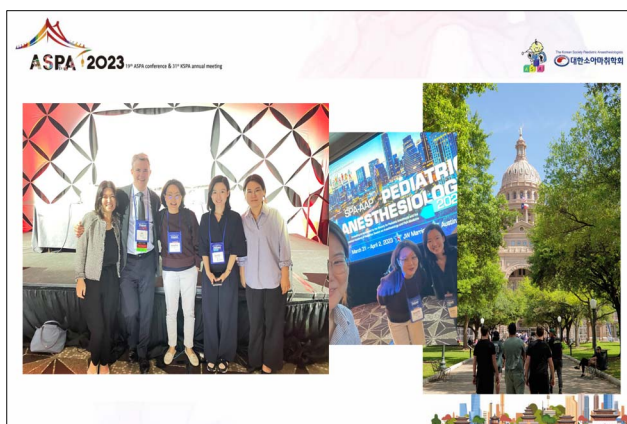
- Misconceptions
- Lack of knowledge
- Failure to follow well-established guidelines regarding the clinical use of NM drugs are commonplace
- What we need is not more complicated monitors, but the application of well-established lessons
- Rather the application of NMB and appropriate reversal



# How to Assess Fluid Responsiveness in Children?

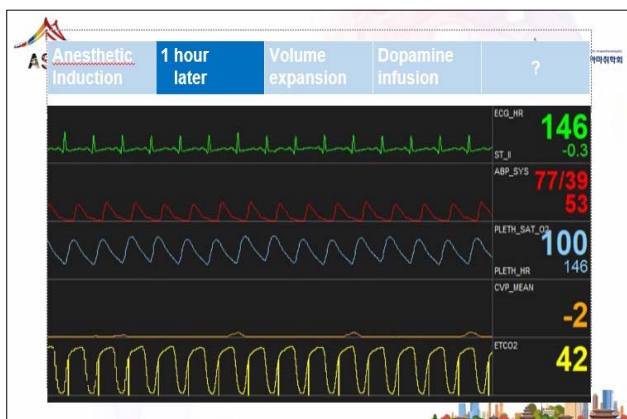
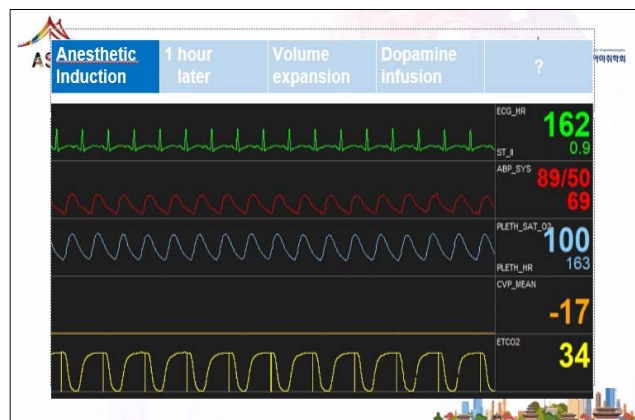
Eun-Hee Kim

Seoul National University Hospital, Korea

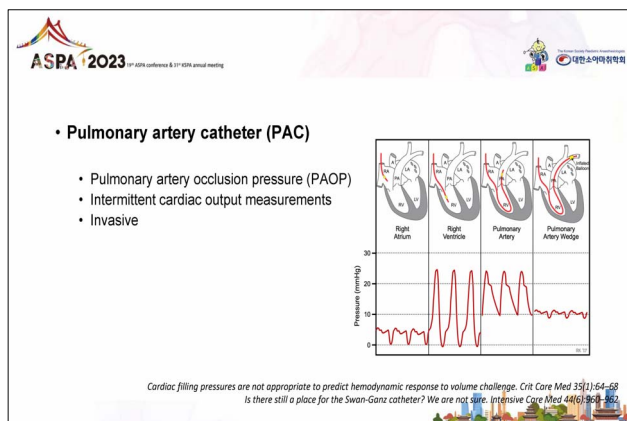
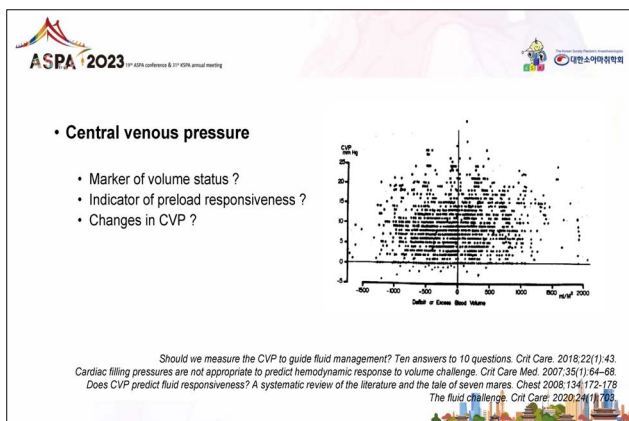
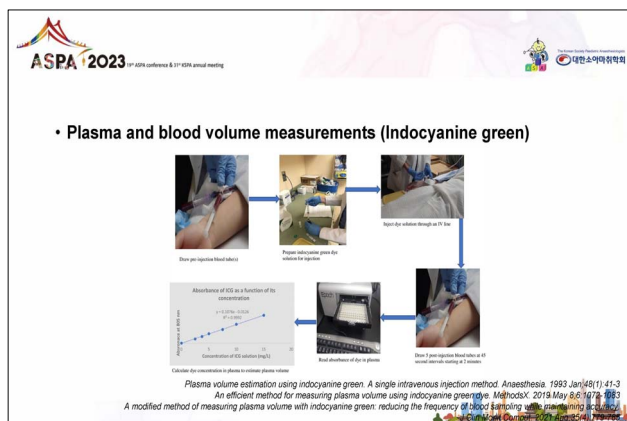
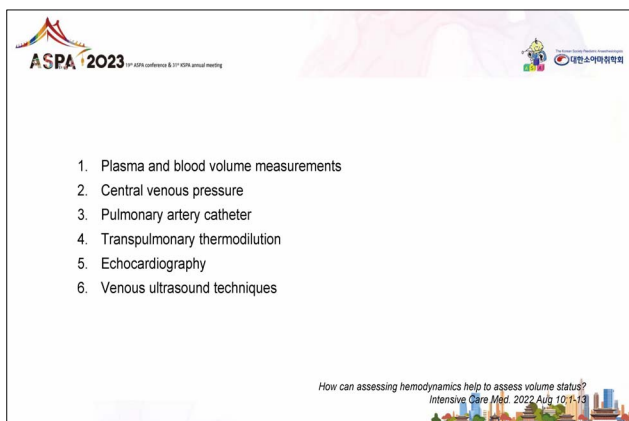
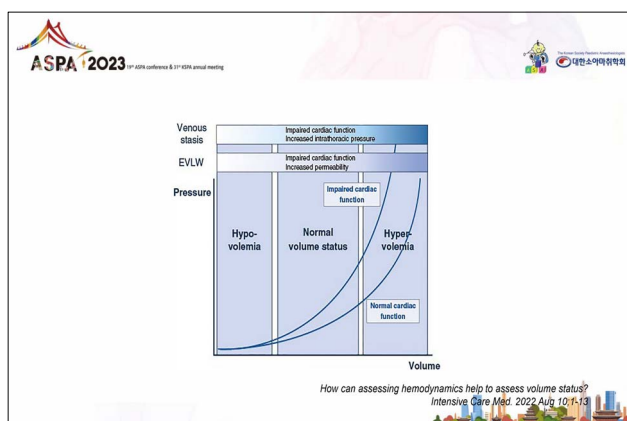
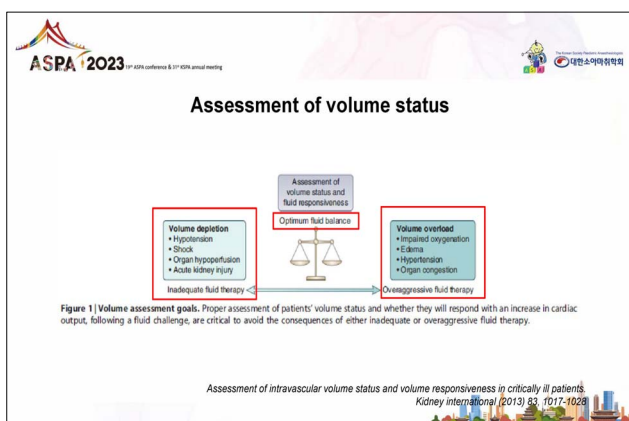
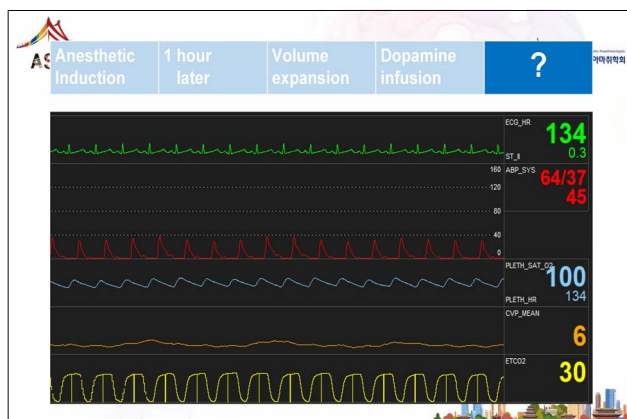
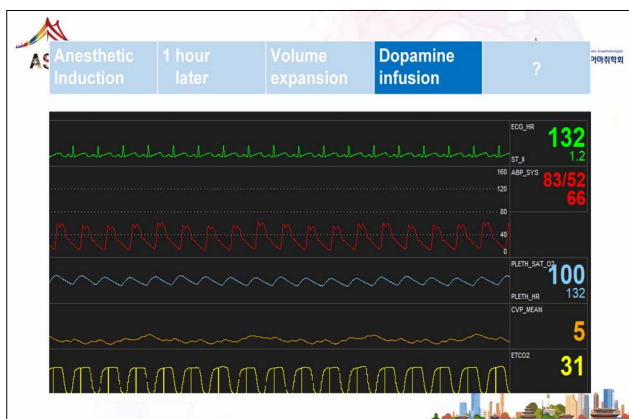


**Case**

- 4 months, female
- 63.4cm, 6 kg
- GA 37+4wks, 3.1kg at birth
- Baseline BP 95/65 mmHg, HR 100-123 bpm, SpO<sub>2</sub> 100% at ward.
- AST/ALT 257/206 IU/L, D.Bil. 7.85 mg/dl (NL 0-0.5)
- Diagnosis: Biliary atresia
- Operation: Kasai operation







## Eun-Hee Kim: How to Assess Fluid Responsiveness in Children?

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**Transpulmonary thermodilution**

- Intrathoracic blood volume
- Extravascular lung water (EVLW)
- Continuous Cardiac output (CO)

After central venous injection the cold bolus sequentially passes through the venous and pulmonary compartments.

Transpulmonary thermodilution: advantages and limits. Crit Care. 2017 Jun 19;21(1):147.

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**Echocardiography**

- Excellent tool to evaluate volume status
- Intravascular volume and pressure
- Cardiac output and function
- Identify fluid responsiveness

"Kissing papillary muscle" end systolic LV cavity obliteration

Hemodynamic monitoring using echocardiography in the critically ill. Springer, Heidelberg

Comparison of echocardiographic indices used to predict fluid responsiveness in ventilated patients. Am J Respir Crit Care Med 195:1022-1032

Cardiovascular clusters in septic shock combining clinical and echocardiographic parameters: a post hoc analysis. Intensive Care Med 45(5):651-667

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**Venous ultrasound techniques**

- Diameter of inferior vena cava
- Flow patterns in hepatic veins, portal vein, renal veins, and femoral veins.
- Impaired right ventricular function or elevated intrathoracic pressure.

Quantifying systemic congestion with point-of-care ultrasound: development of the venous excess ultrasound grading system. Ultrasound J 12(1):16

Alterations in portal vein flow and intrarenal venous flow are associated with acute kidney injury after cardiac surgery: a prospective observational cohort study. Am Heart Assoc 7(19):e009681

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**Volume status ≠ Fluid responsiveness**

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

Fluid responsiveness in the pediatric population. Korean J Anesthesiol 72(5):428-440.

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**How to assess fluid responsiveness in children?**

- Overview
- Spontaneous breathing patients
- Prone position

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**Dynamic variables based on the Heart-Lung interaction**

- PPV, SPV, SVV, ΔDown, ΔUp, ΔPOP, PVI, ΔVpeak, ΔVpeak CA, ΔIVC

Clinical use of respiratory changes in arterial pulse pre-sure to monitor the hemodynamic effects of PEEP. Am J Respir Crit Care Med 199:935-939

Assessment of intravascular volume status and volume responsiveness in critically ill patients. Kidney International (2013) 83:1017-1028

Fluid responsiveness in the pediatric population. Korean J Anesthesiol 72(5):428-440

**ASPA 2023** 19<sup>th</sup> ASPA conference & 31<sup>st</sup> KSPA annual meeting

**Pulse pressure variation**

- False positives
  - Spontaneous ventilation
  - Cardiac arrhythmia
  - Right ventricular failure
- False negative
  - Low tidal volume (< 7ml/kg)
  - Low lung compliance
  - Very high respiratory rate
- Children?

Arterial pulse pressure variation with mechanical ventilation. Am J Respir Crit Care Med 199(1):22-31


Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients. Crit Care Med 2009;37:2842

Respiratory variations in aortic blood flow predict fluid responsiveness in ventilated children. Intensive Care Med 44(5):388-394

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- Stroke volume variation
  - Vigileo monitor and FloTrac sensor
  - LiDCO plus system
  - LiDCO rapid system in children



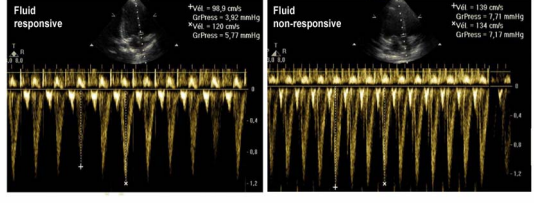
LiDCO system

Intraoperative fluid optimization using stroke volume variation in high risk surgical patients. Crit Care 2010; 14:R118  
 Equipment review: an appraisal of the LiDCO plus method of measuring cardiac output. Crit Care 2004; 8:190-195  
 Low predictability of three different noninvasive methods to determine fluid responsiveness in critically ill patients. Radiat Crit Care Med 2005; 16:e99-94

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- Respiratory variation of aortic blood flow peak velocity ( $\Delta V_{peak}$ )



Fluid responsive:  $\Delta V_{peak} = 98.0$  cm/s,  $\Delta V_{peak} = 3.52$  mm/s,  $\Delta V_{peak} = 1.28$  cm/s,  $\Delta V_{peak} = 5.71$  mm/s

Fluid non-responsive:  $\Delta V_{peak} = 139$  cm/s,  $\Delta V_{peak} = 7.71$  mm/s,  $\Delta V_{peak} = 1.84$  cm/s,  $\Delta V_{peak} = 1.17$  mm/s

Respiratory variations in aortic blood flow predict fluid responsiveness in ventilated children. Intensive Care Med 34(5): 888-894  
 Predicting fluid responsiveness in children: a systematic review. Anesth Analg 117(6): 1380-1392  
 Point-of-care ultrasonography to predict fluid responsiveness in children: A systematic review and meta-analysis. Paediatr Anaesth. 2023 Jan;33(1):24-37. doi: 10.1111/pan.14574. Epub 2022 Oct 1. PMID: 36222222

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- Respiratory variations of inferior vena cava




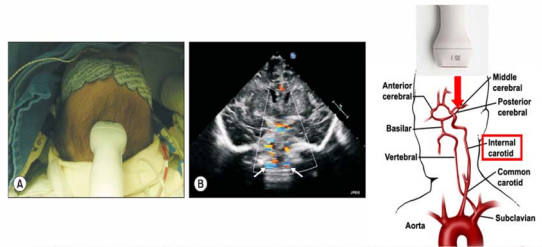
Fig. 20.41 Collapsible IVC >50%.

Fluid responsiveness in the pediatric population. Korean J Anesthesiol 72(5): 429-440  
 Inferior vena cava ultrasound, Monitoring. Smith's anesthesia for infants and children 101

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- Respiratory variation of carotid artery blood flow peak velocity ( $\Delta V_{peak\_CA}$ )



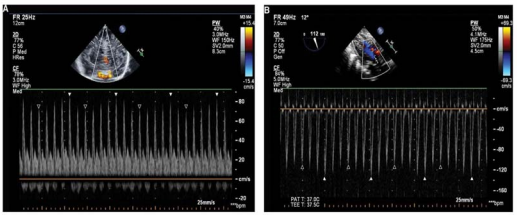
Anterior cerebral, Middle cerebral, Posterior cerebral, Basilar, Internal carotid, Common carotid, Vertebral, Subclavian, Aorta

Respiratory Variation of Internal Carotid Artery Blood Flow Peak Velocity Measured by Transfontanelle Ultrasound to Predict Fluid Responsiveness in Infants: A Prospective Observational Study. Anesthesiology 133(5): 778-787

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- Respiratory variation of carotid artery blood flow peak velocity ( $\Delta V_{peak\_CA}$ )

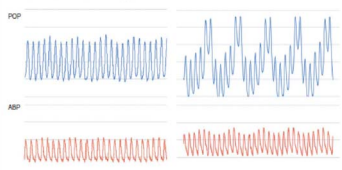


Transfontanelle Ultrasound, Aorta

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- $\Delta POP$  and PVI



POP, PVI

Assessment of intravascular volume status and volume responsiveness in critically ill patients. Kidney International (2013) 83, 1017-1028  
 Assessment of dynamic variables of fluid responsiveness to predict desufflation-induced hypotension during paediatric laparoscopic surgery. Br J Anaesth 2017 Nov 1;119(5): 958-963

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

- $\Delta POP$  and PVI

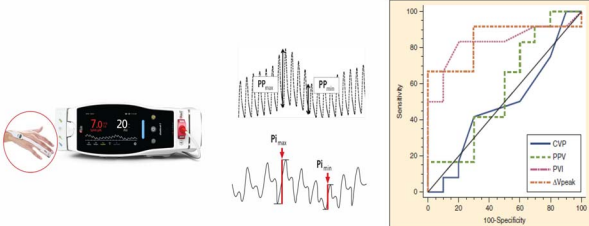


Fig. 18.3 Comparison of Areas Under ROC Curves Before Volume Expansion. Areas under the receiver operating curve (ROC) curve of

Does the plethysmographic variability index predict fluid responsiveness in mechanically ventilated children? Br J Anaesth 2016; 117: 409-410  
 Systolic pressure variation, Monitoring. Smith's anesthesia for infants and children 101

ASPA 2023 17th KSA conference & 17th KSA annual meeting

대한소아마취학회

How to assess fluid responsiveness in children?

- Overview
- Spontaneous breathing patients
- Prone position



**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

• Passive leg raising (PLR)

Prediction of fluid responsiveness. What's new? *Annals of Intensive Care* (2022) 12:46  
Passive leg raising for assessment of volume responsiveness: a review. *Curr Opin Crit Care* 2017 23:237-49

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

• Passive leg raising (PLR) in Children

Index: J Pediatr (2023) 250:1021-1027  
DOI: 10.1016/j.jpeds.2023.102107

**ORIGINAL ARTICLE**

The Passive Leg Raise Test to Predict Fluid Responsiveness in Children -Preliminary Observations

Gangdong Kim, Gangdong Yoon, Yung C Chou, Jihyeon Lee, Eun-Hee Kim, Yoon-Jin Kim

**PEDIATRIC CRITICAL CARE**

Accuracy of Passive Leg Raising Test in Prediction of Fluid Responsiveness in Children

Abirad A D Rameez<sup>1</sup>, Pasant M Farghaly<sup>2</sup>, Huda M Hassan<sup>3</sup>

**RESEARCH ARTICLE**

The clinical value of passive leg raising plus ultrasound to predict fluid responsiveness in children after cardiac surgery

Deqiang Luo<sup>1,2</sup>, Wei Dai<sup>2</sup>, Lai Lai<sup>2</sup> and Xueying Cai<sup>1\*</sup>

Cardiac output	Conclusion
NICOM	The PLR may be helpful in assessing the volume status in children aged >5 years, but not < 5
TTE	PLR is reliable test in < 5 year-old-children if performed appropriately using bedside echocardiography for the measurement of its transient effect

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

• A calibrated abdominal compression

Then the hand press to generate 30 cmH2O of pressure

Diagnostic accuracy of a calibrated i

00:01:78 3r J Anesth 2018 Dec;121(6):1323-1331

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

• Abdominal compression-induced blood pressure change

Prediction of fluid responsiveness based on liver compression-induced blood pressure changes in children after cardiac surgery

Minerva Anestesiol 2021 Sep;31(9):838-846

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

How to assess fluid responsiveness in children?

- Overview
- Spontaneous breathing patients
- **Prone position**

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

Prediction of fluid responsiveness. What's new? *Annals of Intensive Care* (2022) 12:46

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

• Tidal volume challenge

Figure 3. ROC curves of PPV and SVV variation after V.C application (LPPV<sub>100</sub> [blue line] and LSVV<sub>100</sub> [red line]). The ROC curves of PPV (black line) and SVV (grey line) at 1, are also reported in each figure (see text for further explanations). PPV indicates pulse pressure variation; ROC, receiver operating characteristic; SVV, stroke volume variation; V.C, tidal volume challenge.

Assessment of Fluid Responsiveness in Prone Neurosurgical Patients Undergoing Protective Ventilation: Role of Dynamic Indices, Tidal Volume Challenge, and End-Expiratory Occlusion *Int J Anesth* 2020 Nov;133(3):175-184

**ASPA 2023** 19th ASPA conference & 31st KSPA annual meeting

U.S. National Library of Medicine  
**ClinicalTrials.gov**

Study: **Prone Fluid Responsiveness in Children**

Study ID: NCT04408888

Study Dates: Jan 8, 2021 - Jan 12, 2022


Study Description: The safety and scientific validity of this study is the responsibility of the study sponsor and investigator. Listing a study does not mean that it has been endorsed by the U.S. Federal Government, U.S. Department of Health, or any other U.S. government agency. The investigator designed this study to assess the sensitivity and specificity of passive PPV, SVV, and PVI for fluid volume (17) challenge (17) and in predicting fluid responsiveness during machine ventilation.



Fluid Responsiveness Prediction


?

Improve the Clinical Outcome in the Pediatric Population

## Summary

- When we give a fluid to patients, two clinical questions are asked
  - What is the current state of the patient's intravascular volume?
  - And if the patient receives continued resuscitation or a fluid bolus, will physiological variables such as blood pressure, tissue perfusion, and urine output improve?
- Predicting fluid responsiveness is difficult in the pediatric patients
- Respiratory variation in aortic blood flow peak velocity was the most reliable parameter for predicting fluid responsiveness in pediatric patients.
- Several potential parameters can be useful in clinical situations.
- Further researches on the clinical outcomes are needed.




## Operating theatre in SNUH



Labels in image:

- Patient monitor\_PPV
- PVI, PSI, O3
- LIDCO rapid\_SVV, CI
- Transfontanelle ultrasound\_ΔVpeak\_CA





## **Session 3.**

# **Sharing the Knowledge of NORA**

**Chair(s): Vivian Yuen (Hong Kong)**  
**Yong-Hee Park (Korea)**



# Dexmedetomidine<sup>+</sup> Remimazolam Clinical Applications and Limitations

Keira P. Mason

Boston Children's Hospital, Harvard Medical School, USA

## Learning Objectives

- Understand the pharmacology and pharmacokinetic profile of Dexmedetomidine + Remimazolam
- Understand the clinical profile
- Review the relevant literature to aid in clinical delivery
- Share my clinical pearls

## Dexmedetomidine Pharmacology

- $\alpha$ -2 to  $\alpha$ -1 ratio of 1620:1
- intravenous, intramuscular, intranasal, subcutaneous, epidural, transdermal routes
- Crosses blood-brain barrier
- CSF concentration is ~ 8% of the plasma concentration
- Inactive metabolites
- Half life 2-3 hours

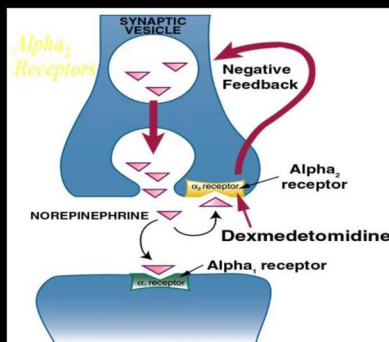
## DEXMEDETOMIDINE



- 1999 approved for ICU
- 2008 approved for sedation
- Bolus 1 mcg/kg over 10 min
- Infusion 0.7 mcg/kg/hr
- 24 Hour Limit

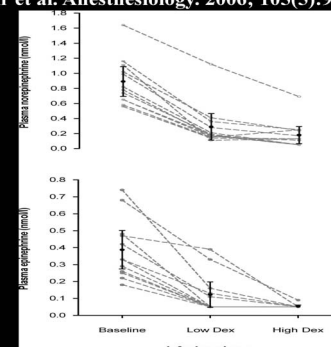
2011  
DEX approved in Europe  
ICU approval only  
NO time limit

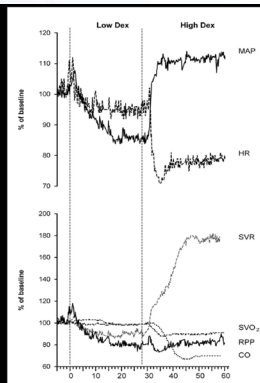
Infusion no Bolus- 1.4 mcg/kg/hr



## DEXMEDETOMIDINE

Effect on Epinephrine & Norepinephrine levels  
Snapir et al. Anesthesiology. 2006; 105(5):902-10





Snapir et al. Anesthesiology. 2006; 105(5):902-10

## Tolerable Rapid Bolus DEX Dose in Children

Dawes J. Ped Anes. 2014

- Healthy children (5-9 yoa)
- Hemodynamic response
- + Response:  $\geq 30\%$   $\Delta$  mean HR, MAP
- 5 second bolus
- ED50 0.49 mcg/kg
- 50 second- max dec in median HR
- 100 second- median inc in median MAP

## AVOID ANTICHOLINERGICS FOR BRADYCARDIA

Mason KP et al. AnesAnal. 108;906-8:2009  
Subramanyam R. Anesth Analg 2015

- All pediatric MRI
- Bradycardia Treatment-prospective (Mason et al)
- Prophylactic Tx –retrospective (Subramanyam et al.)
- Risk transient, marked or sustained hypertension

## DEXMEDETOMIDINE EEG SIMULATES NON-REM SLEEP

Mason KP et al. Paediatr Anaesth. 2009 (12):1175-83  
Mason KP et al. J Pediatr. 2012 (5):927-932

- DEX Sedation
- EEG resembles Stage II Sleep

## Sea Lion

### IM Sedation: Dex+Butorphanol+Versed

Courtesy of: William Van Boon, DVM  
Marine Mammal Center, Sausalito, CA

## SEA LION

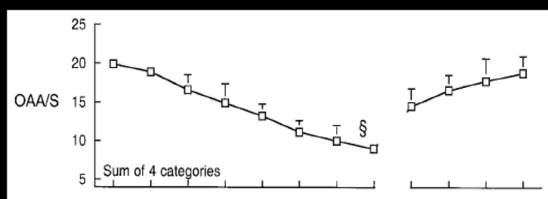
### IM Sedation: Dex+Butorphanol+Versed

Courtesy of: William Van Bonn, DVM  
Marine Mammal Center, Sausalito, CA



## Depth of Sedation Increases with Increasing Dex

Ebert TJ et al. Anesth 2000



## Dex is Not an Amnestic

Mason et al. BJA 2017

BJA

British Journal of Anaesthesia, 118 (2): 254-63 (2017)  
doi: 10.1093/bja/aew421  
Paediatrics

### Feasibility of measuring memory response to increasing dexmedetomidine sedation in children

K. P. Mason<sup>1,\*</sup>, E. R. Kelhoffer<sup>2,3</sup>, R. Prescilla<sup>4</sup>, M. Mehta<sup>2,3</sup>, J. C. Root<sup>2,3,5</sup>, V. J. Young<sup>1</sup>, F. Robinson<sup>6</sup> and R. A. Veselis<sup>2,3</sup>

## BJA 2017

### Dexmedetomidine pharmacodynamics in healthy volunteers: 2. Haemodynamic profile

P. J. Colin<sup>1,2,\*</sup>, L. N. Hannivoort<sup>1</sup>, D. J. Eleveld<sup>1</sup>, K. M. E. M. Reynijens<sup>1</sup>, A. R. Absalom<sup>1</sup>, H. E. M. Vereecke<sup>1</sup> and M. M. R. F. Struys<sup>1,3</sup>

<sup>1</sup>Department of Anaesthesiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, <sup>2</sup>Department of Bioanalysis, Faculty of Pharmaceutical Sciences, Ghent University, Ghent, Belgium and <sup>3</sup>Department of Anaesthesia and Peri-operative Medicine, Ghent University, Ghent, Belgium

\*Corresponding author. E-mail: p.j.colin@umcg.nl

### Hemodynamics Predicted by [Dex] HD as Marker of Sedation Depth

PJ Colin . BJA 2017

- N=18 healthy
- Step up dose of DEX (TCI)
- Hemodynamics described by serum [DEX]
- High correlation between sedation and HD
- Hemodynamics predict sedation/BIS depth
- PKPD Model for HR and MAP effects

### Dexmedetomidine Sedation MRI, CT and Nuclear Medicine

Mason KP et al. Anes Analg 2006  
Mason KP et al. Paediatr Anaesth. 2008  
Mason KP et al. Anes Analg. 108:906-8-2009  
Mason KP et al. Paediatr Anaesth. 2009  
Mason KP et al. Radiology. 2013  
Mahmoud M. Paediatr Anaesth 2014  
Mahmoud M. J Clin Anaesth 2013

- 2-3 mcg/kg bolus (10 min)-2 mcg/kg/hr
- Sedation Achieved:  $8.9 \pm 2.4$  min
- Time to meet discharge criteria:  $31.8 \pm 18$  min

### Bioavailability

Anttila M. Br J Clinical Pharm. 2003  
Iiro T. Eur J Clin Pharm 2011

- Oral- 16%
- Nasal- 65%
- Buccal- 82%
- Intramuscular-104%

### Combination of intranasal dexmedetomidine and oral midazolam as sedation for pediatric MRI

Georgia Coust<sup>1</sup>,  
Lorenza Monesi<sup>2</sup>,  
Nadia Marone<sup>3</sup>,  
Francesca Biondi<sup>4</sup>,  
Andrea Magnifico<sup>5</sup>,  
Francesca Biondi<sup>6</sup>

<sup>1</sup>Institute for Maternal and Child Health (IRCC) Bambino Gesù, Rome, Italy

Stefania Neri<sup>1</sup>,  
Giulia Neri<sup>2</sup>,  
Egle Berti<sup>3</sup>,  
Egle Berti<sup>4</sup>,  
Egle Berti<sup>5</sup>,  
Egle Berti<sup>6</sup>

<sup>1</sup>University of Trieste, Trieste, Italy

Intranasal dexmedetomidine, as midazolam-sparing drug, for  
MRI in preterm neonates

Journal of Clinical Pharmacy and Therapeutics 2018; 43: 143-148

### Pediatric Emergency Care Intramuscular Dexmedetomidine, a Feasible Option for Children With Autism Spectrum Disorders Needing Urgent Procedural Sedation

Georgia Coust, MD  
Andrea Tassone, MD  
Nadia Marone, MD  
Francesca Biondi, MD  
Andrea Magnifico, MD  
Francesca Biondi, MD

<sup>1</sup>Institute for Maternal and Child Health (IRCC) Bambino Gesù, Rome, Italy  
<sup>2</sup>University of Trieste, Trieste, Italy  
<sup>3</sup>University of Trieste, Trieste, Italy  
<sup>4</sup>University of Trieste, Trieste, Italy  
<sup>5</sup>University of Trieste, Trieste, Italy  
<sup>6</sup>University of Trieste, Trieste, Italy

### INTRANASAL DEXMEDETOMIDINE FOR PROCEDURAL SEDATION IN CHILDREN, A SUITABLE ALTERNATIVE TO CHLORAL HYDRATE

Georgia Coust<sup>1</sup>, Stefania Neri<sup>2</sup>, Egle Berti<sup>3</sup>

<sup>1</sup>Institute for Maternal and Child Health (IRCC) Bambino Gesù, Rome, Italy  
<sup>2</sup>University of Trieste, Trieste, Italy  
<sup>3</sup>University of Trieste, Trieste, Italy

### DEX is Synergistic Narcotics, Propofol, Ketamine?

$$1 + 1 = 5$$

SYNERGISM

### BioOne CHEMICAL IMMOBILIZATION AND ANESTHESIA OF FREE-LIVING ASIAN RED GIBBONS (HYLODIPTERUS LEUCOGASTRUS) WITH KETAMINE-DEXMEDETOMIDINE-ALFLOXAN AND ISOFURANE

Jeffrey S. Reagor, MD, PhD, Scott C. Smith, PhD, Anna H. Hsu, PhD,  
A. Brian, DVM, MS, and Lark C. E. Meyer  
Source: Journal of Wildlife Diseases, 56(1):66-72,  
Published by: Wildlife Disease Association  
URL: <http://www.bioscience.org/doi/10.7554/361547-066>



Figure 1. A donkey standing in a field.

### Pharmacokinetics of ketamine and dexmedetomidine in tigers (Panthera tigris)

F. Di Cosimo<sup>1</sup>, F. Caporali<sup>2</sup>, L. Rinaldi<sup>3</sup>, M. Caporali<sup>4</sup>, M.  
Rinaldi<sup>5</sup>, F. Di Cosimo<sup>6</sup>

<sup>1</sup>Department of Health, Animal Science and Food Safety, University of  
Bari, Italy  
<sup>2</sup>Department of Veterinary Medicine, University of Bari, Italy  
<sup>3</sup>Department of Veterinary Medicine, University of Bari, Italy  
<sup>4</sup>Department of Veterinary Medicine, University of Bari, Italy  
<sup>5</sup>Department of Veterinary Medicine, University of Bari, Italy  
<sup>6</sup>Department of Veterinary Medicine, University of Bari, Italy

### Immunization of wild giant pandas (Ailuropus melanoleucus) with dexmedetomidine-Histamine- Zelenoxan

Chang-Ming Tang<sup>1</sup>, Shao-Min Tang<sup>2</sup>, Shao-Min Tang<sup>3</sup>, Shao-Min Tang<sup>4</sup>,  
Shao-Min Tang<sup>5</sup>, Shao-Min Tang<sup>6</sup>

<sup>1</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China  
<sup>2</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China  
<sup>3</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China  
<sup>4</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China  
<sup>5</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China  
<sup>6</sup>The State Key Laboratory of Veterinary Medicine, China Agricultural University, Beijing, China



## Eur J Anaesthesiol, 2020

EJA

Eur J Anaesthesiol 2020; 37:1-8

### ORIGINAL ARTICLE

### The synergistic effect of dexmedetomidine on propofol for paediatric deep sedation A randomised trial

Keira P. Mason, Raymond Seungjoon Park, Cornelius A. Sullivan, Karina Lukovits, Erin M. Halpin,  
Samantha T. Imbrescia, David Cavanaugh, Randy Prescilla and Victor L. Fox

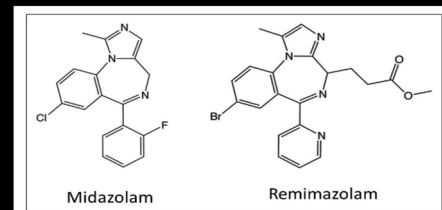


## Remimazolam



- A “soft drug”
- Goal is rapid biotransformation to inactive metabolites
- Ester modified benzodiazepine analog
- Eliminate the active metabolite (alpha hydroxy midazolam) of midazolam

## Ester moiety added to midazolam



## January 2020 Remimaz approved in Japan

- Approved for induction and maintenance of general anesthesia
- 12 mg/kg/hr until targeted level then 1-2 mg/kg/hr infusion
- 0.2 mg/kg bolus as needed

## A placebo- and Midazolam-Controlled phase I Single Descending-Dose Study Evaluating the Safety, Pharmacokinetics, and Pharmacodynamics of Remimazolam (CNS 7056): Part I. Safety, Efficacy, and Basic Pharmacokinetics.

Antonik LJ. Anesth Analg 2012

- Phase 1 clinical trial, healthy adults
- Single, ascending dose study
- .01-.3 mg/kg bolus did not cause hypotension (SBP<80)
- Dose-dependent sedation (MOAA/S scores) with remimazolam  $\geq 0.05$  mg/kg in a single ascending-dose study
- IV remimazolam 0.075–0.20 mg/kg similar sedation depth to 0.075 mg/kg midazolam
- More rapid recovery (5.5–20 vs 40 min)

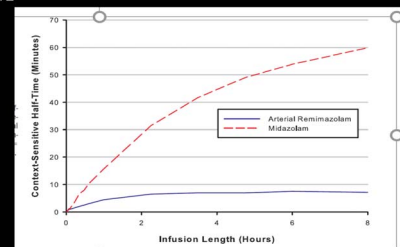
A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part II. Population pharmacokinetic and pharmacodynamic modeling and simulation

Wiltshire HR et al. Anesth Analg 2012

- A phase I, single-center, double-blind, active-controlled, randomized, single-dose escalation study
- n=54 healthy adults, 9 study groups, midaz groups and placebos
- Infusion of remimazolam (0.01–0.3 mg/kg)
- PK and PD study
- Max effect within 3 minutes

## Remimaz phase 1 trials

Wiltshire HR et al. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part II. Population pharmacokinetic and pharmacodynamic modeling and simulation. Anesth Analg 2012



## Journal of Anesthesia, 2020

Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial

Matsuyuki Doi<sup>1</sup> • Kiyoshi Morita<sup>2</sup> • Junzo Takeda<sup>3</sup> • Atsuhiko Sakamoto<sup>4</sup> • Michiaki Yamakage<sup>5</sup> • Toshiyasu Suzuki<sup>6</sup>

Non inferiority study comparing Remimazolam to Propofol for induction and maintenance of GA

- mean age 57
- 6 or 12 mg/kg/hr Remimazolam until LOC then 1-2 mg/kg/hr maintenance titrated
- 2-2.5 mg/kg propofol until LOC then 4-10 mg/kg/hr titrated
- Remimfentanil to both groups
- Primary endpoint- intraop awakening, recall, need for rescue, no body movements

### Non inferiority study comparing Remimazolam to Propofol for induction and maintenance of GA

- Efficacy rates were 100%
- Longer time to LOC (10–15 secs) and extubation (~ 6 min) in Remimazolam group
- No difference in adverse events
- Higher incidence of hypotension (20 vs 49%) with propofol
- 19% pain on injection with propofol, none with Remimazolam

### Pharmacokinetics and Pharmacodynamics of Intranasal Remimazolam—a randomized controlled clinical trial

Marija Pesic, Europ J Clinical Pharm 2020

- Randomized, double-blind, 9-period cross-over design
- PK, PD, and safety
- Single intranasal doses of 10, 20, and 40 mg remimazolam (as powder or solution) vs. IN placebo and 4 mg IV remimazolam.
- IN remimazolam powder had a consistent absolute bioavailability of approximately 50%
- Tmax was 10min
- The higher doses of IN solution decreases relative bioavailability through swallowing and first-pass effect

### A phase III study evaluating the efficacy and safety of remimazolam (CNS 7056) compared with placebo and midazolam in patients undergoing colonoscopy

Douglas K. Rex, GI Endoscopy 2018

- N=461 randomized patients in 12 U.S. sites
- Gastroenterologist delivered
- Less hypotension
- The primary endpoint was met for remimazolam, placebo, and midazolam in 91.3%, 1.7%, and 25.2% of patients,
- Faster recovery

### Remimazolam vs Propofol in Upper Gastrointestinal Endoscopy: A Multicenter, Randomized, Non-inferiority, Phase III trial

Shao-Hui Chen, J Gastroent and Hepatology 2020

- Phase 3 trial- China
- n-384
- Longer time to sedate ~ 1 min
- Shorter recovery ~ 1 min
- Less treatment requiring hypotension (0.5 vs 5.8%)
- Less respiratory depression (1.0 vs 6.8%)
- Fewer adverse events (39 vs 60%)

### Deeper Sedation Induced With Propofol

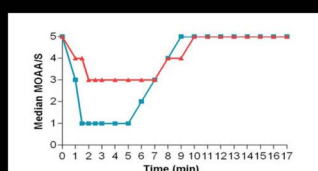


FIGURE 3 Sedation profile. MOAA/S, Modified Observer's Assessment of Alertness/Sedation. —, Remimazolam tosylate; —, Propofol.

### Remimazolam vs Propofol Benefits of Flumazenil

W Luo et al. BMC Anesthesiology 2023

- Prospective RCT
- N=115
- Remimazolam, Remimazolam+Flumazenil, Propofol
- Similar induction time
- Similar recovery between Propofol and Remimazolam+Flumazenil (12 min)
- Less hypotension with Remimazolam (32 vs 68%)
- Less ephedrine and phenylephrine
- Less injection pain

Journal of gastroenterology and hepatology, 2021

### Effect of Remimazolam Tosilate on Early Cognitive Function in Elderly Patients undergoing Upper Gastrointestinal Endoscopy

Tan Yingjie, Ouyang Wen, Tang Yongzhong, Fang Ning, Fang Chao, Quan Chengxuan

First published: 14 December 2021 | <https://doi-org.ezp-prod1.hul.harvard.edu/10.1111/jgh.15761>

- 100 mcg/kg Remimazolam compared to 1-1.5 mg/kg propofol
- No difference in cognitive testing 5 minute post recovery
- Less hypotension (3% versus 48%)
- Average age 66
- Same average recovery 4 minutes

### Psychomotor Recovery Following Remimazolam Induced Sedation and the Effectiveness of Flumazenil as an Antidote

Xia Chen, Clinical Therapeutics 2020

- 87 healthy Chinese
- Phase 1a and 1b trial
- Double blind randomized- midaz vs remi
- 2 hr infusions (BIS 40-60)
- subjects fully alert median 3.5 min after injection of flumazenil, compared with 35 min after

#### Memory Storage Affected

Xia Chen. Clinical Therapeutics 2020

- 20 min verbal word learning test
- Normal responses at 1.5-2 hrs post consciousness
- Diminished word recall at 4 hrs post
- No difference in recall with flumazenil

#### Dosing and Lablling Worldwide

- Europe, USA and China: procedural sedation
  - 5 mg IV bolus over 1 min and then 2.5 mg bolus rescue In Japan and
- South Korea: general anesthesia
  - infusion rate for induction of 12 mg/kg/hour (adjustable)
  - 1 – 2 mg/kg/hour, maintenance

When you're curious, you  
find lots of interesting  
things to do  
- **Walt Disney**





# Needle Free Procedural Sedative Techniques in Pediatric Patients

Jurgen C. de Graaff

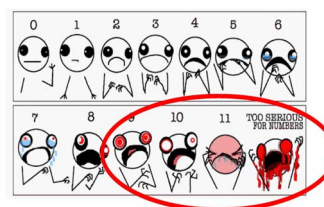
Department of Paediatric Anesthesia, Erasmus MC University Medical Center Rotterdam, Netherlands

## The main goals of safe pediatric PSA

- to reduce and minimize the child's **fear and anxiety**
- to reduce **discomfort and pain** connected with procedures
- to minimize **psychological trauma** (which may include amnesia)
- to control the child's **behavior and movement** for safe and successful completion of the procedure
- to protect the child's **safety during** the procedure and afterwards
- to ensure **safe discharge** from care

Zielinska Ped Anesth 2022; 29:583-590.

## Why needle free?



## Needle free? = non-invasive?

- No pain at application medication:
  - Intravenous
  - Intra muscular medication
- No use of invasive airway
  - Supraglottic airway devices: laryngeal mask of guedell/mayo
  - Tube

## Needle free methods

- Non-pharmaceutical
- Pharmaceutical methods

## Non-pharmaceutical interventions

Bray et al. Insights into Imaging (2022) 13:146  
https://doi.org/10.1186/s13244-022-01278-5

Insights into Imaging

CRITICAL REVIEW

Open Access

Interventions and methods to prepare, educate or familiarise children and young people for radiological procedures: a scoping review

Lucy Bray<sup>1</sup>, Lisa Booth<sup>2</sup>, Victoria Gray<sup>3</sup>, Michelle Maden<sup>4</sup>, Jill Thompson<sup>5</sup> and Holly Saron<sup>1</sup>

## Non-invasive interventions

- **Information**  
Prepare, educate or familiarize children
- **Distraction**

## Non-invasive interventions

- Information

Prepare, educate or familiarize children

- **Information:** video, colour book, photo-diary booklet, story-book, meet staff and environment
- **Technology:** Music, Smartphone applications, Interactive videos, Animations, Virtual reality

- **Distraction**



Hoxhallari, Plastic and reconstructive Surgery 201

Felemban BMC Oral Health 2021

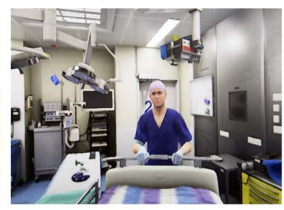
## Non-invasive interventions

- Information

Prepare, educate or familiarize children

- Information: video, colour book, photo-diary booklet, story-book, meet staff and environment
- Technology: Music, Smartphone applications, Interactive videos, Animations, Virtual reality: **preparation**

- **Distraction**



Eijlers Eur J Anaesthesiol 2019

## SYSTEMATIC REVIEW

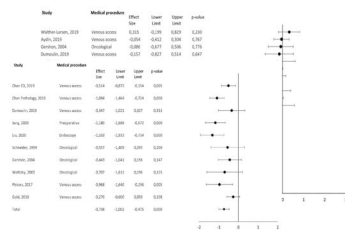
Pediatric Anesthesia WILEY

## Virtual reality in pediatrics, effects on pain and anxiety: A systematic review and meta-analysis update

Floris Q. Tas<sup>\*</sup> | Cynthia A. M. van Eijk<sup>\*</sup> | Lonneke M. Staals | Jeroen S. Legerstee  
Bram Dierckx

## Reduction on

- Pain +
- Anxiety +



## Non-invasive interventions

- Information

Prepare, educate or familiarize children

- **Information:** video, colour book, photo-diary booklet, story-book, meet staff and environment
- **Technology:** Music, Smartphone applications, Interactive videos, Animations, Virtual reality

- **Distraction**



- Facilitate play
- Provision of information: play specialists/child life specialists, nurse, paediatrician, medical social worker, volunteers, child life specialist etc.
- Opportunities to practice: Mock scanner
- **Feed and Swaddle < 6 months**

### Definitions of drug-induced sedation

- **Minimal sedation** calming of the child and reduction of fear during which the patient is conscious and responds normally
- **Moderate sedation** depression of consciousness during which the patient is sleepy but responds purposefully to verbal commands or light tactile stimulation
- **Deep sedation** depression of consciousness during which the patient is asleep and cannot be easily roused but does respond to repeated or painful stimulation (may require assistance to maintain a patent airway and spontaneous ventilation)
- **General anesthesia**

Needle free sedation:

- **Minimal sedation** calming of the child and reduction of fear during which the patient is conscious and responds normally
- **Moderate sedation** depression of consciousness during which the patient is sleepy but responds purposefully to verbal commands or light tactile stimulation
- **Deep sedation** depression of consciousness during which the patient is asleep and cannot be easily roused but does respond to repeated or painful stimulation (may require assistance to maintain a patent airway and spontaneous ventilation)
- **General anesthesia**

## SPECIAL INTEREST ARTICLE

WILEY Pediatric Anesthesia

# Safe pediatric procedural sedation and analgesia by anesthesiologists for elective procedures: A clinical practice statement from the European Society for Paediatric Anaesthesiology

Marzena Zielinska<sup>1</sup> | Alicja Bartkowska-Sniatkowska<sup>2</sup> | Karin Becke<sup>3</sup> |  
Claudia Höhne<sup>4</sup> | Nadia Najafi<sup>5</sup> | Eva Schaffrath<sup>6</sup> | Dusica Simic<sup>7</sup> | Maria Vittinghoff<sup>8</sup> |  
Francis Veyckemans<sup>9</sup> | Neil Morton<sup>10</sup>

Zielinska Ped Anesth 2019;29:583–590

Purpose sedation: Assess requirements?

- Cooperation
- Reduced awareness
- Lack of movement
- Duration
- Analgesia
- Anxiolysis
- Fear reduction
- Movement
- Required depth
- Emergence
- Location

Zielinska *Ped Anesth* 2019;29:583–590

## Assessment for PSA

- Medical status and past medical history
- Current comorbidities and surgical problems
- Psychological and developmental status
- Past sedation and anesthesia history including family history
- Current and previous medication, nutraceuticals
- Allergies
- Age, weight, and height
- Focused examination of: airways, lungs and heart
- Increased risk for complications: **Airway!**
- Urgency of the procedure
- Fasting status; elective

6h: solid meal  
4h: milk/light meal  
3h: breast milk  
1h (0?): clear liquids

(not for minimal sedation: level 1)

Zielinska Ped Anesth 2019;29:583-590  
Eur J Anaesthesiol 2022; 39:4-25

## Consult specialist!

- Increased intracranial pressure
- Risk of aspiration: esophageal disease, polyhandicap, duration of fasting for solids and liquids
- Difficult airway due to anatomical or functional problems! (hypotonia, obstructive sleep apnea?)
- Respiratory compromise
- ASA-PS III or greater
- Young age, especially infants (birth to age 1 year)
- Severe anxiety
- Autism spectrum disorder
- Developmental delay

Zielinska Ped Anesth 2019;29:583-590

## Preparation

### Information and consent

- Patient and parents
- Risks
- Benefits
- Alternatives

### Psychological preparation

- Developmental stage
- Expectations from parents

## Requirements healthcare professionals:

### Knowledge & skills

- Pediatric PSA drug pharmacology
- Assessment of children
- Monitoring of children
- Recovery care of children!
- Pediatric PSA complications:
  - advanced pediatric life support
  - **airway management**

### Practical

- Effectively delivering PSA technique
- Using, interpreting, and responding to monitoring equipment
- Managing its complications
- Observing clinical signs in children
  - airway patency, breathing rate and depth, pulse, pallor and cyanosis, and depth of sedation
- Using, interpreting, and responding to monitoring equipment

## Facilities and equipment

- Pulse-oximeter
- ECG
- NIBP
- Oxygen supply and delivery equipment
- Capnography

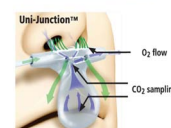
- Oral or nasopharyngeal airway
- Face masks and other suitable supraglottic airway devices
- Bag with self-inflating reservoir
- Endotracheal tubes & laryngeal masks
- Laryngoscope

### Suction device!

- Emergency medication
  - atropine, epinephrine, dopamine, flumazenil, naloxone, muscle relaxant, neostigmine, local anesthetics, sugammadex, calcium, glucose 10%, balanced electrolyte solution
- Intravenous catheters/lines/infusion pumps
- Thermometer/active warming system
- **Easily available:** blood gas analysis, blood glucose measurements, intraosseous needles and defibrillator

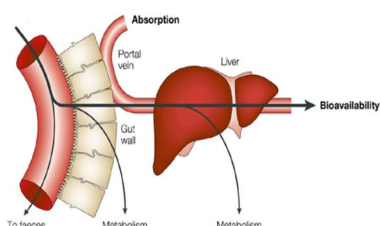
## Monitoring and documentation

Moderate sedation	Deep sedation
Pulse oximetry	Pulse oximetry
Heart rate	Heart rate
Respiratory rate	ECG
Strongly recommended:	Respiratory rate
ECG	Blood pressure
End-tidal carbon dioxide/ capnography	End-tidal carbon dioxide/ capnography



## Needle free pharmaceutical methods : Routes of application

- Oral & rectal: bioavailability: 0-100%
  - Non-invasive?



## Needle free pharmaceutical methods : Routes of application

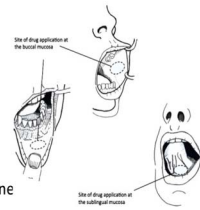
- Oral & rectal
- Nasal
  - Atomizer
  - Max: 0,3 ml per dose !!!





## Needle free pharmaceutical methods : Routes of application

- Oral & rectal
- Nasal
- Buccal: swallow!
- Inhalation: nitrous oxide
- Transdermal
  - Topical anesthesia for lacerations: lidocaine, adrenaline
  - Tissue adhesive for laceration repair: dermabond



## Chloral hydrate (CH)

- Discovered in 1832, administered to children since 1869
- Most widely used: imaging studies
- Dose & onset time & duration of action
  - Oral & rectal: good absorption!
  - 50-100 mg/kg; 30-60 min; 2-8 h & 24 h
  - Elimination half-life:
    - Children: 4-12 h
    - Infants: 28 h
    - Preterm: 37h
- Side effects: oxygen desaturation
- Adverse event:
  - Case reports serious respiratory depression!
  - Significant morbidity and even death following procedural sedation
  - In patients with significant respiratory illness!
- Anesthesiologists: Do not use!
- Safe and short-acting alternatives



## Midazolam

- Oral, nasal, buccal, rectal
- 0.25, 0.5, 0.75, or 1 mg/kg
- Onset time: 10-45 min
- Duration of action: 45-60 min
- Eliciting paradoxical reactions:
  - dysphoria, inconsolable violent crying, agitations, struggling needing restraint, disorientation, restlessness: 1-5%
- Non-responders, despite adequate plasma concentrations
- pH: 3.5! Acid and irritating!
  - => Ozalin/ADV6209: wild orange & sucrose registered 2018 EU 6 – 17 yrs; 0,25 mg/kg



Williamson Drugs &amp; Therapy Persp 2019

## (Es-)Ketamine

- Bioactivity & dose:
  - Oral: 20%,
  - Rectal: 25%
  - Nasal: 50%; 0.5-2.0 - 5 mg/kg
- Analgesic!
- Side effects:
  - oxygen desaturation (90%)
- Adverse events: Hypersalivation, bradycardia, drowsiness, dysphoria/dissociation, unpleasant taste, dizziness, nausea/vomiting, vision changes, laryngospasm: 0.3%, apnea: 0.8%

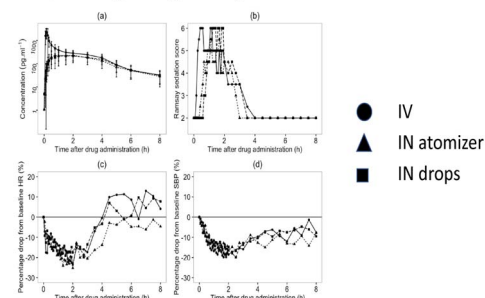
Green Ann Emerg Med 2009  
Alanazi Am J Emerg med 2022

## Dexmedetomidine

- Alpha 2 receptor agonist
- Bioactivity & dose & onset – duration time:
  - Oral: 16%
  - Buccal: 82%; 1-3 µg/kg; 20-40 min
  - Nasal: 65%; 1-3 µg/kg; 20-40 min
- Side effects
  - Bradycardia, desaturation,
  - Anticholinergic reactions
  - Easily wake up
- Contraindications: digoxin, beta blockers, amiodarone, calcium channel blockers or other medications predispose bradycardia or hypotension



## Pharmacokinetic and pharmacodynamic study of intranasal and intravenous dexmedetomidine

British Journal of Anaesthesia,  
120 (5): 960-968 (2018)A. Li<sup>1,2,3</sup>, V. M. Yuen<sup>2,3,4</sup>, S. Goulay-Dufay<sup>1,3,5</sup>, Y. Sheng<sup>3,5</sup>, J. F. Standing<sup>3,6</sup>,  
P. C. L. Kwok<sup>3,6</sup>, M. K. M. Leung<sup>3</sup>, A. S. Leung<sup>3</sup>, I. C. K. Wong<sup>3,10</sup> and M. G. Irwin<sup>2</sup>

## Nitrous oxide

- Inhalation anesthetic: “laughing gas,”
- Discovered in 1772, first used in 1884 for dental extractions

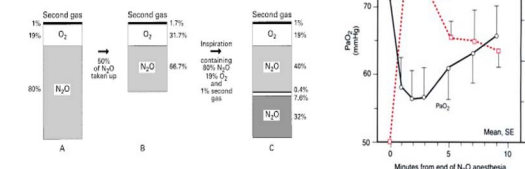


## Nitrous oxide

- Inhalation anesthetic: “laughing gas,”
- Discovered in 1772, first used in 1884 for dental extractions
- Concentration effect => diffusion hypoxia!

## Concentration effect (second gas effect) Diffusion hypoxia = Fink effect

Minimum: 30% oxygen & 70% N<sub>2</sub>O  
Entonox: 50% oxygen & 50% N<sub>2</sub>O



## Nitrous oxide

- Inhalation anesthetic: "laughing gas,"
- Second gas effect: diffusion hypoxia!
- Popular
  - pediatric dentists
  - Emergency room: fractures
- Success dependent on: temperament
- Lower success: mental disabilities
- Adverse events: vomiting!



## Painful procedures in emergency room

- Distraction: telephone app / video/VR
- Inhalation Nitrous oxide
- (Es) ketamine: intranasal



## Radiologic procedures

- Distraction & education:
  - mock scanner: > 6 – 9 yrs
  - Feed and swaddle: < 6 months



### ORIGINAL ARTICLE

#### Experience with a "Feed and Swaddle" program in infants up to six months of age

Leah B. Templeton<sup>1</sup> | Michael J. Norton<sup>1</sup> | Eduardo J. Goenaga-Diaz<sup>2</sup> | Douglas H. McLaughlin<sup>1</sup> | Michael E. Zapadka<sup>2</sup> | T. Wesley Templeton<sup>1</sup>



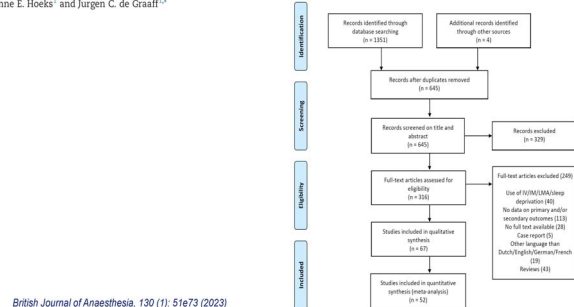
	% Overall	Median ASA status	Median day of life at time of scan (Range)	Median weight kg (Range)	Mean length of scan (min)	Non-contrast	Contrast	Outpatient	Inpatient
<60 (n = 124)	91.1% (84.8%-95.0%)	3	30 (1-68)	4.0 (2.0-4.4)	39 ± 22	89.1% (82/92)	96.9% (92/95)	93.8% (90/95)	90.2% (85/95)
Diagnostic (95% CI)									
Nondiagnostic	8.9% (1.1-24)	3	53 (3-67)	4.6 (3.2-5.6)	52 ± 23	10.9% (10/92)	3.1% (3/95)	6.2% (6/95)	9.8% (9/92)
>60 (n = 40)	95.0% (88.4%-98.6%)	2	158 (90-174)	6.3 (4.1-9.5)	36 ± 20	96.8% (28/29)	90.9% (30/33)	92.3% (32/35)	96.3% (26/27)
Diagnostic (95% CI)									
Nondiagnostic	5.0% (2-10)	2	153 (124-179)	6.1 (4.9-7.3)	57 ± 45	3.4% (1/29)	9.3% (1/11)	7.7% (1/13)	3.7% (1/27)

< 6 Months

Acta Anaesthesiol Scand. 2020; 64:63-68.

#### Needle-free pharmacological sedation techniques in paediatric patients for imaging procedures: a systematic review and meta-analysis

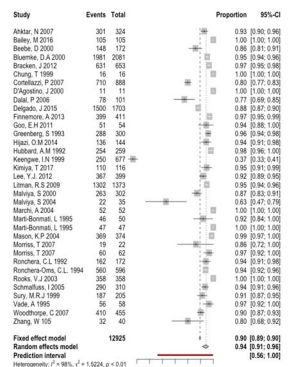
Ingeborg de Rovere<sup>1,2</sup>, Jasper Willeman<sup>1,3,4</sup>, Jaap J. Dogger<sup>1</sup>, Wichor M. Bramer<sup>2</sup>, Sanne E. Hoeks<sup>1</sup> and Jurgen C. de Graaf<sup>1,2</sup>



British Journal of Anaesthesia, 130 (1): 51e73 (2023)

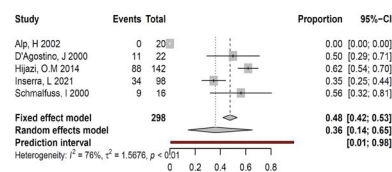
## Choral hydrate

- pooled proportion of success of 0.94 (95% CI, 0.91-0.96)

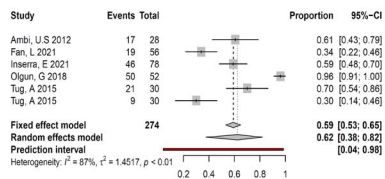


## Midazolam oral/IN/rectal

- Pooled proportion of success of 0.36 (95% CI, 0.14-0.65)
- Onset time was 53±41 minutes,
- Sedation lasted 59-76 minutes.
- Recovery time was reported as 113±48 minutes.

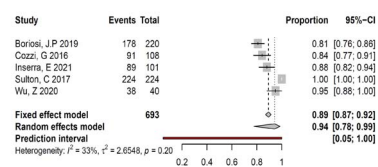


## Dexmedetomidine IN: 2-4 µg/kg



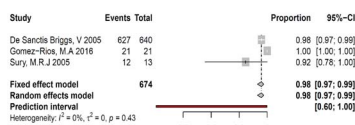
- Pooled proportion of success of 0.62 (95% CI, 0.38-0.82)
- >20% decrease in baseline heart rate
- 10% experienced bradycardia
- 3% oxygen desaturation.

## Dexmedetomidine: 3µg/kg &amp; midazolam: 0.3mg/kg



- Pooled proportion of success: 0.94% (95% CI, 0.78-0.99)
  - Onset time: 9-39 min.
  - Sedation duration: 58-118 min.
  - Recovery time: 61-91 min.
  - Nausea and vomiting 2-5%
  - Bradycardia in 6-8%
- Hypotension: 3%  
Oxygen desaturation: 3-5%

## Sevoflurane



- Pooled proportion of success of 0.98 (95% CI, 0.97-0.99)
- 1 MAC sevoflurane = anesthesia
- No proper airway management => not Safe  
Do not use!



## Conclusion Radiologic procedures

- Distraction & education: mock scanner & feed and swaddle
- Intranasal:
  - Dexmedetomidine 3µg/kg & midazolam 0.3 mg/kg
- IV contrast!
  - Selection of patients
- Parents love it!
- General anesthesia easier  
faster and 100% succes ☺



## Conclusion:

- Adequate medication
  - Adequate dose
  - Route of application
  - Parents compliance!
  - Full examination: airway
  - Airway skills
  - Adequate monitoring
  - Adequate recovery facilities
  - Adequate time
- Painful procedures
    - Nitrous oxide
    - IN: Esketamine 0.5-2mg/kg
  - Radiologic procedures
    - < 6 months: feed & swaddle
    - > 6 – 9 yrs: mock scanner
    - Other ages
      - IN: Dexmedetomidine 3µg/kg & midazolam 0.3 mg/kg
      - (Sevoflurane + IV + LMA)

## ESPA CONGRESS

13<sup>th</sup> European Congress for Paediatric Anaesthesiology

September 28–30, 2023  
Prague, Czech Republic  
[www.espacongress.com](http://www.espacongress.com) | [www.euroespa.com](http://www.euroespa.com)

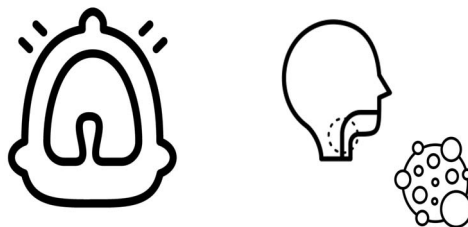




# How to Deal with Challenging Sedation Cases

Eun-Young Joo

Asan Medical Center, Korea



## CASE 1

- 15/M
- 166.5cm/50.4kg
- EEG for Epilepsy
- Known Autism
- No snoring or history of sleep apnea
- Recurrent Hx. of failed sedation
- PR 98 SpO<sub>2</sub> 100% on Room air

- VIMA with Sevoflurane, accompanying security agents
- IM Dexmedetomidine 150mcg
- Total sedation time: 120 min
- Discharge without complication

## CASE 2

- 10/M
- 124.3cm/23.5kg
- Whole body MRI for Neurofibromatosis
- s/p C2-6 Laminoplastic laminotomy
- Severe Craniovertebral and C4-5 kyphoscoliosis
- No snoring or history of sleep apnea
- 126/69 PR 48 SpO<sub>2</sub> 96% on Room air
- Airway exam : Severely limited neck extension

- IV Dexmedetomidine 1.5mcg/kg loading for 10min
- IV Dexmedetomidine 1.5mcg/kg/hr continuous infusion
- O<sub>2</sub> 4L/min by Oxymask
- BP, SpO<sub>2</sub>, ETCO<sub>2</sub> monitoring
- Total scan time: 70 min
- PACU time: 20 min
- Discharge without complication

### CASE 3

- 5/F
- 94cm/12.7kg
- Heart CT for FSV
- FSV s/p BCS
- OSAS considering CPAP
- Hx. of intubation failure d/t Trismus
- 99/63-84-28-82% on Room air
- Airway exam : mouth opening 1FB, retrognathia

- IV Propofol 12mg ivs
- Oral airway insertion → I-gel # 1.5 change
- BP, SpO<sub>2</sub>, ETCO<sub>2</sub> monitoring
- Total scan time: 15min
- PACU time: 35 min (I-gel removal after 7 min of arrival)
- Discharge without complication

### CASE 4

- 5/F
- 112.7cm/15.6kg
- Face MRI for Lymphangioma
- Being able to sleep only in a right-side lying position
- Hx. of failure of sedation d/t airway obstruction
- 122/82-101-24-98% on Room air
- Airway exam : Stridor (+), Mallampati's class IV

- IV Propofol 30mg + succinylcholine 30mg
- Intubation using Video laryngoscope with e-tube #4.5
- Maintenance : Sevoflurane + IV rocuronium 20mg
- BP, SpO<sub>2</sub>, ETCO<sub>2</sub> monitoring
- Total scan time: 55 min
- Extubation at PICU (after 1hr of arrival)
- Discharge without complication

## CASE 5

- 9/M
- 130cm/25kg
- Brain MRI for Brain abscess
- DORV, PA s/p BCS, s/p One and a half repair
- Lt. main bronchus stenosis
- SVC syndrome d/t BCS stenosis
- HF induced Protein losing enteropathy
- Home vent: Nasal iVAPS mode (EPAP 6cmH2O, O2 1L/min)
- 89/56-101-27-85%

- Hx. of Apnea after sedation during Heart CT
- Performing Brain MRI without sedation
- Using Inroom Viewing Device
- Minimizing scanning time: about 15min
- Using Home vent with extended, non-magnetic device





# NORA for Children with Special Needs

Ina Ismiarti Binti Shariffuddin

Department of Anaesthesiology, University Malaya, Malaysia

## OUTLINE

- NORA -What is it?
- Who are "children with special needs"?
- Concerns of anaesthesia
- Peri-procedural Management
- Conclusion



## NORA: NON OPERATIVE ROOM ANAESTHESIA

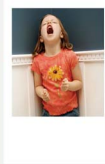
- Non-operating room anaesthesia(NORA) is the **provision of anaesthesia and sedation outside the operating theatre.**
- Common procedures done in remote locations include:
  - Radiology procedures: (MRI, CT scan & interventional radiography).
  - Oncology (radiotherapy, bone marrow aspiration and/or intrathecal injections).
  - Endoscopy
  - Radiotherapy and chemotherapy



## CHILDREN WITH SPECIAL NEEDS

For the purpose of this talk, this term encompasses children with:

- learning disability (IQ<70)
- language and communication disorder
- Any disability that prevents a child from coping well with new experiences.



Judith Alison Shore, MD, CP FRCPA, Anaesthesia for children with special needs, including autistic spectrum disorder, Continuing Education in Anaesthesia Critical Care & Pain, Volume 13, Issue 4, August 2013, Pages 107-112.

## INCIDENCE

- Intellectual and developmental disabilities (IDD) in children affect **5.5% to 9.7 %** of the population in the world.
- In Malaysia, intellectual and developmental disabilities (IDD) affect **34.8% of children with disabilities** in Malaysia.

1. Altunac M, Saroha E. Lifetime prevalence of learning disability among US children. *Pediatrics*. 2007;119 Suppl 1:S77-83.  
2. Ying K, et al. Health-Related Quality of Life and Family Functioning of Primary Caregivers of Children with Cerebral Palsy in Malaysia. *International Journal of Environmental Research and Public Health*. 2021;18(5):2351.

## CHILDREN WITH LD

- is more prevalent in the Asian community.
- There is a slight male preponderance. (1.3-1)

**Robust physical health**  
-Autism

**Congenital abnormalities or syndrome**  
-Down syndrome  
-Cerebral palsy



Gillberg C, Soderstrom H. Learning disability. *Lancet* 2003;362: 811-821.

## ANAESTHESIA CONCERNS

Patient



Environment



Personnel



## CHALLENGES IN PATIENTS WITH SPECIAL NEEDS



- Polypharmacy
  - On stimulants and anti-psychotics.
  - Ritalin & Olanzapine
- Psycho-social challenge:
  - They may be very anxious
  - They may have **difficulty conforming** to the usual pattern of hospital care.

"Hospital attendance is often stressful".

## ANAESTHESIA CONCERNS

### Patient

- Frequently associated with multiple co-morbidities that necessitates diagnostic imaging or therapeutic procedures
- Patients are often admitted as day case.

Table 4  
Coexisting medical problems in learning disability

Condition	Frequency
Epilepsy	Up to 44% (42)
Psychiatric conditions	Up to 50% (31)
Eating disorders	– (31)
Self harming	– (31)
Attention deficit hyperactivity disorder	18% (32)
Schizophrenia	– (33)
Depression	– (34,35)
Sensory disorders	
Visual impairment	10x greater (36)
Hearing loss	40x greater (36)
Cerebral palsy	Common (5)
Miscellaneous	
Hypothyroidism	– (37)
Gastroesophageal reflux	49% (39)
Malformations – stomach, gall-bladder, esophagus, thyroid, connective tissue	– (38)
Nonischemic cardiac disorders	– (40)
Poor dentition	– (41)

Difficult Airway

COURTMAN, S. P., & MUMBY, D. (2008). Children with learning disabilities. *Pediatric Anaesthesia*, 18(3), 198–207.

## WHO CAN BE TREATED IN NORA (DAY SURGERY SETTING)?

- The child should be well, with **only mild and well controlled comorbidities**.
- Children with relatively complex needs, provided:
  - They are stable with **minimal cardiorespiratory problems**.
  - Do not have features of **difficult airway**.

\*Royal College of Anaesthetists. Guideline for the provision of paediatric anaesthesia services. 2019. <https://www.rcogan.ac.uk/document-store/guidelines-the-provision-of-paediatric-anaesthesia-services-2019>

## ANAESTHESIA CONCERNS

### Environment

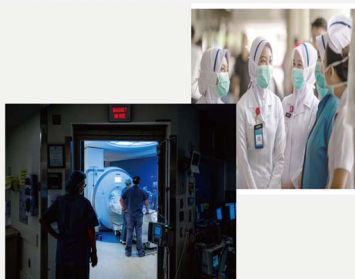
- Limited resuscitative and monitoring facilities.
- Cramped and congested work area.
- Low ambient temperature with risk of hypothermia in small babies.
- Inadequate space, monitoring facilities and trained staff at recovery bay.
- Unfamiliar working environment.



## ANAESTHESIA CONCERNS

### Personnel

- Lack of trained assistance to assist anaesthetist.
- The anaesthetist may not be familiar with the environment or the equipment provided.
- Lack of knowledge/expertise in handling patients with special needs.



## PROBLEMS



Limitation of staff awareness  
Inadequate training of staff about children with learning disability



Lack of suitable equipment & environment

Prolonged waiting times for operation date  
Prolonged waiting on the day of operation  
Lack of private space  
Lack of non-invasive equipment

Teghzadeh et al. Paed Anaesthesia, Vol 29, Issue 9, Sept 2019

## PRE-ADMISSION MANAGEMENT:

Adopt a flexible and holistic approach to care

Coordinate interventions required by multiple specialities

Consider family's & patient's needs

Collect Information over the phone to avoid preoperative admission anxiety

## PRE-OPERATIVE MANAGEMENT:

### Communication between staff and family

- Ensure good communication
  - i. Clear plans & explanations
  - ii. Staff should show empathy

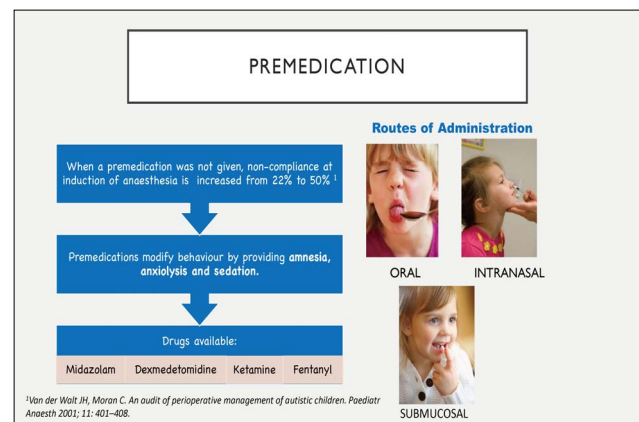
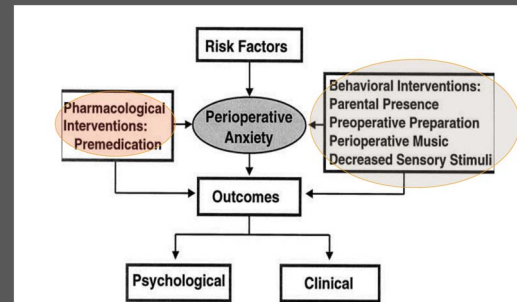
### Individualized care within the hospital framework

- Health providers have to be flexible with standard protocols
  - i. Avoiding unnecessary blood pressure measurements
  - ii. Not changing into hospital gowns.





### ANXIOUS IN UNFAMILIAR ENVIRONMENT



DOSE		
DRUG	DOSE	Duration of action
MIDAZOLAM <sup>1</sup>	Oral 0.5-0.75 mg/kg Max at 15-20 mg IN: not recommended	Onset 10 mins Peak 30 mins
DEXMEDETOMIDINE <sup>2</sup>	IN 2mcg/kg	Onset: 20-30 min
KETAMINE <sup>1</sup>	Oral- 5-6mg/kg Need administration with anticholinergic Atropine 0.02 mg/kg	Onset: 10 mins
FENTANYL <sup>1</sup>	Oral 5-15 mcg/kg PONV	Onset: 10 mins

Pasin L et al. Dexmedetomidine vs midazolam as preanesthetic medication in children: a meta-analysis of randomized controlled trials. Paediatr Anaesth. 2015 May; 25(5):468-76.  
<sup>1</sup>Cole CJ. Preoperative preparation and premedication BJA 1999; 83, 16-28  
<sup>2</sup>Yuen et al.

Anaesthesia 2012, 67, 1210-1216 doi:10.1111/j.1365-2044.2012.07309.x

### Original Article

#### A randomised comparison of two intranasal dexmedetomidine doses for premedication in children

V. M. Yuen,<sup>1</sup> T. W. Hui,<sup>1</sup> M. G. Irwin,<sup>2</sup> T. J. Yao,<sup>3</sup> L. Chan,<sup>4</sup> G. L. Wong,<sup>5</sup> M. Shahnaz Hasan<sup>6</sup> and I. I. Shariffuddin<sup>6</sup>

#### Conclusion:

- In children aged 1-4 years: IN DEX in doses of 1 and 2mcg/kg produced a similarly high rate of satisfactory sedation.
- In children aged 5-8 years, **IN DEX 2mcg/kg** was associated with a higher proportion of satisfactory sedation than 1mcg/kg without causing adverse haemodynamic effects

### ANAESTHESIA

Anaesthesia drugs used will be determined by any co-existing morbidity.

Minimize postoperative nausea and vomiting:

- Administer antiemetic agent
- Adequate hydration with isotonic crystalloid fluid bolus.

### ANALGESIA

- Simple analgesics should be adequate.
- Be aware of sensitivity of certain syndromes with opioids.



## EMERGENCE DELIRIUM

- ED may have a correlation with preoperative anxiety.
- The odds of experiencing emergence delirium might increase with the increased in pre-operative anxiety.
- Children with special needs may be super anxious.
- Treatment: mainly pharmacological

## Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment

S. Nair<sup>1,\*</sup> and A. Wolf<sup>2</sup>

BJA Education, 18(1): 30–33 (2018)

doi: 10.1016/j.bjae.2017.07.001

Table 4 Drugs used to prevent ED

Agent	Route/time of administration
Propofol	I.V. TIVA/end of surgery
Midazolam	P.O./i.v. at end of surgery
Clonidine	P.O. (preoperative)/i.v. (intra-/postoperative)
Dexmedetomidine	I.V. pre-/intraoperative
Fentanyl	I.V./intra-nasal intraoperative
Gabapentin	P.O./preoperative
Magnesium infusion	I.V./intraoperative
Dexamethasone	I.V./preoperative
Ketamine	Intra-nasal preoperative/i.v./intrathecal

IV 0.3 mcg/kg of DEX at the end of surgery reduces the incidence of ED from 47% to 5%. DEX has been shown to be superior to a propofol bolus of 1 mg/kg at the end of surgery.

## RECOVERY

- May become agitated on regaining consciousness due to anxiety, pain or nausea which may be hard to diagnose.
- The caregiver should be brought to the child early to allay any fears and assist with communication.
- All fluid and drug administration should be completed promptly in recovery.
- Early removal of the IV cannula
- Should be discharge to their normal home environment as soon as possible.



## CONCLUSION

Careful selection of patients for NORA is very important to ensure benefits for these children.

Children with special needs require a multidisciplinary approach to ensure optimal care.

Awareness and understanding of their special requirements is essential when devising a management plan.

Identifying barriers to care can help guide improvement in the care of these children.

# Neonatal Sedation for MRI

Yu Cui

Chengdu Women and Children's Central Hospital, China

## Disclosure

None

## Chengdu Women's and Children's Central Hospital



## The numbers of patients in 2021

Outpatients	Inpatients	Total
8,616	14,524	23,141

Among them, lung function (6,362) · CT (1,989) · Echo (4,745) · MRI (5,027) · Hearing screening (3,931) · others (1,087)

411 neonates underwent MRI sedation

## The numbers of patients in 2022

Outpatients	Inpatients	Total
11,870	6,879	18,749

Among them, lung function (5,334) · CT(1449) · Echo (3,559) · MRI(4,792) · Hearing screening (2,594) · others (1,021)

429 neonates underwent MRI sedation

## Contents

- Summary of the latest research in neonatal MRI sedation
- Our own experience in neonatal sedation for MRI from more than 1,000 cases (from 2020.1-2022.4)

**Drugs?**

OR

**Others?**

## A survey from Italian Society of Pediatric and Neonatal Anesthesia (SARNePI)

- 106 institutions met minimal criteria for MRI procedures on pediatric patients
- To NICU neonates, 53 centers performed less than 3 MRI procedures per week, while 12 centers performed more than 3 procedures MRI per week.

Table 5 First choice Sedation technique in NICU centers

Sedation in NICU centers n. 65			
Drug Sedation	Yes n. 43 (66%)	Midazolam n. 9 (21%)	None n. 22 (34%)
	Sevoflurane n. 21 (49%)		
	Thiopental n. 4 (9%)	Multi-drug <sup>a</sup> n. 9 (21%)	
Pharmacological premedication	Yes n. 8 (18%)		None n. 57 (82%)
	Perindolol n. 8 (100%)		
Airway devices	Endotracheal Tube n. 4 (9%)	Laryngeal Mask n. 3 (7%)	External device n. 36 (84%)

<sup>a</sup> Center with no premedication or with use of multiple drugs association (even both volatile and intravenous agents)

Baraglia F, Spinazzola G, Adduci A, et al. Children and neonates anesthesia in magnetic resonance environment in Italy: an active call survey. BMC Anesthesiol. 2022;22(1):279. doi:10.1186/s12871-022-01821-3

## A survey from North American physician members of the Society

- The final results represented 59 institutions from 26 U.S. states, the District of Columbia and three Canadian provinces.
- In neonates undergoing MRI, 46% of respondents reported attempting feed and bundle in all patients, with most (35%) using a single swaddling attempt before sedation.
- Sedation was most often used for neonatal **interventional procedures** (93%).
- More than half of respondents (63%) reported an average success rate of greater than 50% when using neonatal sedation for MRI.

Hwang M, Barton K, Kim JS, et al. Utilization of neonatal sedation and anesthesia: an SPR survey. Pediatr Radiol. 2022;52(13):2630-2635. doi:10.1007/s00247-022-05423-6

## Can we reduce anesthesia exposure? Neonatal brain MRI: Swaddling vs. sedation, a national survey

- This is a national survey of NICUs in the United States with a Neonatology Fellowship Program.
- The questions were as follows, including sedation, GA, and swaddling without medication.

• Sedation (not general anesthesia) is used, what is the primary sedative used for the MRI?  
 • Who is responsible for assessing the patient during the MRI (NRS) (if not applicable)?  
 • Is a different or different brain MRI scan used than general anesthesia is administered (to obtain adequate images before a patient may wake up)?  
 • Is a more profound sedation (not general anesthesia) used when other sedation does not seem to correct a case to general anesthesia (or reintubate a patient to receive general anesthesia)?  
 • How your institution used MRI with only a first and variable technique and decided to use general anesthesia?  
 • Why do you think your institution used general anesthesia for brain MRI versus other methods?  
 • Have you ever in a constant before on any cases you could like to administer on or discuss, (or quantify frequency) which you think you have been able to enter alone?  
 • Why is it important for neonatal MRI patients who they receive MRI? (check all that apply)  
 • What method do you use to keep patient's position?  
 • Is a different or different MRI scan used than when general anesthesia is administered (to obtain adequate images before a patient may wake up)?  
 • If sedation and Swaddling method is used, how often would you estimate an MRI fails to yield an acceptable result?  
 • Is a first and variable method used to yield acceptable images when the MRI is repeated?

Heller BJ, et al. Can we reduce anesthesia exposure? Neonatal brain MRI: Swaddling vs. sedation, a national survey. J Clin Anesth. 2017;38:119-122. doi:10.1016/j.jclinane.2017.01.034

- In the feed and swaddle group, 81% reported that a failure to obtain useful images occurred < 25%; 11% reported that it occurred 25–75%; and 5% reported that it occurred >75%.
- In the drug sedation and GA group, 100% reported failure to obtain useful images occurred rarely.

## Drug sedation

## Midazolam Sedative effect of intranasal midazolam in neonates undergoing MRI

- A total of 70 neonates were randomized into an observation group and a control group, with 35 cases in each group.
- The observation group received intranasal drops of midazolam (0.3 mg/kg), and the control group received intramuscular injection of phenobarbital sodium (10 mg/kg).
- Ramsay sedation scores are as follows.

Group	10min	20min	30min	40min	50min	60min	70min
Phenobarbital	2.8 ± 0.6	3.0 ± 0.6	3.4 ± 0.6	3.4 ± 0.8	3.4 ± 0.8	3.3 ± 0.9	3.2 ± 1.0
Midazolam	3.5 ± 0.8	3.9 ± 0.5	3.7 ± 0.7	3.7 ± 0.8	3.6 ± 0.9	3.5 ± 1.0	3.3 ± 1.1
P values	<0.001	<0.001	0.020	0.206	0.419	0.398	0.735

Wang FH, et al. Sedative effect of intranasal midazolam in neonates undergoing magnetic resonance imaging: a prospective single-blind randomized controlled study. Zhongguo Dang Dai Er Ke Za Zhi. 2020;22(5):441-445.

## Dexmedetomidine Intranasal administration is an alternative route explored.

53 neonates (at ≤32 weeks of gestation or with a birth weight of ≤1500 g)

The historical midazolam group received sedation with boluses of intranasal (0.1-0.2 mg/kg) or intravenous (0.05-0.1 mg/kg) midazolam.

The dexmedetomidine sedation group received a single dose of intranasal dexmedetomidine 3ug/kg, with intranasal or intravenous midazolam as rescue therapy.

The report shows that dexmedetomidine spares the use of midazolam in preterm neonates undergoing MRI at term equivalent age.

Bua J, et al. Intranasal dexmedetomidine, as midazolam-sparing drug, for MRI in preterm neonates. Paediatr Anaesth. 2018;28(8):747-748.

## Sevoflurane

### Advantages

A sevoflurane concentration of approximately 1.5–2% can provide a success rate of 97.9%.

### Disadvantages

0.4% severe airway-related adverse events, and 0.2% had severe respiratory apnea.

De Sanctis Briggs V. Magnetic resonance imaging under sedation in newborns and infants: a study of 640 cases using sevoflurane. Paediatr Anaesth. 2005;15(1):9-15.  
 Lei H, et al. Serious airway-related adverse events with sevoflurane anesthesia via facemask for magnetic resonance imaging in 7129 pediatric patients: A retrospective study. Paediatr Anaesth. 2019;29(6):635-639



**A solution based on melatonin, tryptophan, and vitamin B6 can be used for newborns during brain MRI**

Thirty minutes before MRI assessment, they administered Melamil Tripto® oral solution, Humana Italia S.p.A, Milan, Italy

Regardless of body weight.

1 mg of melatonin	20mg of tryptophan	1.4 mg of vitamin B6
0.5ml		

**Table 3** Effect of melatonin administration during MRI performing and patient evaluation after MRI

	2 mg (32)	3 mg (72)	4 mg (52)	p-value
Quality of MRI				
Positive (patient, %)	26 (81.2%)	67 (92.9%)	5 (100%)	
Difficult (patient, %)	6 (17.8%)	2 (2.7%)	0 (0%)	
Negative (patient, %)	0 (0%)	3 (4.3%)	0 (0%)	0.04
Waking state after MRI				
Awake, tends to fall asleep	10 (31.2%)	16 (22.2%)	0 (0%)	
Awake if stimulated	3 (9.3%)	7 (9.7%)	0 (0%)	
Awake	19 (59.5%)	49 (68%)	5 (100%)	0.0

Picone S, et al. A solution based on melatonin, tryptophan, and vitamin B6 (Melamil Tripto®) for sedation in newborns during brain MRI. Ital J Pediatr. 2019;45(1):122.

一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新

# Non-drug sedation


一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新

**Cardiovascular MRI using a feed-and-sleep technique in neonates and infants**

- Case-series study
- The infant has been fasted for a period of 4 h prior to the scan.
- Fed just prior to the procedure.
- The infant is swaddled with one or two sheets before being placed within a vacuum immobilizer.

**Conclusion**

- Using this technique, infants younger than 6 months can complete a cardiovascular MRI without the need for sedation or general anesthesia




**Fig. 1** Photo of an infant swaddled in a MedVac bag prior to being placed in the scanner

Windram J, et al. Cardiovascular MRI without sedation or general anesthesia using a feed-and-sleep technique in neonates and infants. Pediatr Radiol. 2012;42(2):183-187.

一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新

**Application of vacuum stretcher combined with feeding in cranial magnetic resonance imaging examination for neonates**

- Neonates with a gestational age of >34 weeks underwent MRI
- The neonates were randomly divided into a vacuum stretcher combined with feeding group and a conventional sedation group(10% chloral hydrate 0.5mg/kg)



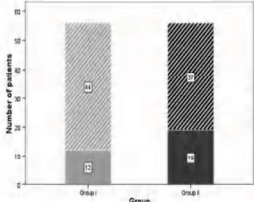
	10% chloral hydrate (n=40)	Vacuum stretcher combined with feeding (n=40)	P value
Successful	30	37	0.034
Interrupt during procedures	3	8	0.105
MRI duration	6.0(6.0, 25.8)	6.0(6.0, 6.8)	0.493

Shen XX, et al. Zhongguo Dang Dai Er Ke Za Zhi. 2020;22(5):435-440.

一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新

**Oral 30% glucose provides sufficient sedation in newborns during MRI**

- Group 1: 0.5-3 ml 30% glucose orally
- Group 2: 0.1 mg/kg midazolam



**Fig. 1** Comparing the efficacy of the techniques according to the number of patients for groups

Eker HE, et al. Oral 30% glucose provides sufficient sedation in newborns during MRI. J Anesth. 2017;31(2):206-211.

一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新


# Our own experience

一切为了妇女儿童健康 海纳百川 厚积薄发 永攀创新

**Choice 1: Non-drug techniques**

**Sleep deprivation**

About 20% neonates could be successfully sedated by non-drug techniques during MRI.



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**Choice 2: Chloral Hydrate**

1148 neonates were retrospectively analyzed

2019.12 to 2022.12

Characteristics	Values
Males[n(%)]	697 (60.7)
Birth days, days	11.0 (6.0, 16.0)
Weight, kg	3.3(3.0, 3.7)
Source[n(%)]	
Outpatients	211 (18.4)
Inpatients	937 (81.6)
Sedation history[n(%)]	104 (9.0)
Procedures[n(%)]	
MRI	998 (86.9)
MRI and Auditory brainstem response (ABR)	148 (12.9)
MRI and Echo	1 (0.1)
MRI and Hearing screen	1 (0.1)
Route[n(%)]	
Oral	1035 (90.2)
Intranasal	64 (5.6)
Gastric tube	31 (2.7)
Rectal	18 (1.6)

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	Numbers (n=1148)
Initial dose of chloral hydrate, mg/kg	49.4 (48.1, 50.0)
Initial success rate, n(%)	91.0%
Complications, n(%)	
Vomiting	65(5.6)
Delayed awakening(>2h)	23(2.0)
Respiratory depression	8(0.7)
Choking	3(0.3)
Severe adverse events	0 (0.0)

### Choice 3: Midazolam

More than 100 neonates were successfully sedated by oral midazolam during MRI.

0.5mg/kg midazolam syrup provides a sedation success rate of 100% for neonates.





## **Session 4.**

# **Perioperative Concerns in Pediatric Anesthesia**

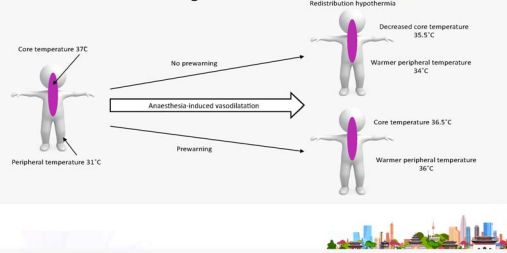
**Chair(s): Tae-Hun Ahn (Korea)**

**Woo Suk Chung (Korea)**





### Effect Of Anesthesia Induced Vasodilation on Core & Peripheral Temperature With & Without Prewarming



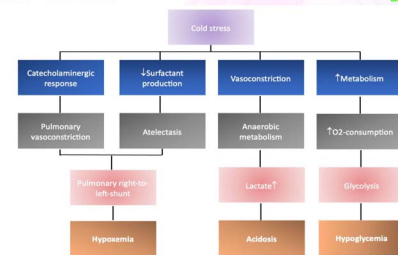
### Pediatric proneness (especially neonate) to perioperative hypothermia:

- Greater heat loss:
  - Regulatory capacity is less effective than in adults
  - Reduced weight-to-surface-area (WSA) ratio
  - Increased heat loss from the head
  - Limited stores of subcutaneous fat for thermal insulation
  - Neonates are have no behavioural regulation.
- Increased basal metabolic rate (compared with adults).
- Effector mechanisms of skeletal muscle stimulation are minimal → heat generation depend on non-shivering thermogenesis
- ELBW neonates have poor vasomotor control at birth (unable to exhibit peripheral vasoconstriction to preserve heat)
- (+) general anaesthesia → lowers the threshold for vasoconstriction and other compensatory mechanisms including NS thermogenesis.
- During surgery: Cold OR, administration of cold fluids, the application of dry anaesthetic gases, and wound exposure.

### ASPA 2023 ADEVERSE EVENT

- Discomfort to morbidity & mortality
- Concern in:
  - pharmacokinetics and pharmacodynamics (essentially muscle relaxants)
  - platelet function, coagulation, and blood loss,
  - cardiovascular & respiratory complications,
  - wound healing and surgical site infections (SSI), and
  - thermal discomfort
- possible consequences: apnoea and need for mechanical ventilation, arrhythmias, increased risk of infections, prolonged length of hospital stay, poor neurologic outcome, death.

### ASPA 2023 PATOPHYSIOLOGY PATHWAY



### ASPA 2023 SOLUTION ?

- RISK FACTOR IDENTIFICATION
- MONITORING
- MANAGEMENT & PREVENTION

### ASPA 2023 RISK FACTOR

- Low body weight
- Prematurity
- major intestinal surgery, invasive procedures
- OR temperature less than 23 °C
- Neonates receiving interventional cardiac procedures
- type & duration of surgery (e.g., major orthopedic surgery)
- Low baseline temperature
- High blood loss & transfusion requirement
- Inadequate core temperature monitoring.

### ASPA 2023 MONITORING

Pre-OP	Intra-OP (General Anaesthesia)	Post-OP
<ul style="list-style-type: none"> <li>Oral, axillary (rectal)</li> <li>(Tympanic)</li> </ul>	Continuous methods: <ul style="list-style-type: none"> <li>Oesophageal</li> <li>Nasopharyngeal</li> <li>Non-invasive methods based on ZHF technology</li> <li>Bladder, rectal</li> </ul>	Serial measurements: <ul style="list-style-type: none"> <li>Oral, axillary (rectal)</li> <li>(Tympanic)</li> <li>Hypothermic patients: Continuous methods, e.g., non-invasive methods based on ZHF technology</li> <li>Intubated patients: see Intra-OP</li> </ul>

### ASPA 2023 Evidence-based Studies on Methods for Preventing Hypothermia

Author(s)	Study Type	Number of Cases	Method	Result
Lars Witt et al. (2013)	Prospective multicenter observational study	130	Intraoperative Hot Air Blown System	Decrease in unwanted hypothermia
Wong et al. (2007)	RCC	103	Preoperative period	Decrease unwanted hypothermia carbon polymer bed reduced blood loss
Leeth et al. (2010)	RCC	105	Postoperative period; hot air blowing system	Body temperature is the same amount of increase in thermal comfort, cost reduction
De Witte et al. (2010)	RCC	26	Preoperative period; carbonfiber blanket body temperature increase	Postoperative period; hot air blown
Hooven (2011)	Cohort	149	Postoperative period; hot air blowing system	An increase in body temperature

## PREVENTION & MANAGEMENT

1. Warming Therapy during Transport
  - Dressed for as long as possible & covered with blankets, (optional) a warming pad
  - Ideally: prewarmed bed, provided with radiant heater or warming mattress.
  - Especially preterm infants & neonates → warmed incubator.
  - Keep incubator plugged in during the surgical procedure
2. Warming before Induction of Anesthesia
  - OR 'warm' enough → In general, a room temperature:
    - 32 °C for neonates
    - 24 °C and 30 °C for infants.
  - start active warming therapy before induction of anesthesia.



3. Warming Therapy during Anesthesia
  - active warming therapy must be continued
  - irrigation solutions should be warmed to body temperature.
4. Infusion Warming
  - warm fluids and blood products with a blood and fluid warmer
  - Concern: length of the infusion tubing
5. Warming Therapy after Anesthesia
  - extubation should not be performed when children are hypothermic.
  - If hypothermic → should be rewarmed during anesthesia & then extubated.
  - Postoperative phase: core temperature should be measured regularly



## CONCLUSION

- Pediatric today still often become hypothermic, due to their vulnerable physiology & insufficient perioperative hypothermia prevention/management.
- A good perioperative prevention strategy must be planned.
- With risk identification, good monitoring and prevention, It is possible to avoid perioperative hypothermia .



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# Emergence Agitation & Long Term Behavioral Consequences

Agnes Ng

KK Women's and Children's Hospital, Singapore

## AGITATION (symptom)

DSM-5 "excessive motor activity associated with a feeling of inner tension.

*Unpleasant state of extreme arousal (stirred up or excited), increase tension and irritability*

Pain, Hunger, Physiological compromise,  
or  
Fear or Anxiety, absence of a primary caregiver or unfamiliar surroundings

## DSM-5

*Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5)*

- A. **Disturbance in attention** (i.e., reduced ability to direct, focus, sustain, and shift attention) and **awareness** (reduced orientation to the environment).
- B. The disturbance develops over a short period of time (usually hours to a few days), **represents an acute change from baseline attention and awareness**, and tends to fluctuate in severity during the course of a day.
- C. An additional **disturbance in cognition** (e.g. memory deficit, disorientation, language, visuospatial ability, or perception).
- D. *The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.*
- E. There is evidence from the history, physical examination or laboratory findings that the disturbance is *a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.*

## Emergence Delirium

Mental disturbance during recovery

- Dissociated state of unconsciousness
- Altered cognitive perception
- Agitated behaviour

## Incidence and Etiology of Postanesthetic Excitement: Clinical Survey James E. Eckenhoﬀ et al Anesthesiology 1961

Excitement: Restlessness, disorientation, crying, moaning or irrational talking,

Delirium: Wild thrashing, shouting and screaming

Incidence 5.3% in 14,436 patients; adults and children (12-13%),

### Contributing factors:

- Age (3-9 yr)
- ASA 1
- Premed: barbiturate and scopolamine premed
- Cyclopropane or ether anesthesia
- Operative procedures associated with pain or emotional stress

## Emergence Delirium

- Has been described with every anaesthetic agent ( especially ether and cyclopropane)
- Decreased markedly with halothane
- Incidence EXPLODED with sevoflurane (& desflurane)

What parents

**Say:** "whatever I did, didn't help....please take him away and give me my child back"

**Describe:** "the devil having jumped into him – he was pitch black"

**Experience:** "fear and insecurity, feelings of powerlessness and guilt

Wells & Rasch Anesth Analg 1999;88:1308-10  
Ringblom Scand J Caring Sci 2022;36:1104-1112

## Emergence Delirium

Generally self limiting

- May result in physical harm to patient & caregiver
- Dislodgement of drains & IV sites
- Pain and bleeding of surgical sites
- Distressing to all

## Why incidence varies?

### PAED Scale

- 1 The child makes eye contact with the caretaker
- 2 The child's action are purposeful
- 3 The child is aware of his surroundings  
(implies consciousness & cognition)
- 4 The child is restless
- 5 The child is in inconsolable  
(reflects psychomotor behaviour & emotion  
e.g. pain or apprehension)

0= extremely  
1= very much  
2= quite a bit  
3= just a little  
4= not at all

0= not at all  
1= just a little  
2= quite a lot  
3= very much  
4= extremely

Anesthesiology 2004; 100:1138-45

© 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

#### Development and Psychometric Evaluation of the Pediatric Anesthesia Emergence Delirium Scale

Nancy Sikich, M.Sc., R.N.,\* Jerrold Lerman, B.A.Sc., M.D., F.R.C.P.C., F.A.N.Z.C.A.T

### Cravero Emergence Agitation scale

Level	Description
1	Obtunded with no response to stimulation
2	Asleep but responsive to movement or stimulation
3	Awake and responsive
4	Crying (>3 minutes)
5	Thrashing behaviour that requires restraint

### Watcha Behavior scale for emergence delirium

Level	Description
1	Calm
2	Crying, but can be consoled
3	Crying, cannot be consoled
4	Agitated and thrashing around

- All three scales correlated reasonably well with each other
- PAED score >12 appears to provide greater sensitivity and specificity than a PAED score ≤10.
- Watcha scale appears to be a practical tool to use and assess ED in the PACU

## Hypoactive Delirium ICU-delirium

Quiet, confused, disorientated, no eye contact  
Minimal movements when awake, non-communicative and do not respond to social interaction

### RESEARCH REPORT

Pediatric Anesthesia WILEY

#### An observational study of hypoactive delirium in the post-anesthesia recovery unit of a pediatric hospital

Paul F. Lee-Archer<sup>1,2,3</sup> | Britta S. von Ungern-Sternberg<sup>4,5,6</sup> | Michael C. Reade<sup>2</sup> | K.C. Law<sup>1</sup> | Deborah Long<sup>3,7</sup>

Pediatric Anesthesia. 2021;31:429-435.

The Cornell Assessment of Pediatric Delirium (CAP-D) was developed as an adaptation and extension of the PAED scale and is a rapid screening tool for pediatric delirium in the hospital setting (Figure 1). The additional items that are included to assess hypoactive delirium are as follows:

1. Does the child communicate needs and wants?
2. Is the child underactive—very little movement while awake?
3. Does it take the child a long time to respond to interactions?

PAED detected 57 cases  
CAP-D 74 cases 1.7%  
57 cases using PAED  
17 (23%) represent cases of hypoactive ED

Significance yet to be explored

#### Clinical Implications

##### What is already known about this topic

- Emergence delirium is a common problem in children recovering from general anesthesia.
- Hypoactive delirium has been well-described in children in the intensive care unit but has not been widely studied in the recovery setting.

##### What this study adds

- Nearly a quarter of all cases of emergence delirium in a single pediatric hospital were found to be hypoactive in nature.
- The Cornell Assessment of Pediatric Delirium is a rapid, easy-to-use tool that is an extension of the Pediatric Assessment of Pediatric Delirium scale. It can detect hyperactive and hypoactive delirium and may be an appropriate measure for use in recovery units.

## Emergence Delirium lead to long term Psychological Harm?



- Higher risk
- Less neurocognitive reserves

## Long term effects of ED

### Maladaptive behaviour

e.g. general anxiety, night-time crying, enuresis, sleeping and eating problems

- 10 point increase of state anxiety scores increases odds by 10% of having marked ED and 12.5% one or more new onset post-op maladaptive behaviour changes
- Parents at high risk of preoperative anxiety, ED and maladaptive behaviour are more anxious in the holding area
- Children with marked ED OR 1.43 having one or more new onset post-op maladaptive behaviour changes

Kain et al Anesth Analg 2004;99:1648-54

Received: 30 December 2020 | Revised: 10 May 2021 | Accepted: 10 June 2021  
DOI: 10.1111/pan.14259

## RESEARCH REPORT

Journal of Paediatric Anaesthesia  
WILEY



Volume 31, Issue 10  
Pages 1, 1059–1105  
October 2021

### Behavioral changes after hospital discharge in preschool children experiencing emergence delirium after general anesthesia: A prospective observational study

Jonghae Kim<sup>1</sup> | Sung Hye Byun<sup>2</sup> | Jun Won Kim<sup>3</sup> | Ji-Yoon Kim<sup>4</sup> | Yun Jin Kim<sup>5</sup> | Nayeon Choi<sup>6</sup> | Bong Soo Lee<sup>1</sup> | Seungcheol Yu<sup>1</sup> | Eugene Kim<sup>1</sup>

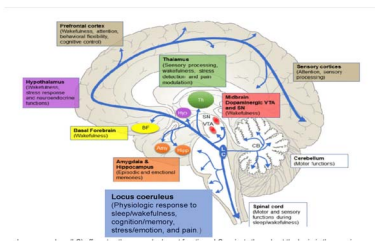
**Results:** Children with emergence delirium ( $n = 58$ ) had higher postoperative behavior checklist scores than children without emergence delirium ( $n = 42$ ) [mean (SD), 22.8 (17.5) vs. 14.0 (12.1); mean difference (95% CI), 8.8 (1.5–16.2)]. Increases in preoperative anxiety level [regression coefficient (b) (95% CI) = 0.241 (0.126–0.356)] and peak delirium-specific score [b = 0.789 (0.137–1.442)] were associated with an increase in behavior checklist score 1 week after surgery, while pain-related score, type of surgery, premedication, and age were not.

**Conclusion:** Children with emergence delirium develop more severe behavior changes 1 week after surgery than those without emergence delirium. High preoperative anxiety level and emergence delirium scores were associated with posthospital behavioral changes.

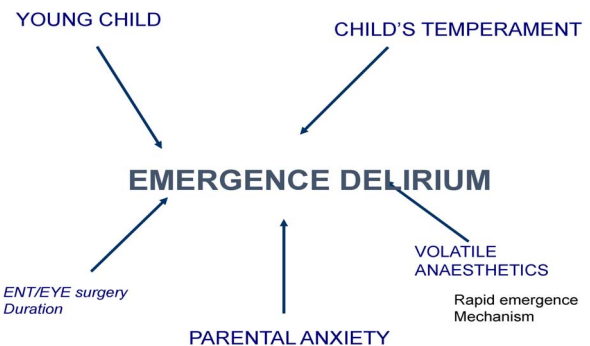
But results  
Incidence ED 58%  
ED needed more analgesics 89.7% vs. 47.6%

## Emergence Delirium - possible etiological factors

Emergence from general anesthesia is not a PASSIVE reversal process  
Now reconsidered, distinct and as an active and controllable process.



Escape From Oblivion: Neural Mechanisms of Emergence From General Anesthesia. I  
Max B. Kelz  
Anesth Analg. 2019 April



### Frontal electroencephalogram activity during emergence from general anaesthesia in children with and without emergence delirium

Jonghae Kim<sup>1</sup>, Hyung-Chul Lee<sup>1</sup>, Sung-Hye Byun<sup>1</sup>, Hyunyoung Lim<sup>1</sup>, Minkyu Lee<sup>1</sup>, Yoojin Choung<sup>2</sup> and Eugene Kim<sup>1\*</sup>

British Journal of Anaesthesia, 126 (1): 293–303 (2021)

#### Editor's key points

- Electrical oscillations between the cortex and thalamus, and between cortical regions and hemispheres, appear to provide important information on different states of consciousness, including general anaesthesia and delirium.
- Emergence delirium is a challenge in paediatric anaesthesia, and it occurs commonly in children during emergence from general anaesthesia.
- This research shows that certain EEG patterns before emergence from anaesthesia are strongly associated with emergence delirium in children, including high relative delta power and an increased ratio of low-frequency (i.e. delta and theta) to high-frequency (i.e. alpha and beta) oscillations.

Transitioning rapidly from deep anaesthesia to wakefulness, reflected by the absence of an EEG pattern resembling non-rapid eye movement stage 2 sleep, might predispose children to emergence delirium.

### Alterations in the Functional Connectivity of Frontal Lobe Networks Preceding Emergence Delirium in Children

Jonghae Kim, B.Sc., B.R., David T. Lin, M.B., ChB., Ph.D., A. Shyn-Hwang, M.D., B.S., A.C.P., Lark-Kyung, B.Sc., Ph.D., Jeeun W. Song, M.B., ChB., F.F.A.R.C.S., F.A.N.Z.C.A., F.J.T.C.M., M.D., Andrew J. Henderson, M.B.B.S., M.D., F.A.N.Z.C.A., Grad Dip Bio Stat.

Anesthesiology, V 121 • No 4

#### What This Article Tells Us That Is New

- In children without emergence delirium, an electroencephalogram pattern of sleep or drowsy states was observed before prefrontal functional connectivity.
- In children with emergence delirium, arousal with critical delirium occurred before observation of electroencephalogram patterns of sleep.
- Frontal regional functional connectivity was significantly elevated in emergence delirium compared with that of matched controls shortly after discontinuation of anaesthesia.

Absence of sleep EEG pattern associated with ED

## Management of Emergence Delirium

Determine incidence in your own institution  
Ensure departmental Analgesic and PONV strategy

### Evaluation of emergence delirium in Asian children using the Pediatric Anesthesia Emergence Delirium Scale KKH

The incidence of ED is approximately **10%** in our population of healthy, unpremedicated Asian children undergoing day surgery.

Young age, poor compliance at induction, lack of intraoperative fentanyl use and rapid time to awakening were predictive risk factors for ED in our population.

A PAED Score of  $\geq 10$  correlated to clinically significant ED

Choon L. Bong Pediatric Anesthesia 2009 19: 593–600

Anaesthesia 2015, 70, 393–399

doi:10.1111/anae.12867

## Original Article

Overall incidence ED 39.2%

A comparison of single-dose dexmedetomidine or propofol on the incidence of emergence delirium in children undergoing general anaesthesia for magnetic resonance imaging\*

C. L. Bong,<sup>1</sup> E. Lim,<sup>2</sup> J. C. Allen,<sup>3</sup> W. L. H. Choo,<sup>4</sup> Y. N. Siow,<sup>1</sup> P. B. Y. Teo<sup>5</sup> and J. S. K. Tan<sup>2</sup>

<sup>1</sup> Consultant, <sup>2</sup> Senior Consultant, Department of Paediatric Anaesthesia, <sup>3</sup> Senior Staff Nurse, <sup>4</sup> Nurse Manager, Department of Diagnostic Imaging, KK Women's and Children's Hospital, Singapore

<sup>5</sup> Assistant Professor, Centre for Quantitative Medicine, Office of Clinical Sciences, Duke-NUS Graduate Medical School, Singapore

#### Summary

Emergence delirium is a significant problem in children regaining consciousness following general anaesthesia. We compared the emergence characteristics of 120 patients randomly assigned to receive a single intravenous dose of dexmedetomidine 0.3  $\mu\text{g}\cdot\text{kg}^{-1}$ , propofol 1  $\text{mg}\cdot\text{kg}^{-1}$ , or 10 ml saline 0.9% before emerging from general anaesthesia following a magnetic resonance imaging scan. Emergence delirium was diagnosed as a score of 10 or more on the Paediatric Anaesthesia Emergence Delirium scale. The incidence of emergence delirium was 42.5% in the dexmedetomidine group, 33.3% in the propofol group and 41.5% in the saline group ( $p = 0.671$ ). Three patients in the dexmedetomidine group, none in the propofol group and two in the saline group required pharmacological intervention for emergence delirium ( $p = 0.202$ ). Administration of neither dexmedetomidine nor propofol significantly reduced the incidence, or severity, of emergence delirium. The only significant predictor for emergence delirium was the time taken to awaken from general anaesthesia, with every minute increase in wake-up time reducing the odds of emergence delirium by 7%.



## Preemptive strategy

Non pharmacologic interventions  
Premedication  
Parental presence, video distraction etc  
Above measure allays anxiety but may not reduce ED

Appropriate anaesthesia techniques  
Good pain strategies

Pharmacologic agents  
Adjunct agents



## Effects of sevoflurane versus other general anaesthesia on emergence agitation in children

Halothane  
RR 0.51, 95% CI 0.41 to 0.63

Propofol TIVA  
RR 0.35, 95% CI 0.25 to 0.51

Propofol after Sev Induction  
RR 0.59, 95% CI 0.46 to 0.76



David Costi et al  
Cochrane Database of Systematic Reviews, Sept 2014



## TIVA only?

## INTERVENTIONS

### Elective adjuncts for reducing the risk of EA during sevoflurane anaesthesia

Dexmedetomidine,  
851 participants  
RR 0.37, 95% CI 0.29 to 0.47

Clonidine  
739 participants  
RR 0.45, 95% CI 0.31 to 0.66

Opioids, in particular  
fentanyl  
1247 participants  
RR 0.37, 95% CI 0.27 to 0.50



SEVOFLURANE ALONE

David Costi et al  
Cochrane Database of Systematic Reviews, Sept 2014

## Adjuncts for reducing EA during sevoflurane anaesthesia

Effective Medication	Dosage	Route/Timing of Admin
Dexmedetomidine	1-2 ug/kg 0.5-1.0 ug/kg 0.2 ug/kg/hr	IN premed IV intraop/End IV infusion
Clonidine	2 ug/kg	IV intraop/End
Fentanyl Remifentanyl	1-2 ug/kg 0.05-0.015 ug/kg/min	IV intraop/End IV intraop
Propofol *	2 - 3 mg/kg	IV/End
Ketamine*	0.25mg/kg	IV/End
Melatonin	0.2 - 0.4mg/kg	Oral premed

\*Costi: Paediatric Anaesth. 2015 May;25(5):517-23.

## SUMMARY

### Prevention:

#### Identify at risk child

- Consider sedation premedication
- **EFFECTIVE** prevention of postoperative pain and nausea and vomiting
- Recover the child in a silent environment
- Avoid verbal and physical stimulation during transfer and recovery

#### Child at risk

- Consider TIVA
- If volatiles used, use adjuncts

# Anesthesia-induced Neurotoxicity: Recent Updates and Preclinical Research Trends

Woosuk Chung

Department of Anesthesiology and Pain Medicine, Chungnam National University, Korea

## Anesthesia-induced Neurotoxicity



FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women

### Safety Announcement

[12-14-2016] The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains.

## PANDA, MASK, GAS studies

3 representative studies which prospectively evaluated the effects of a single exposure of general anesthesia for surgery



Although these studies differed in several aspects, the primary outcome was identical

: General intelligence (IQ)

**MASK study**  
(Mayo Anesthesia Safety in Kids)

**GAS study**  
(General Anesthesia and Spinal)

All 3 studies reported the same results

: A single, short exposure to general anesthesia for surgery in pediatric patients *did not affect general intelligence*

## After the PANDA, MASK, GAS studies...

### EDITORIAL VIEWS

Tindt et al. *Anesthesiology*. 2019

### GAS, PANDA, and MASK

No Evidence of Clinical Anesthetic Neurotoxicity!

### THE OPEN MIND

Bernier et al. *A & A*. 2019

### "Pediatric Anesthetic Neurotoxicity": Time to Stop!

"Human evidence suggests that any effect of well-conducted pediatric anesthesia is insignificant or nonexistent."

"... the possibility of harm from prolonged or multiple anesthetic exposures, hypotheses which can never be disproven."

"Neither funds nor researchers are unlimited; we must recognize that an unjustified research commitment in one area has an opportunity cost for other, perhaps more valuable, areas."



FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women

### Safety Announcement

[12-14-2016] The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains.

### Safety Announcement

[4-27-2017] The U.S. Food and Drug Administration (FDA) is notifying the public that we have approved previously announced label changes regarding the use of general anesthetic and sedation medicines in children younger than 3 years. These changes include:

### Use of anaesthetics in young children

Consensus statement of the European Society of Anaesthesiology, the European Society for Paediatric Anaesthesiology, the European Association of Cardiothoracic Anaesthesiology and the European Safe Tote Anaesthesia Research Initiative

**EJA**

... The evidence to support such warning is currently insufficient and incomplete. Therefore, this FDA warning is not shared by the European Societies.

## Why is there a continuous concern for early anesthetic exposure?

Normal brain function results from a conserved sequence of developmental processes of cell division, migration, network formation and maturation.



Disturbance in the balance between excitation and inhibition synaptic transmission (*E/I imbalance*) during critical sensitive periods act as an important mechanism for neurodevelopmental disorders, such as autism and ADHD.

Lipton et al. *Annu. Rev. Pharmacol. Toxicol.* 2021 Nelson et al. *Trends in Neuroscience*. 2020.

*Animal studies consistently show that early anesthetic exposures induce changes in synaptic transmission in mice.*

## Can early anesthesia induce long-lasting changes?

*Thus, we don't know what to look for!*

### Anesthesia-induced Neurotoxicity

#### Animal



General Anesthesia

Neuronal cell death  
Excitatory/Inhibitory imbalance  
Altered neurogenesis, synaptic structure  
Altered neuronal activity  
Long-lasting behavioral changes



## Is there a phenotype for Anesthesia-induced Neurotoxicity?

Early clinical studies mostly focused on **intelligence, academic achievements** (based on animal studies and general concerns).

More recent studies have performed wide-range of tests, trying to identify a possible **phenotype due to early anesthetic exposure**.

: Educational Outcomes, Cognitive functions, **Motor abilities**, **Social and Behavioral outcomes**, etc

Several studies suggest that **although early anesthesia does not alter general cognitive function (intelligence), but it may affect specific behaviors**.

Warner. Anesthesiology. 2018 Anesthesiology. 2020; Wallden et al.

## Recent studies suggest possible changes in specific behaviors

Prospectively assessed neurodevelopmental outcomes in studies of anaesthetic neurotoxicity in children: a systematic review and meta-analysis

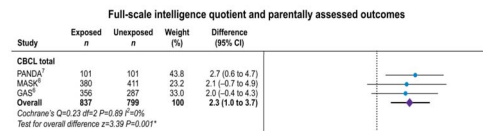
BJA. 2021; Ing et al.

A meta-analysis was performed using the results of PANDA, MASK, GAS

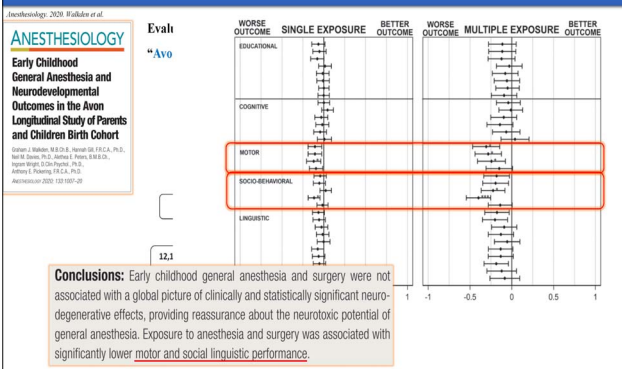
Child Behavior Checklist (CBCL)

: a checklist for the parents (118 questions), detect emotional and behavioral problems in children.

**Increased behavioral problems in patients who received early anesthesia**



## Recent studies suggest possible changes in specific behaviors



Based on these recent updates, **what should be considered when studying anesthesia induced neurotoxicity in young animals?**

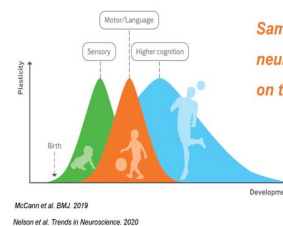
1. What is the appropriate age of animals to study anesthesia-induced neurotoxicity?
2. Could there be other phenotypes caused by early anesthetic exposures?
3. Are we using an appropriate anesthetic depth in young animals?

Based on these recent updates, **what should be considered when studying anesthesia induced neurotoxicity in young animals?**

1. **What is the appropriate age of animals to study anesthesia-induced neurotoxicity?**
2. Could there be other phenotypes caused by early anesthetic exposures?
3. Are we using an appropriate anesthetic depth in young animals?

## Anesthetic exposure during neurodevelopment

The effects of early anesthesia may differ depending on the developing stage of the child.



**Same anesthetic exposures may affect neurodevelopment differently depending on the age of patients.**

## Anesthetic exposure during neurodevelopment: What to consider?

Most concerns about anesthetic induced developmental neurotoxicity has been focused on **toddlers and infants** because this is a time of critical development.

Thus, it is natural that preclinical research should also study animals with similar neurodevelopment compared to human infants.

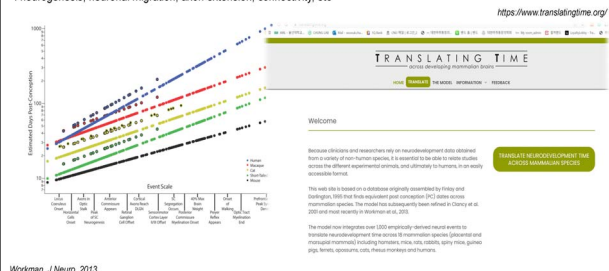
Is it possible to compare the neurodevelopment between humans and animals (mice, primates)?



## Comparing the neurodevelopment between animals and humans

A scientific approach would be comparing important neurodevelopmental events between species...

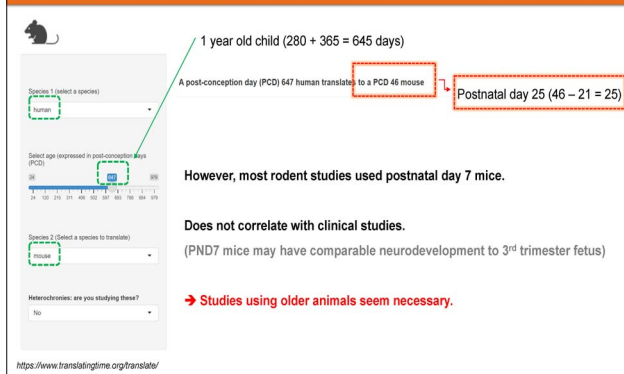
: neurogenesis, neuronal migration, axon extension, connectivity, etc



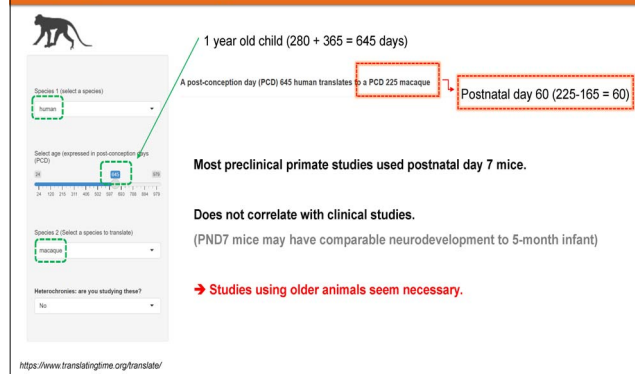


## Woosuk Chung: Anesthesia-induced Neurotoxicity: Recent Updates and Preclinical Research Trends

## Comparing the neurodevelopment between animals and humans

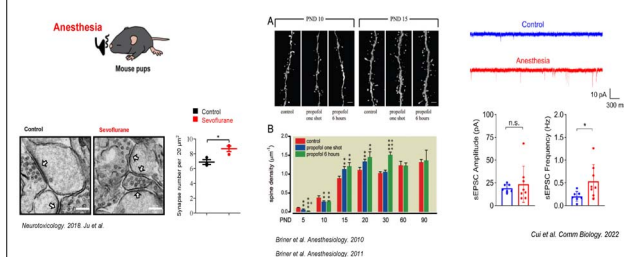


## Comparing the neurodevelopment between animals and humans



## What do previous studies using older animals suggest?

Anesthesia-induced increase in dendritic spine density was associated with changes in excitatory and inhibitory synaptic transmission (Excitatory/inhibitory imbalance)



Based on these recent updates, what should be considered when studying anesthesia induced neurotoxicity in young animals?

1. What is the appropriate age of animals to study anesthesia-induced neurotoxicity?
2. Could there be other phenotypes caused by early anesthetic exposures?
3. Are we using an appropriate anesthetic depth in young animals?

## Behaviors affected by early anesthetic exposures?

Recent clinical studies suggest that specific behaviors rather than general cognition may be affected by early anesthetic exposures.

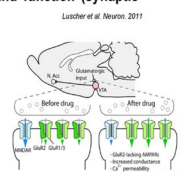
What kind of behavior should we be evaluating?

Maybe.... Addiction???

Use of addictive drugs leads to changes in neuronal structure and function (synaptic transmission) → associated with addiction behavior.

Thus, drugs that cause changes in synaptic transmission may influence addiction behavior later in life.

General Anesthesia!!!



## Early Anesthesia &amp; Addiction: A possible connection?

Our hypothesis:

The synaptic changes that occur after anesthetic exposures during neurodevelopment may affect addiction behavior later in life.

Choice of drug: Ketamine

Ketamine is often used in pediatric patients

Ketamine induces changes in synaptic transmission

Ketamine is also a recreational drug (called special K), and abused world-wide.

J of Anesthesia 2021. Lee et al.

Addiction 2012. Morgan et al.



## Can early ketamine anesthesia affect addiction behavior in later life?

Young mice (PND 16) received NSS or Ketamine (35mg/kg, ip) for 5 consecutive days

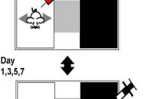
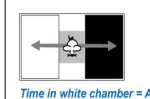


## Behavior test for drug reward: Conditioned Place Preference (CPP) test

Pre-conditioning phase  
(15 minutes)  
: no injection

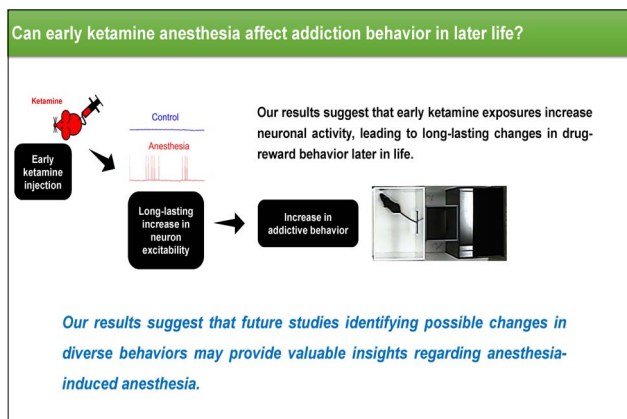
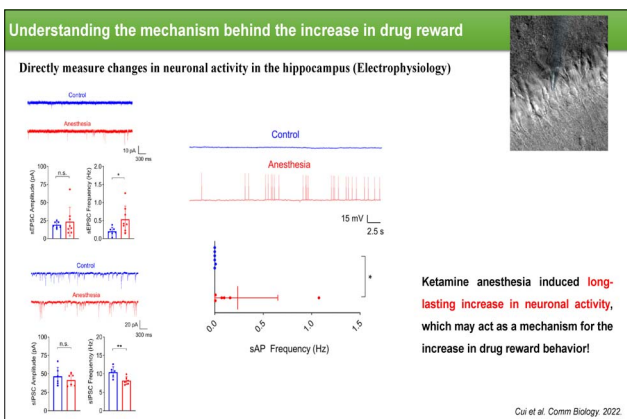
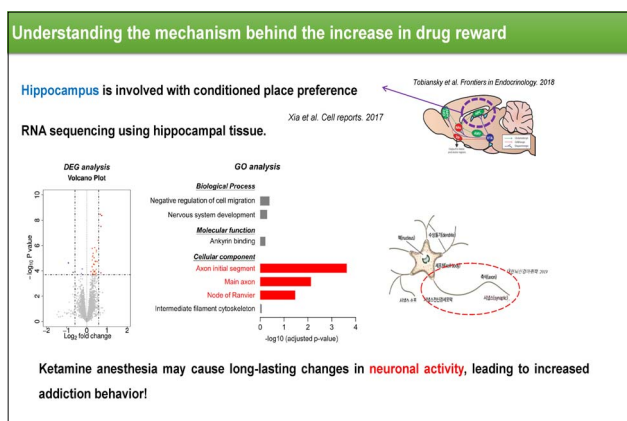
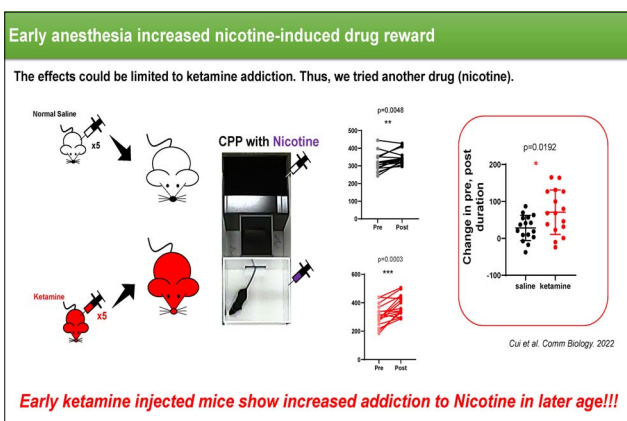
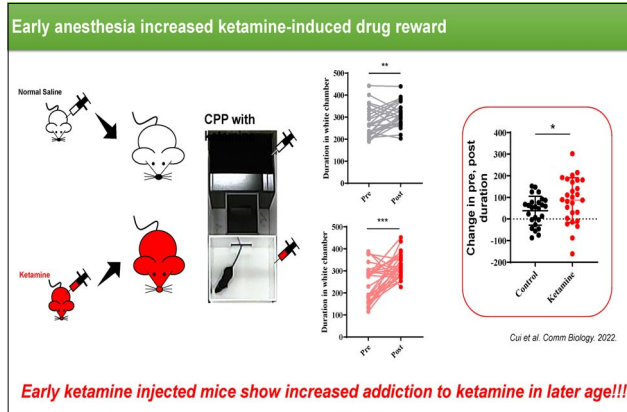
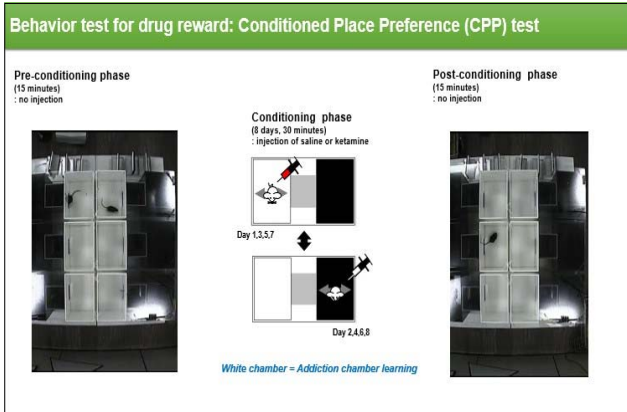
Conditioning phase  
(8 days, 30 minutes)  
: injection of saline or ketamine

Post-conditioning phase  
(15 minutes)  
: no injection



White chamber = Addiction chamber learning

Addiction can be measured by measuring the increase in time spent in the white chamber (B-A)



Based on these recent updates, what should be considered when studying anesthesia induced neurotoxicity in young animals?

1. What is the appropriate age of animals to study anesthesia-induced neurotoxicity?
2. Could there be other phenotypes caused by early anesthetic exposures?
3. Are we using an appropriate anesthetic depth in young animals?

### Depth of anesthesia in neurotoxicity research

pEEG monitoring is widely used for controlling anesthetic depth in adult patients, and recent studies suggest the unnecessary depth of anesthesia (causing burst suppression) is associated with worse clinical outcomes.

Pawar et al. Front Syst Neurosci. 2022.

Although pEEG monitoring is unreliable in pediatric patients due to changes in EEG during neurodevelopment, previous studies show that anesthetic overdose (burst suppression) often occurs also in pediatric patients (30-60%).

Yuan et al. Current Anesth Reports. 2023.

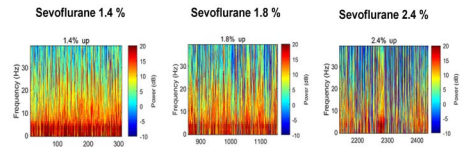
While long-term adverse affects of unnecessary depth of anesthesia remain undetermined, future studies may need to evaluate the appropriate anesthetic dose when studying neurotoxicity in young animals.

## Woosuk Chung: Anesthesia-induced Neurotoxicity: Recent Updates and Preclinical Research Trends

## Depth of anesthesia in neurotoxicity research

Regarding **sevoflurane**, most preclinical studies use a concentration of **2.5%** when studying neurotoxicity in both rodents and primates.

**Sevoflurane 2.5%**, when administered in PND 17 mice induces robust burst-suppression.



Ju et al. Unpublished data

## Depth of anesthesia in neurotoxicity research

Is burst suppression associated long-lasting behavioral changes?

Experimental paradigm

P17

Surgery and anesthesia

8wk

Behavioral experiment

Group1 : control

Group2 : No Burst Suppression Anesthesia (Sevo 1.4%) + Surgery

Group3 : Burst Suppression Anesthesia (Sevo 2.4%) + Surgery

Learning and Memory, Anxiety, Sociability

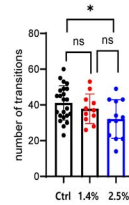
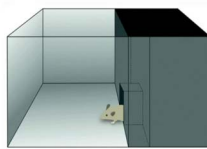


Jiang et al. Unpublished data

## Depth of anesthesia in neurotoxicity research

Mice that received surgery under deep anesthesia showed changed anxiety levels in the light-dark box test

Light-dark box test



Jiang et al. Unpublished data

## Conclusion

Evidence strongly suggests that the effects of anesthesia on general cognition is subtle.

Recent studies also suggest that early anesthetic exposures may have a more **significant effect in specific aspects of development**.

Thus, further studies identifying **possible changes in diverse developmental behaviors** may provide valuable insights regarding the potential neurotoxic effects of early anesthesia.

Also, future preclinical studies should also **attempt to mirror clinical settings by considering factors** such as the age of animals and the appropriate anesthetic dose.



**19th Conference of Asian Society of Paediatric Anesthesiologists &  
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