

# **Sudden Infant Death Syndrome: Research and Risk Reduction**



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Chair, California SIDS Advisory Council

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Children's Hospital Los Angeles



**No Conflicts of Interest to Disclose**

October is **Sudden Infant Death Syndrome** Awareness Month





**“And this woman's son  
died in the night ...”**

**1 Kings 3: 19  
(950 B.C.)**

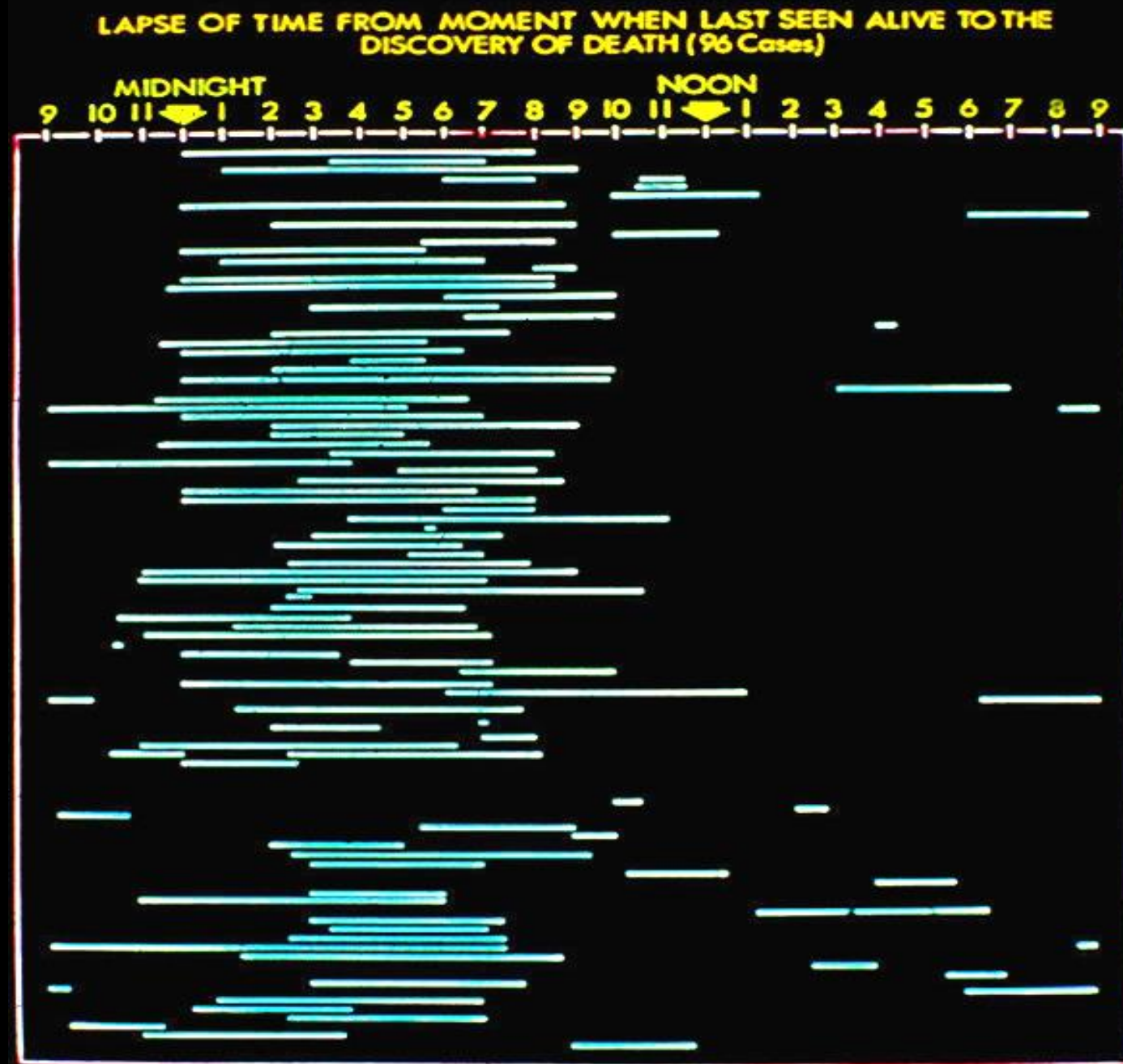
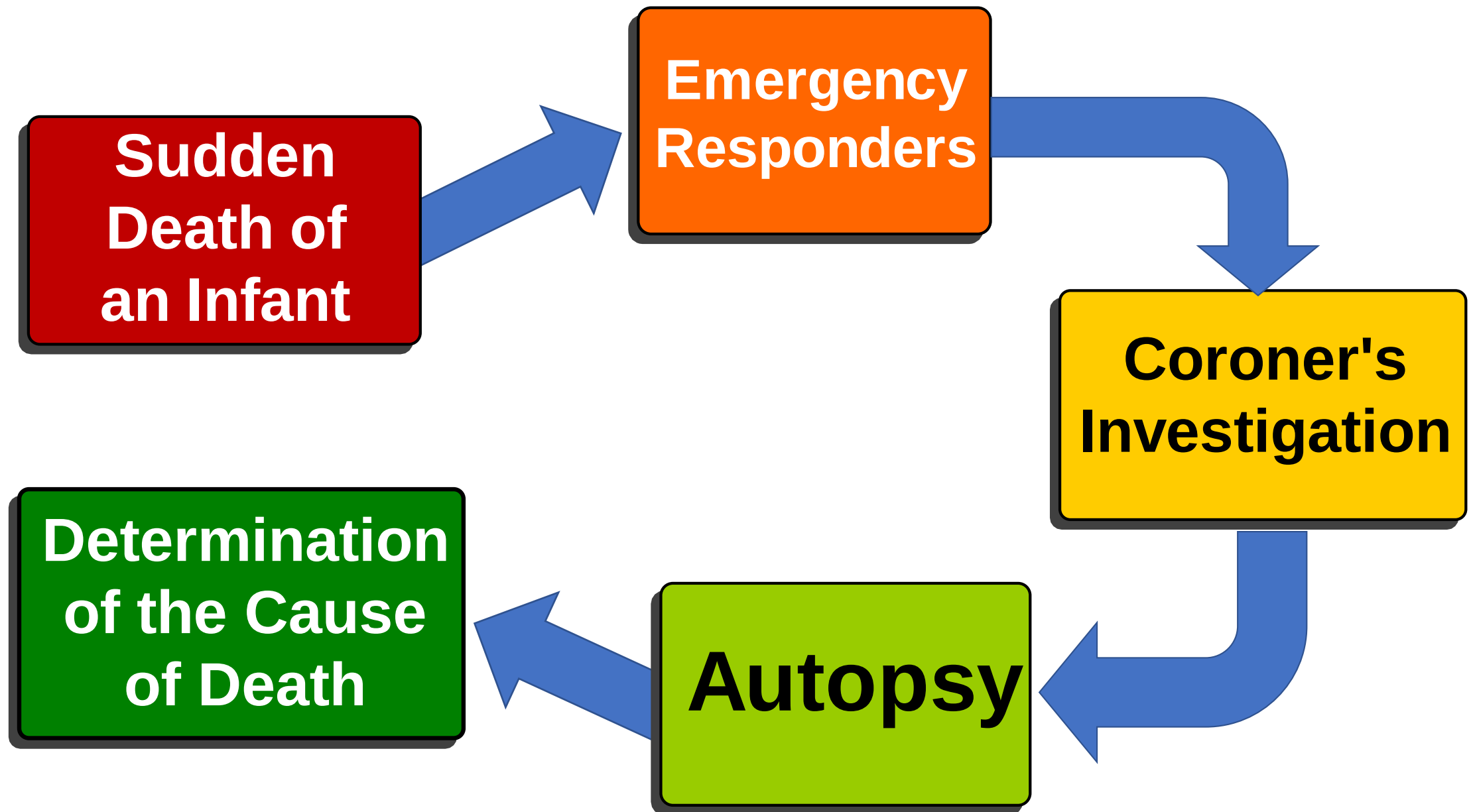


**Figure Courtesy of Doctor Maria Valdes-Dapena**





# Sudden Infant Death Syndrome



**The sudden unexpected death of an infant, under one-year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including performance of a complete autopsy, and review of the circumstances of death and the clinical history.**



**Krous, H.F., J.B. Beckwith, R.W. Byard, T.O. Rognum, T. Bajanowski, T. Corey, E. Cutz, R. Hanzlick, T.G. Keens, and E.A. Mitchell. *Pediatrics*, 114: 234-238, 2004.**

# What Shall We Call them?



- From blaming parents: Ancient Greece and Rome through the Middle Ages.
- To natural causes: Late 1800's and early 1900's.
- To blaming parents again: Early to mid 1900's.
- To natural causes again: Late 1900's and early 2000's.
- Now to unsafe, accidental causes.



# Different Coroners Use Different Diagnoses for these Infants



When diagnosing the cause of death in an infant dying suddenly and unexpectedly during sleep, the following terms are considered synonymous:

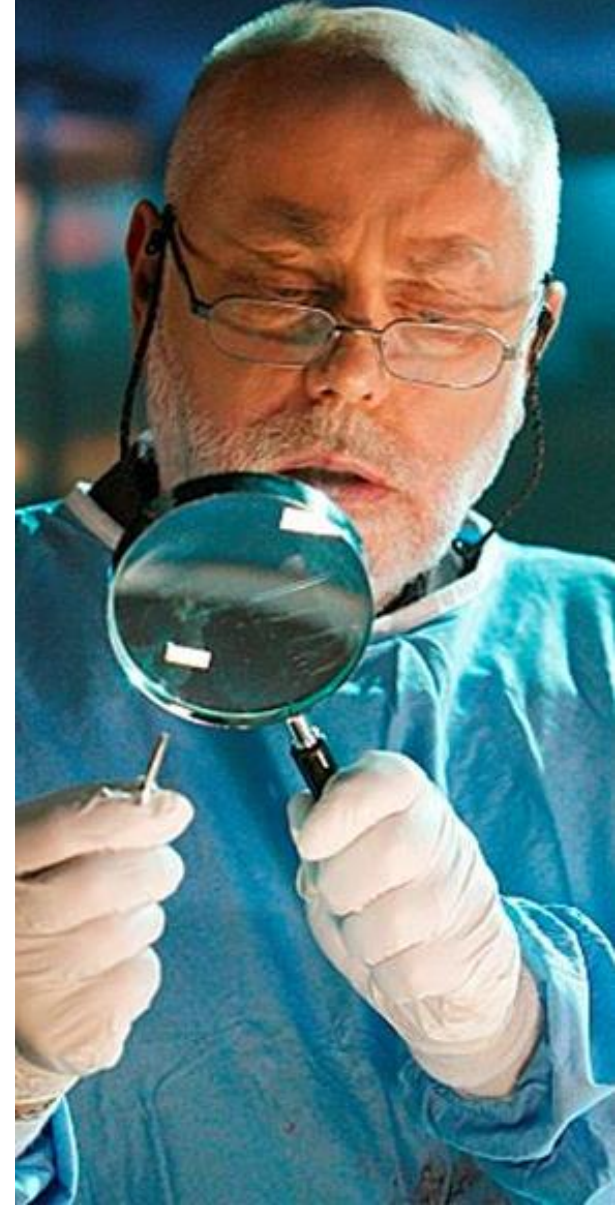
- SIDS
- SUID
- SUDI
- Undetermined

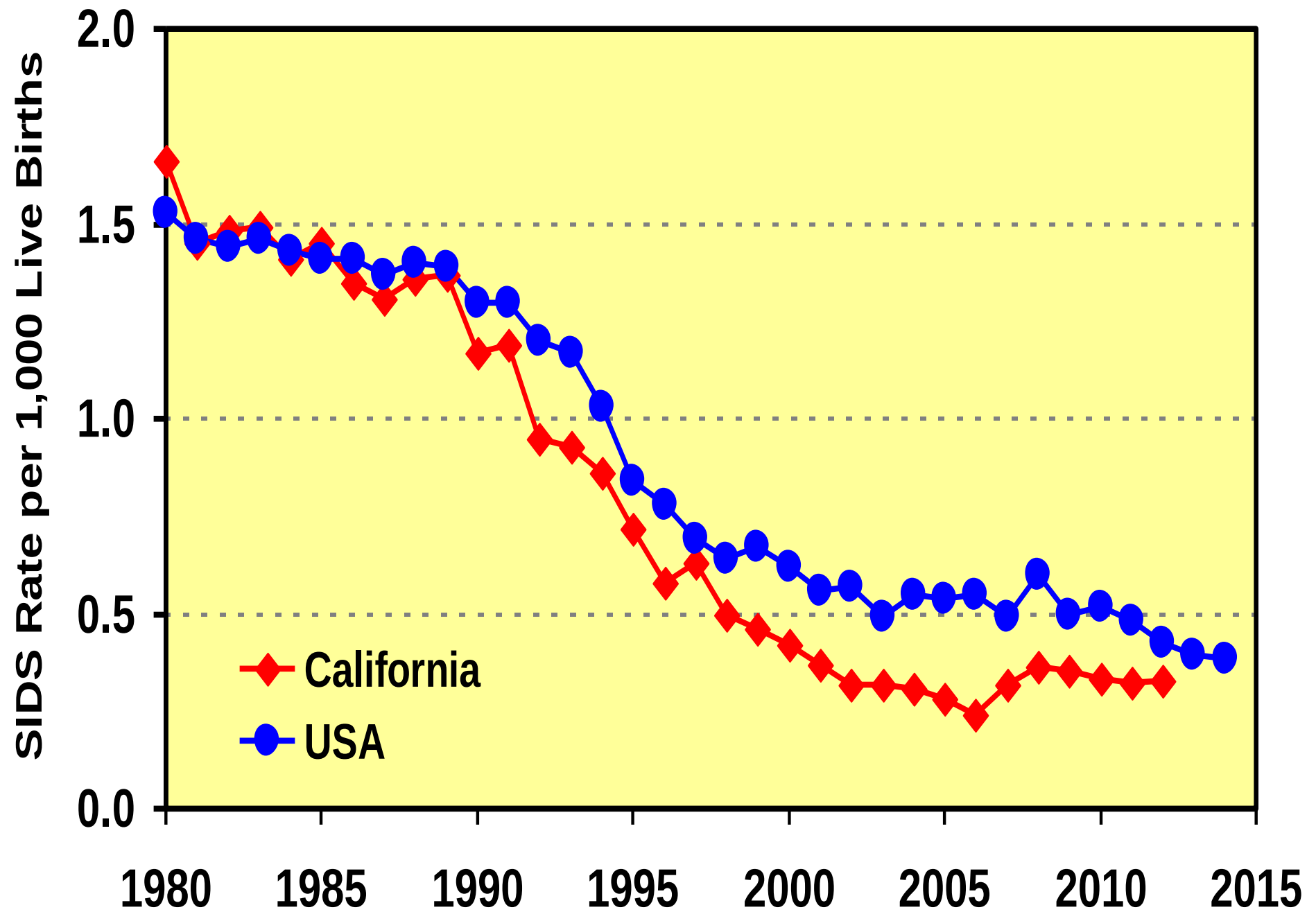
They all mean the same thing; that the infant's death is *unexpected* and *unexplained*.

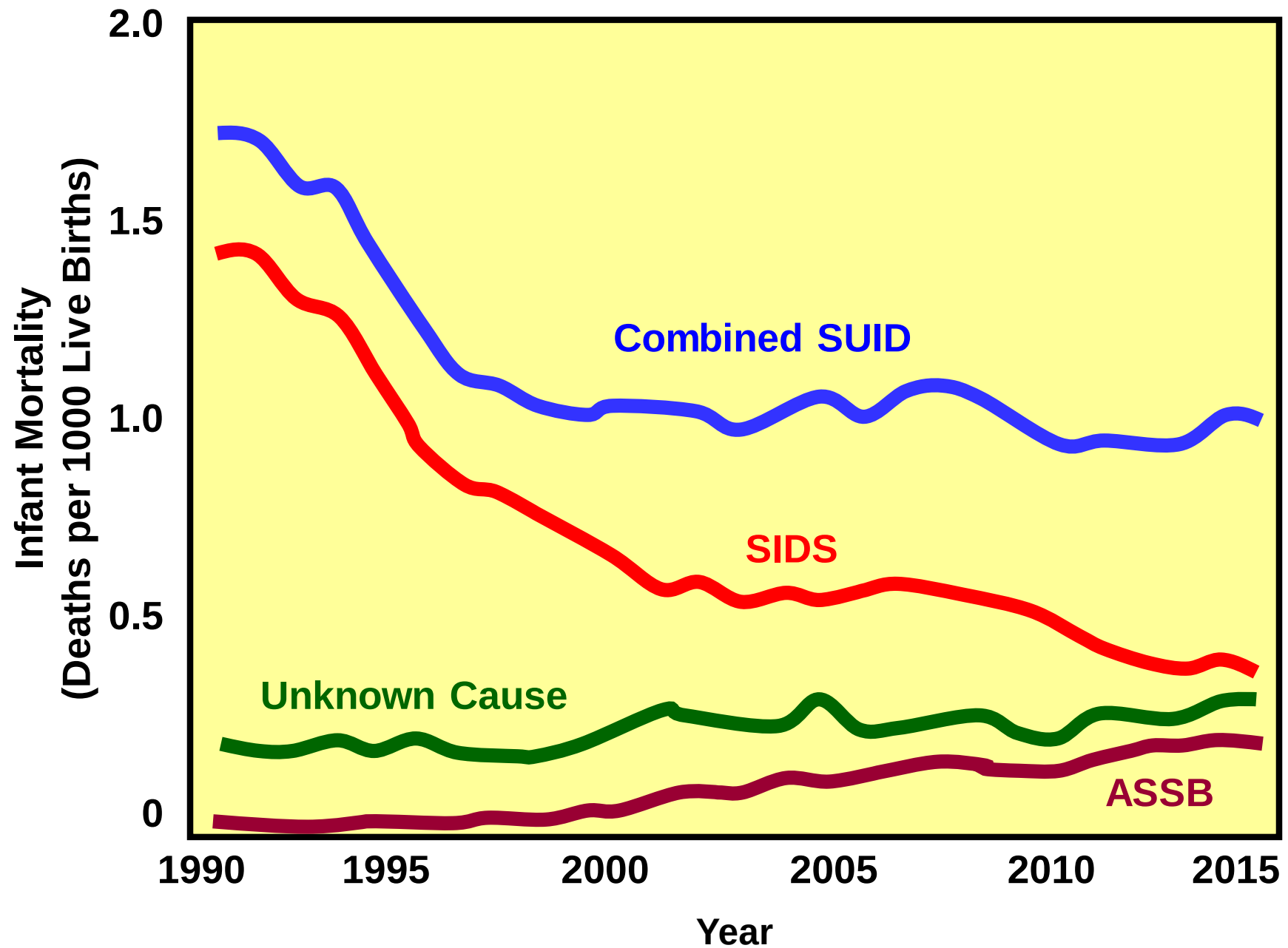
Krous, H.F. *Forensic. Sci. Med. Pathol.*, 9: 91–93, 2013.

Cutz, E. *JAMA Pediatr.*, 170: 315-316, 2016.

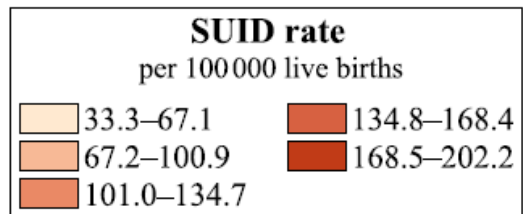
Goldstein, R.D., et al. *For. Sci. Med. Pathol.*, 15: 622-628, 2019.

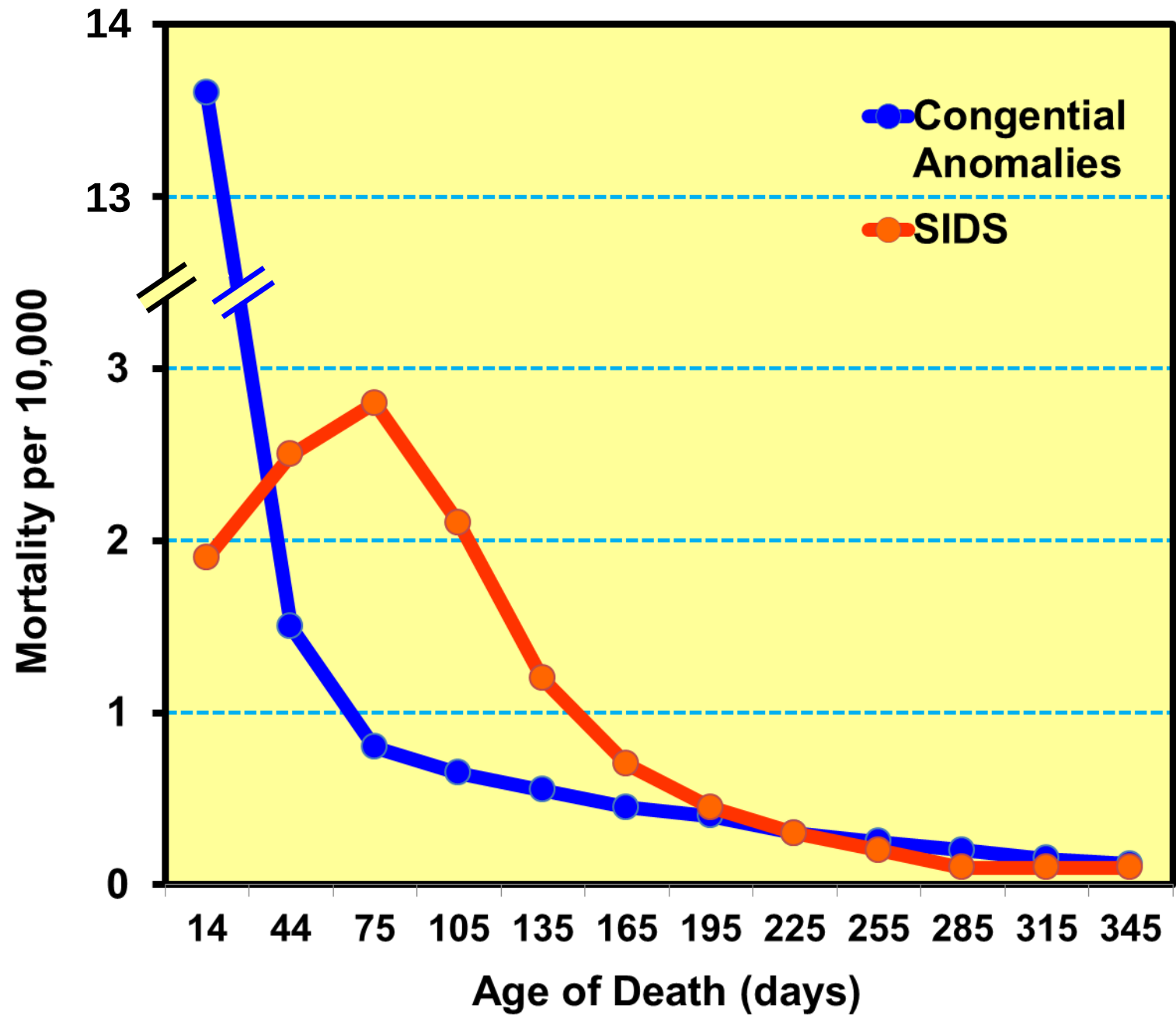




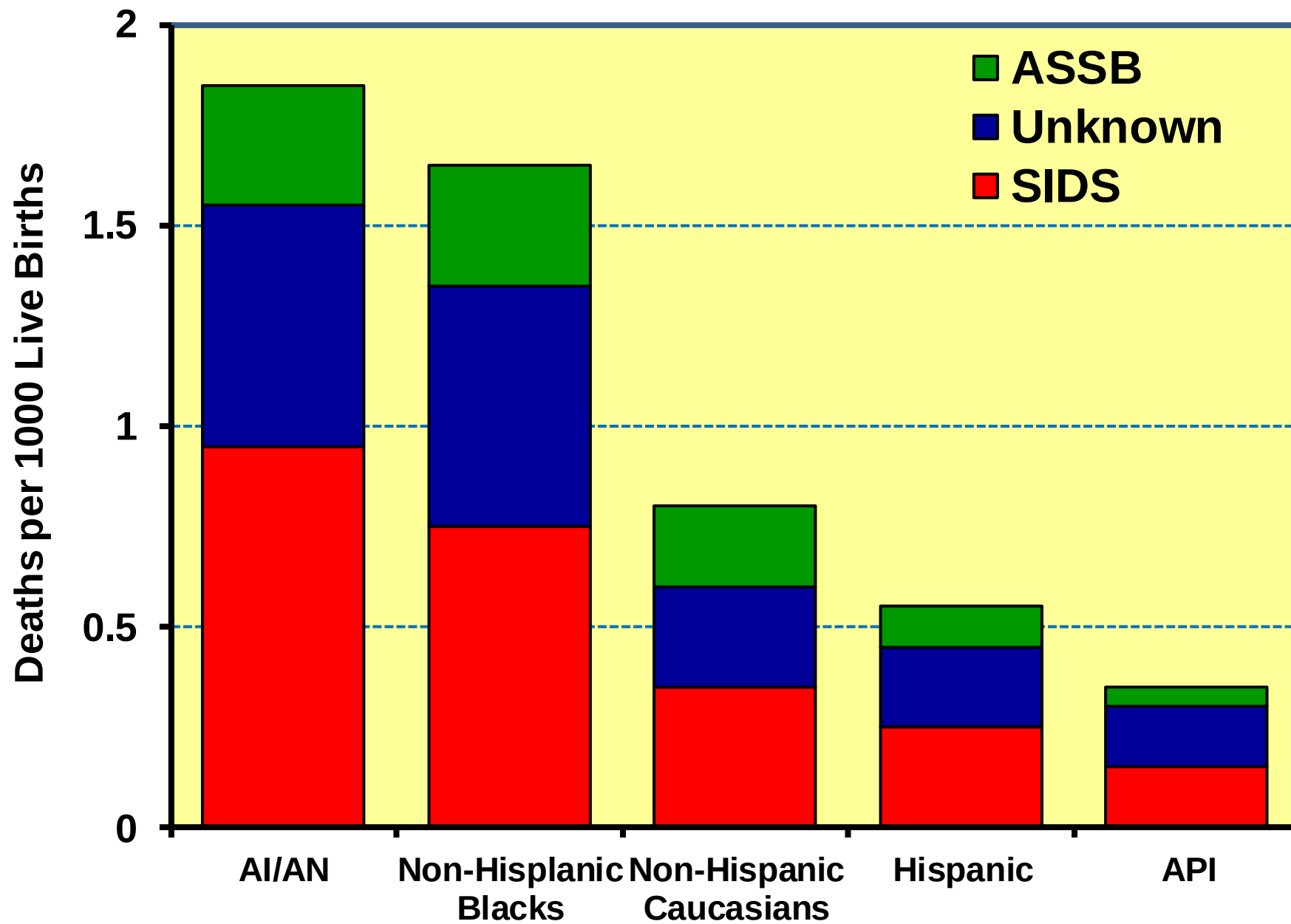


2013-2015

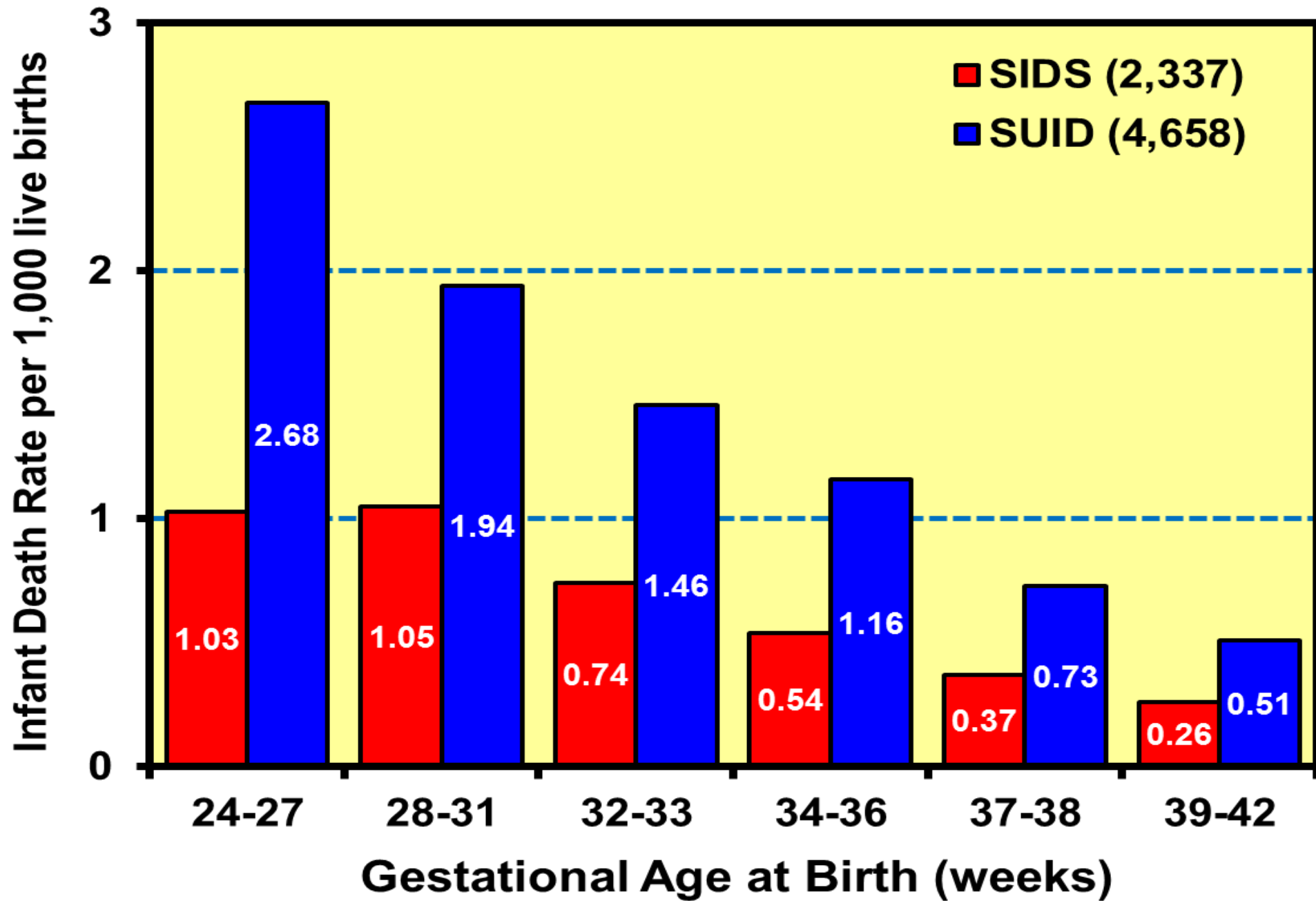




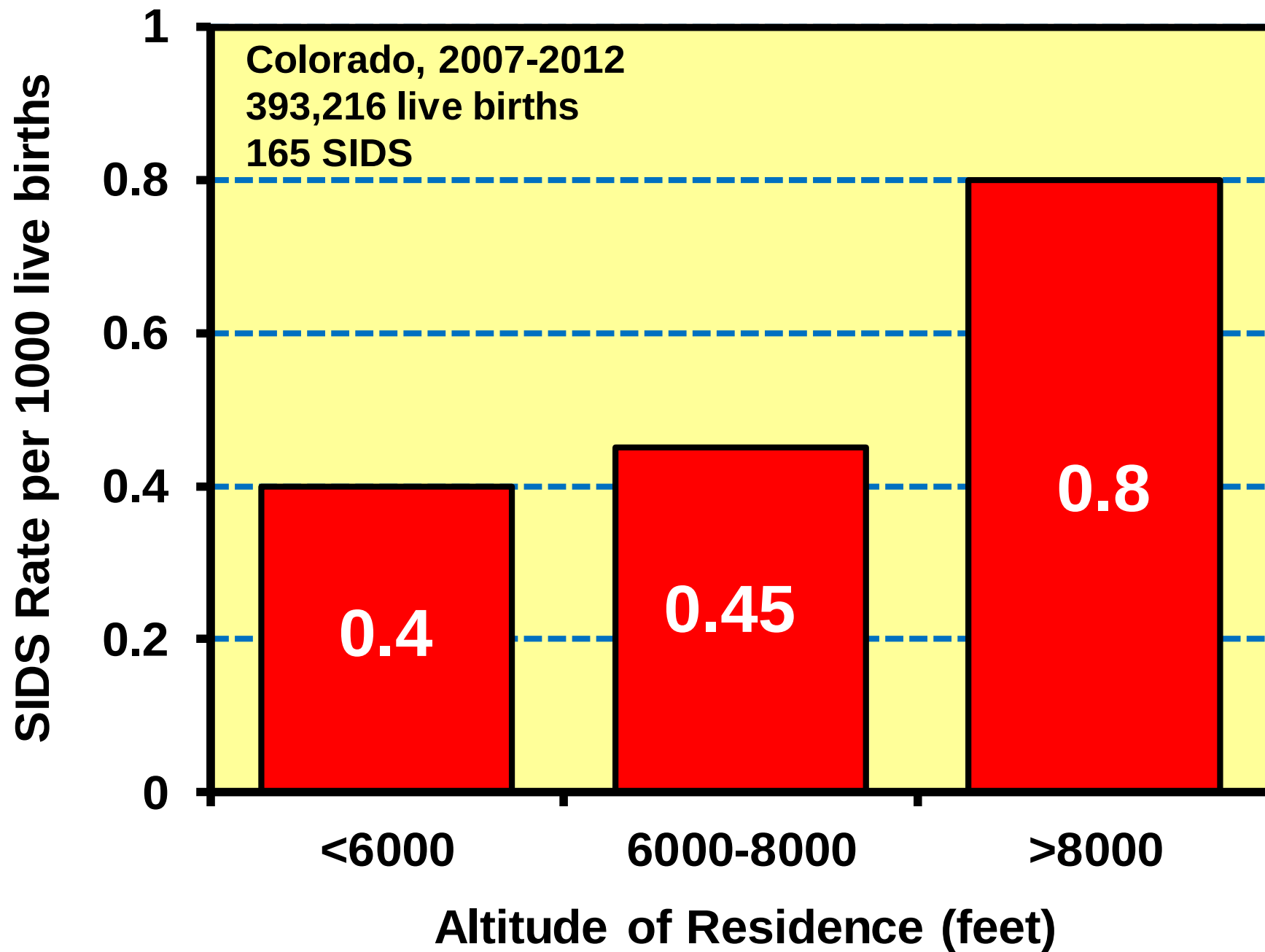
Guntheroth, W.G., and P.S. Spier. *Pediatrics*, 110: 110;e64, 2002.



<https://www.cdc.gov/sids/data.htm>



Ostfeld, B.M., et al. *Pediatrics*, 140: e20163334, 2017.



- **No identifiable cause of death.**
- **No signs of severe illness.**
- **No signs of significant stress.**
- **Diagnosis of exclusion**

# How Are We to Understand SIDS?



**Imagine a car driving up a  
steep mountain road.**

**The car has stopped.**

**Why can't the car continue  
up the hill?**

Modified after Professor Jacopo P. Mortola. McGill University.

# How Are We to Understand SIDS?



Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

## **Medical Model.**

- There is a flat tire.
- Identify the problem.
- Find a solution to the problem.
- Fix the problem.

Modified after Professor Jacopo P. Mortola. McGill University.

- **Cardiac causes.**
- **Respiratory causes.**
- **Arousal disorders.**
- **Metabolic disorders.**
- **Infections.**
- **Vitamin deficiency.**
- **Environmental toxins.**



# How Are We to Understand SIDS?

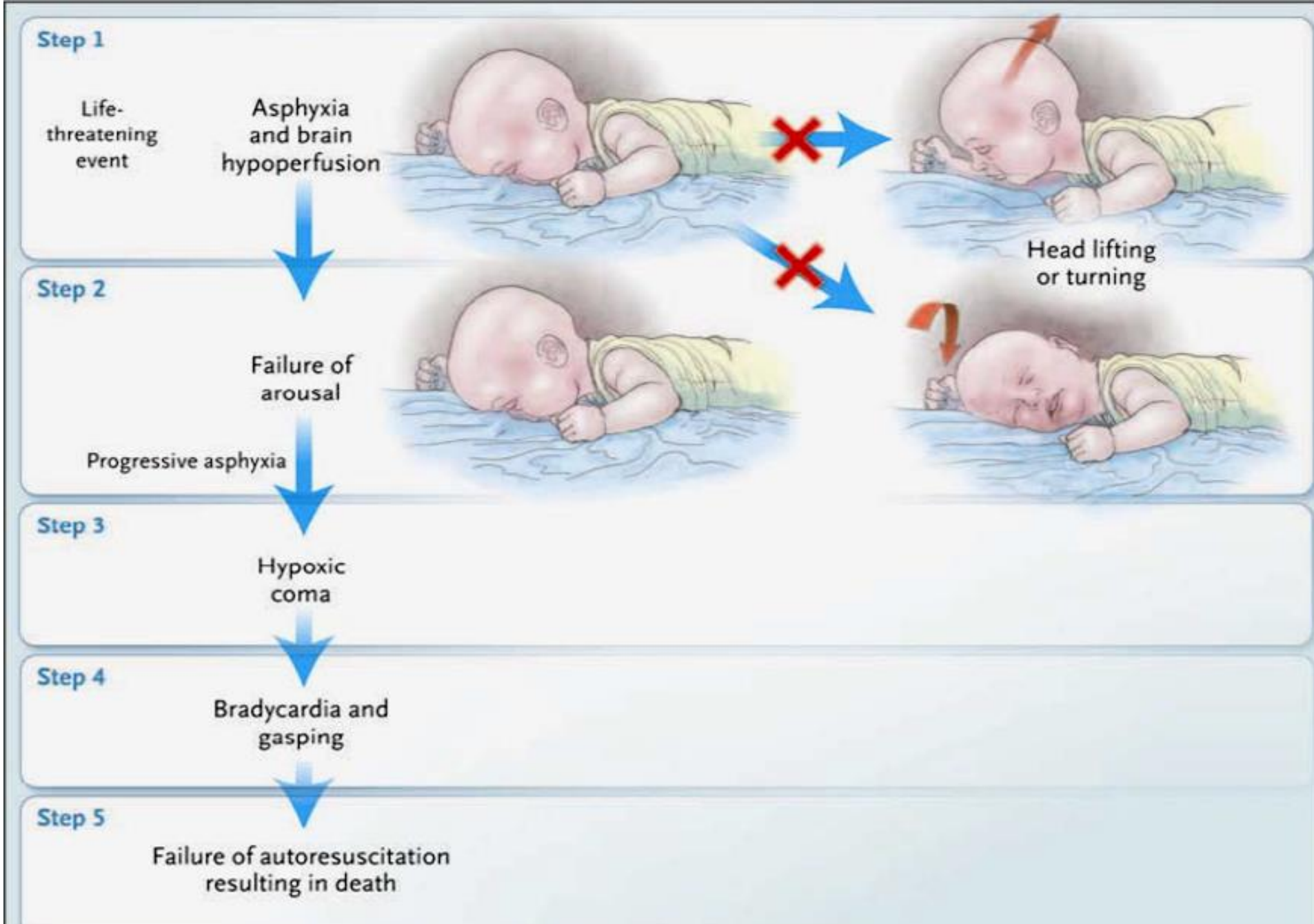


Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

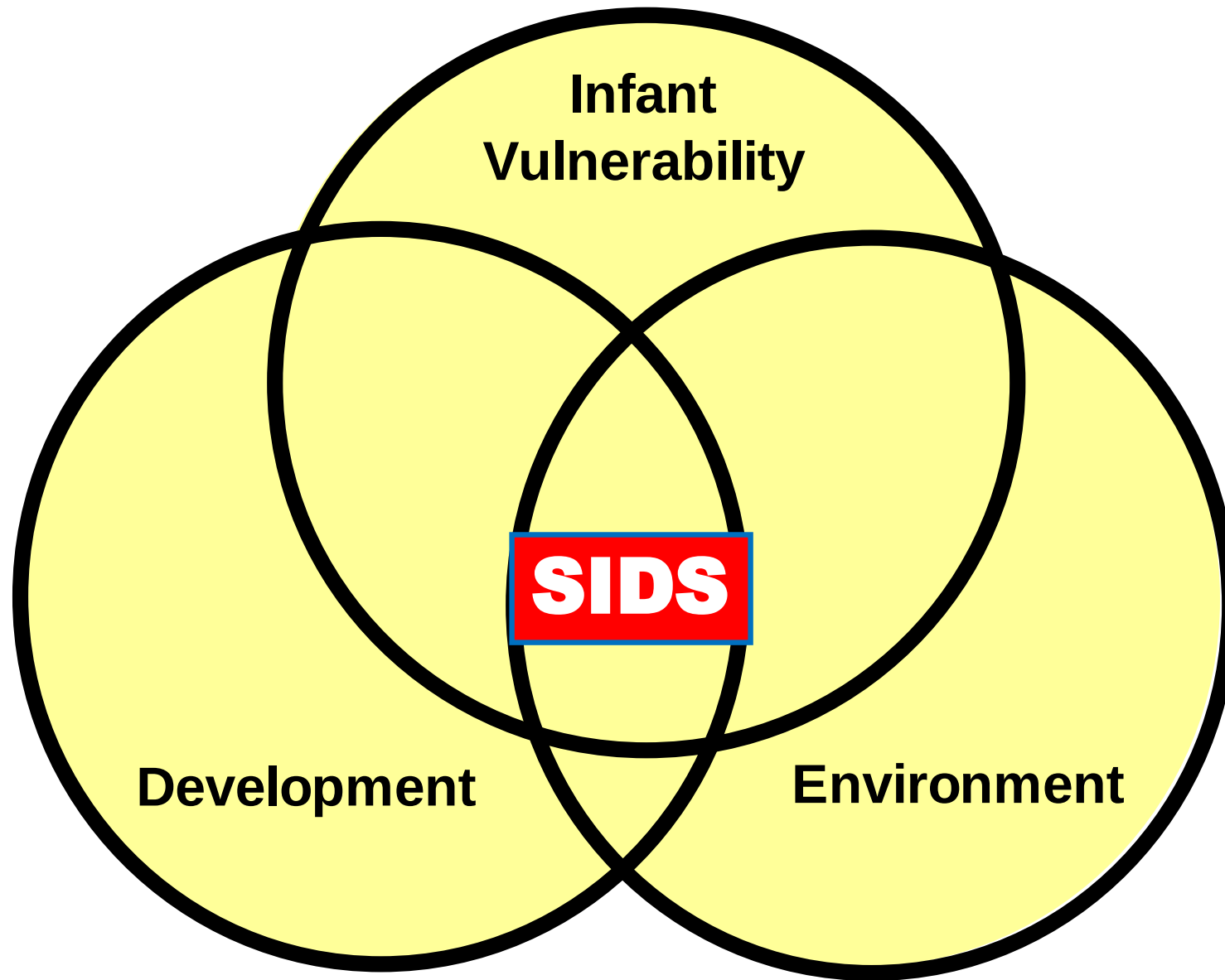
## **A New Way of Thinking.**

- There are too many passengers.
- The engine is not powerful enough.
- The road is too rocky.
- The road is too steep.

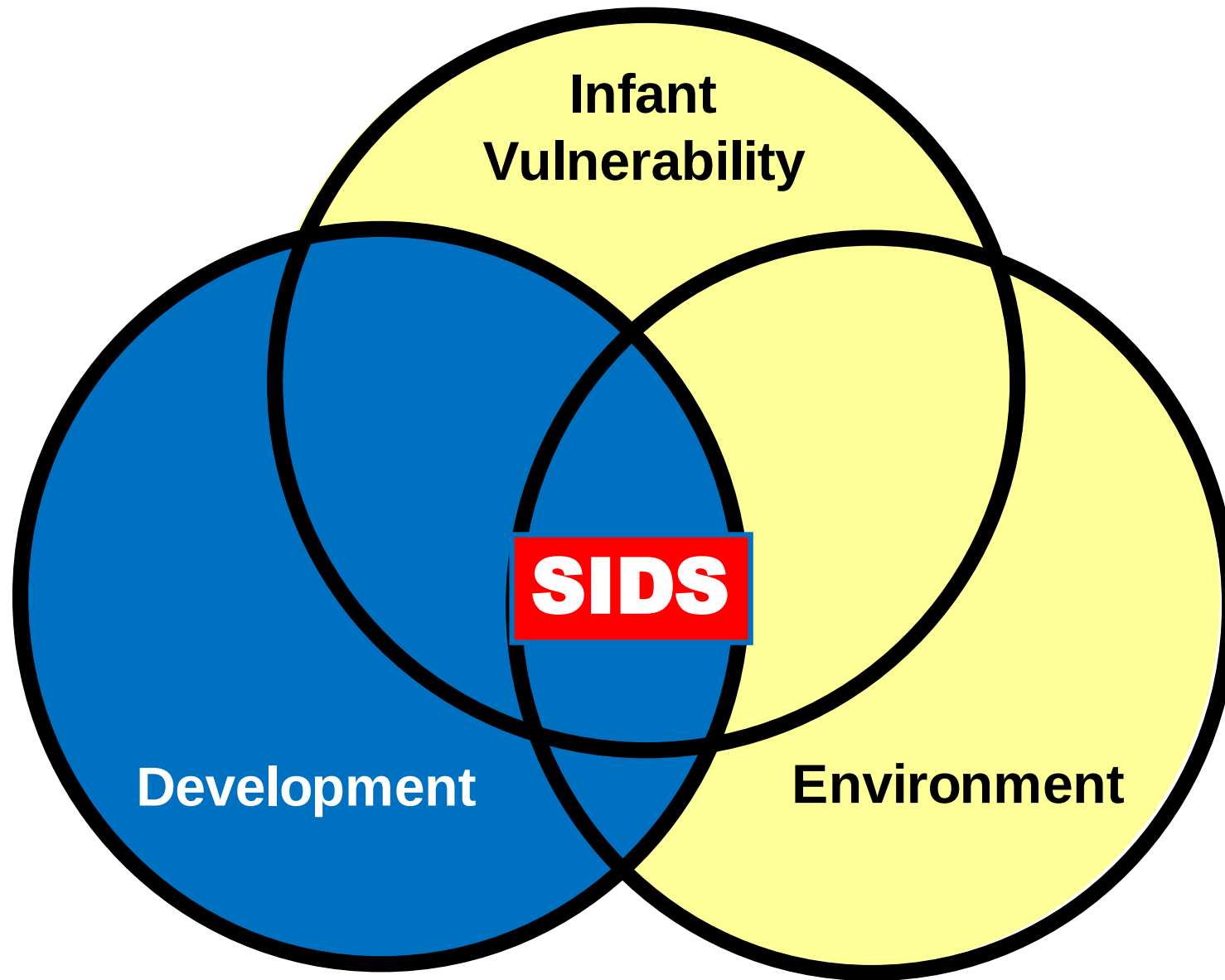
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Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

# Developing Infant Cardiorespiratory Physiology is Unstable



- **Any system in transition is intrinsically unstable.**
- **Infant cardiorespiratory physiology undergoes rapid changes in the first 3-6 months of life.**
- **Thus, infant physiological responses are immature and do not function optimally.**

# The CHIME Study

- **Clinical Sites.**
  - **Los Angeles, California.**
  - **Chicago, Illinois.**
  - **Honolulu, Hawaii.**
  - **Cleveland, Ohio.**
  - **Toledo, Ohio.**
- **Clinical Trial Operation Center.**
- **Data Coordinating and Analysis Center.**
- **NICHD.**

- **Clinical Sites.**



- **Los Angeles, California.**



- **Chicago, Illinois.**
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- **Clinical Trial Operation Center.**
- **Data Coordinating and Analysis Center.**
- **NICHD.**



# **CHIME Steering Committee**

## **NICHD, Bethesda, Maryland, U.S.A. *July, 1992.***





# **CHIME Steering Committee**

**NICHD, Bethesda, Maryland, U.S.A. *July, 1992.***



**USC**  
University of  
Southern California



# CHIME Study: USC-CHLA Team



# The CHIME Study

|                             |                                                       |
|-----------------------------|-------------------------------------------------------|
| <b>Healthy Term Infants</b> | Home monitoring up to 66 wks PCA (age 6 months).      |
| <b>Preterm Infants</b>      | Home monitoring up to 56 wks PCA (age 4 months).      |
| <b>ALTE Infants</b>         | Until infant has no real alarms for 3-months.         |
| <b>SIDS Siblings</b>        | Until 66 wks PCA, or 4 wks past age of death of SIDS. |

- **Respiratory Inductance Plethysmography.**
- **Central and Obstructive Apneas.**
- **Electrocardiogram.**
- **Pulse Oximeter.**
- **Body Position.**
- **Computer to record events and normative data.**

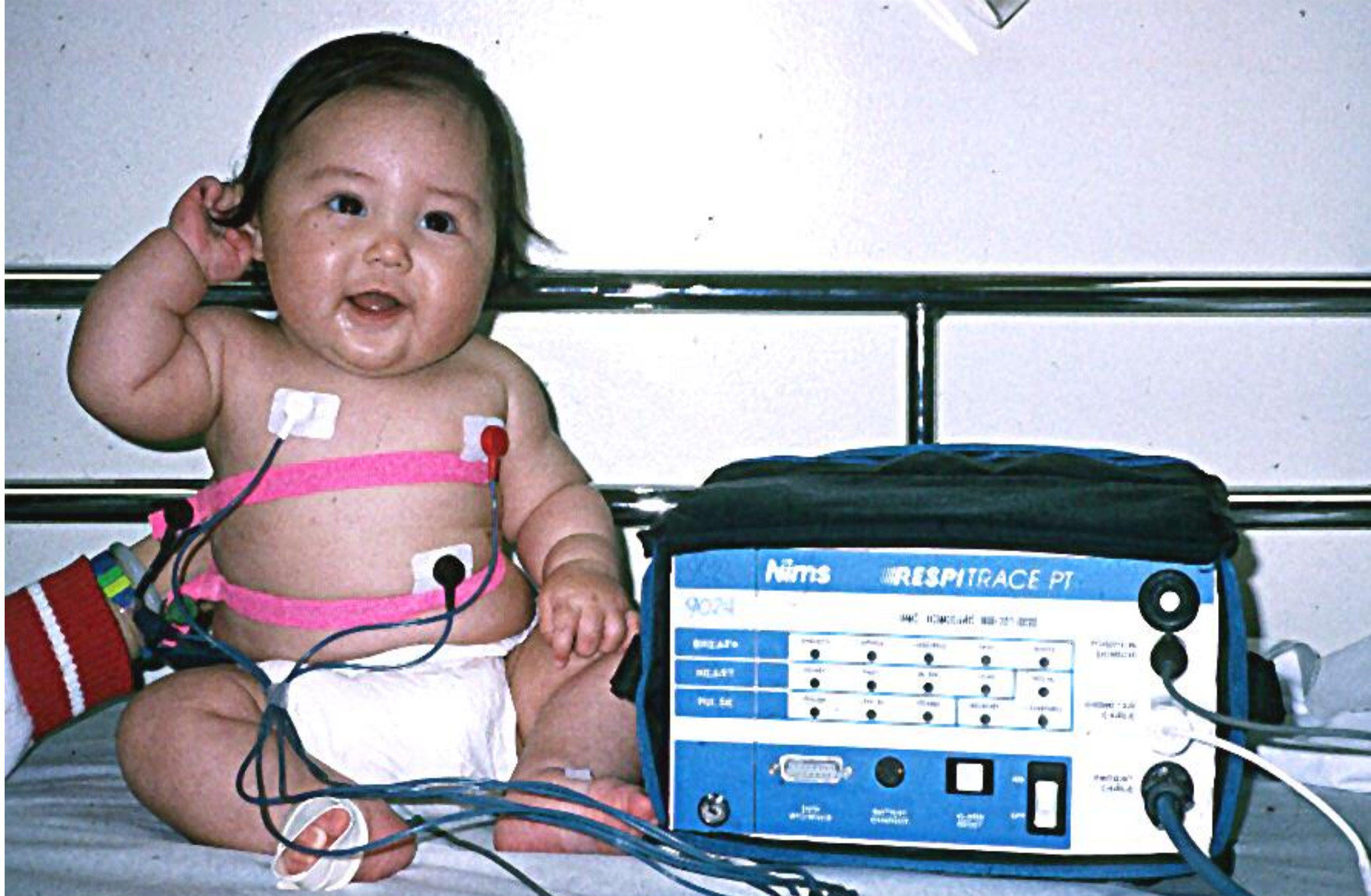
Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.  
Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.



**The CHIME Home Monitor (Non Invasive Monitoring Systems, Miami, Florida, U.S.A.)  
Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.**



Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.



Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.

215 %Vt

Vt

215 %Vt

RC

215 %Vt

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0 BM

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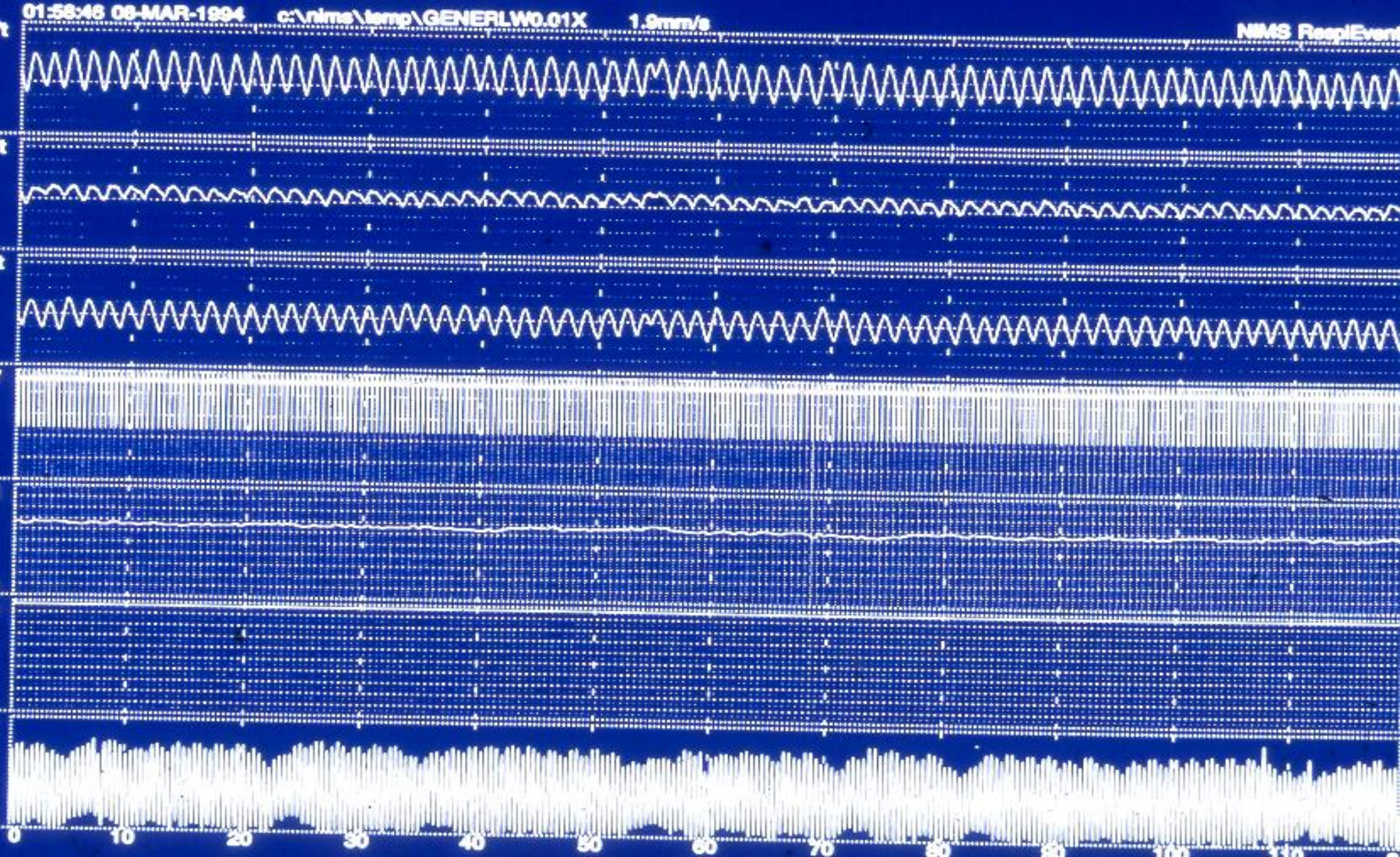
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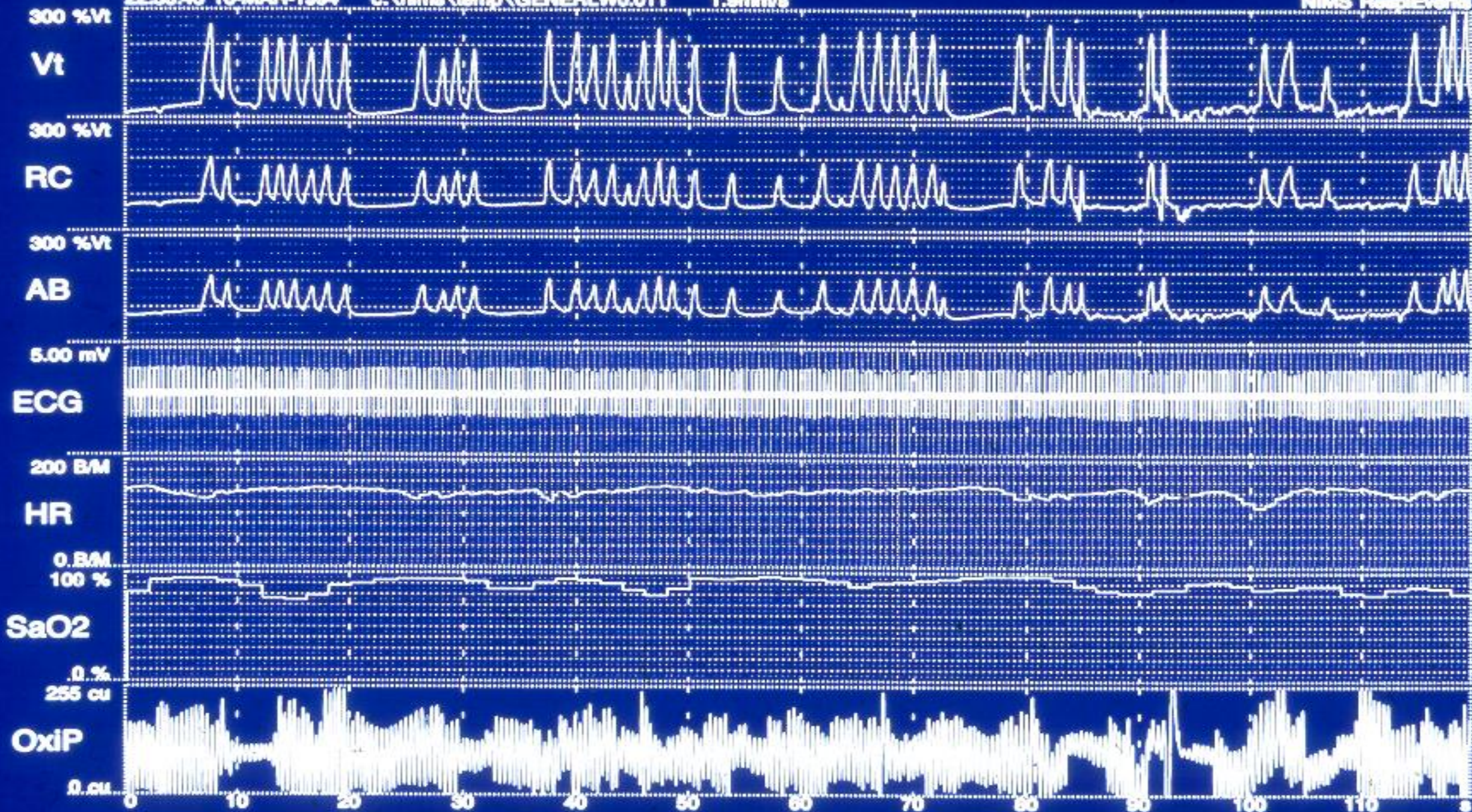
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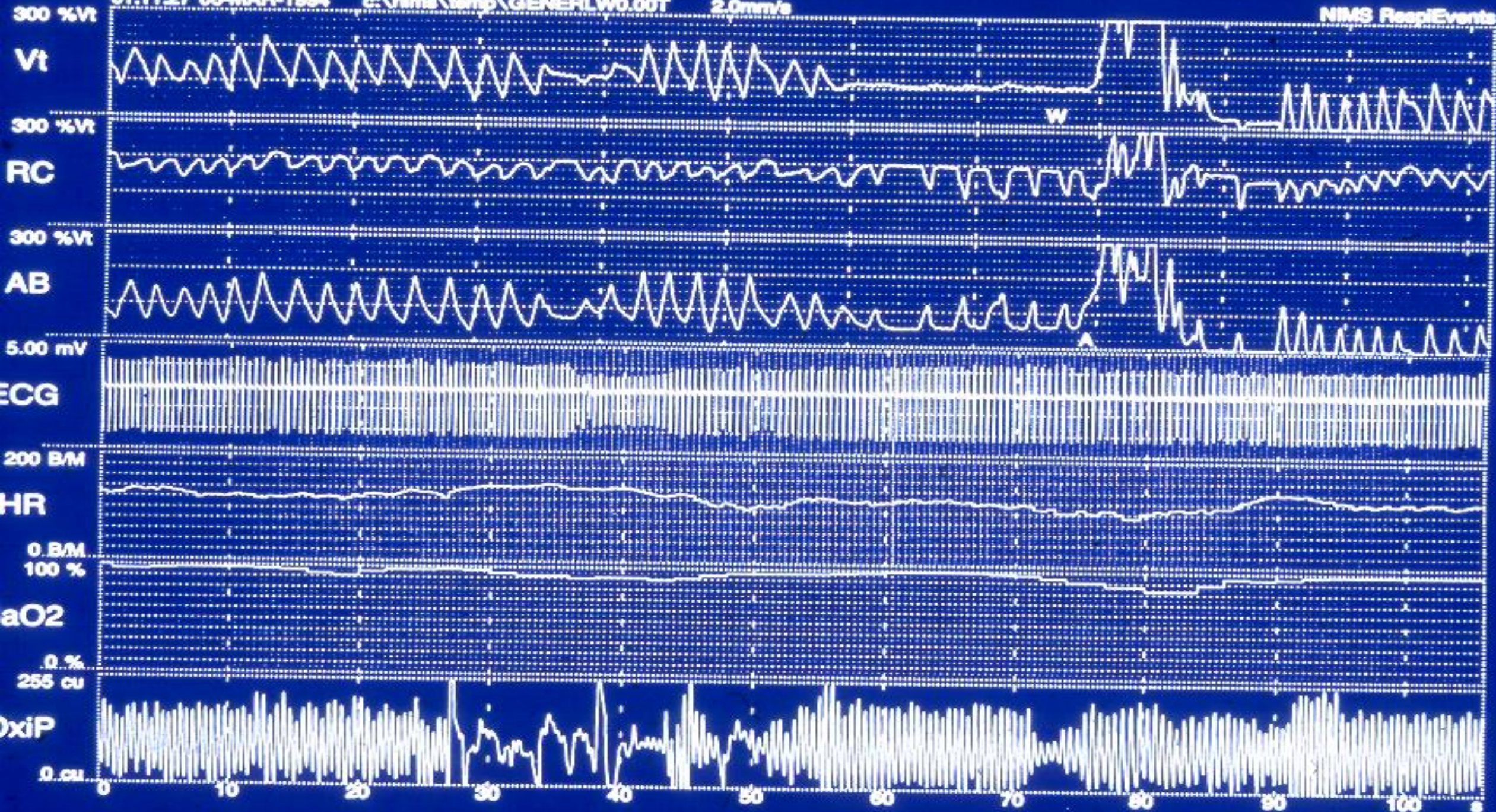


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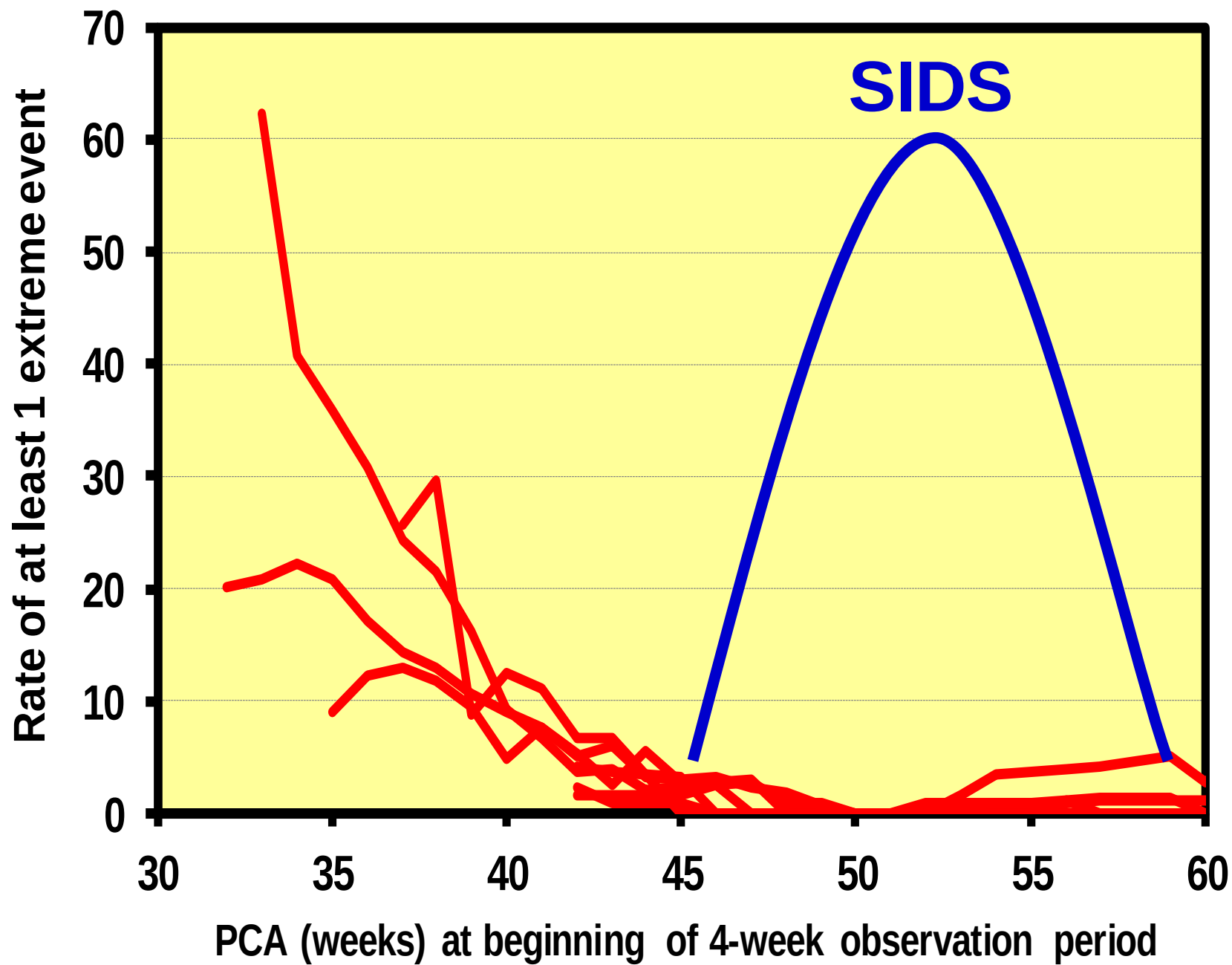
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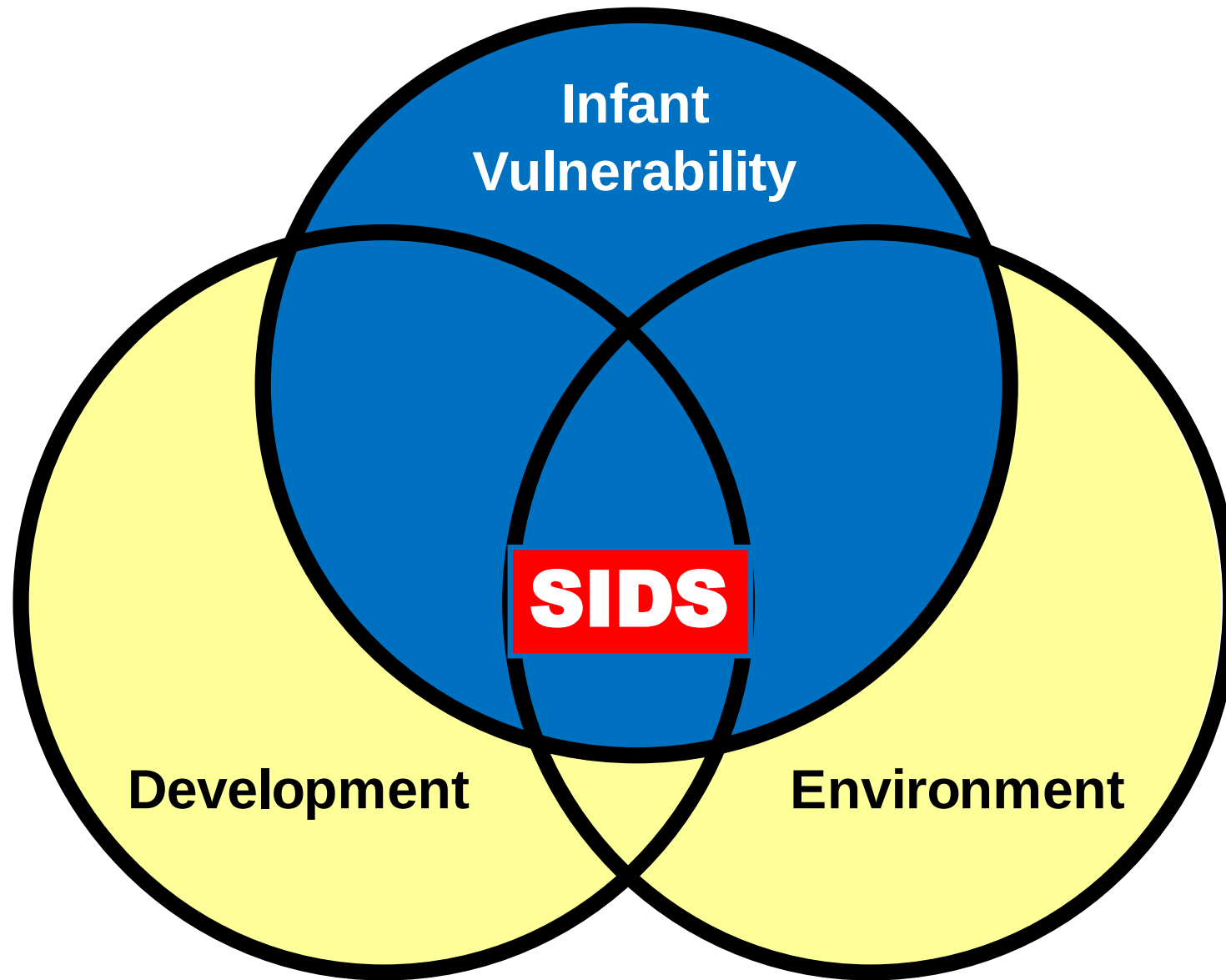
# **Is SIDS a Catastrophic Physiologic Crisis?**



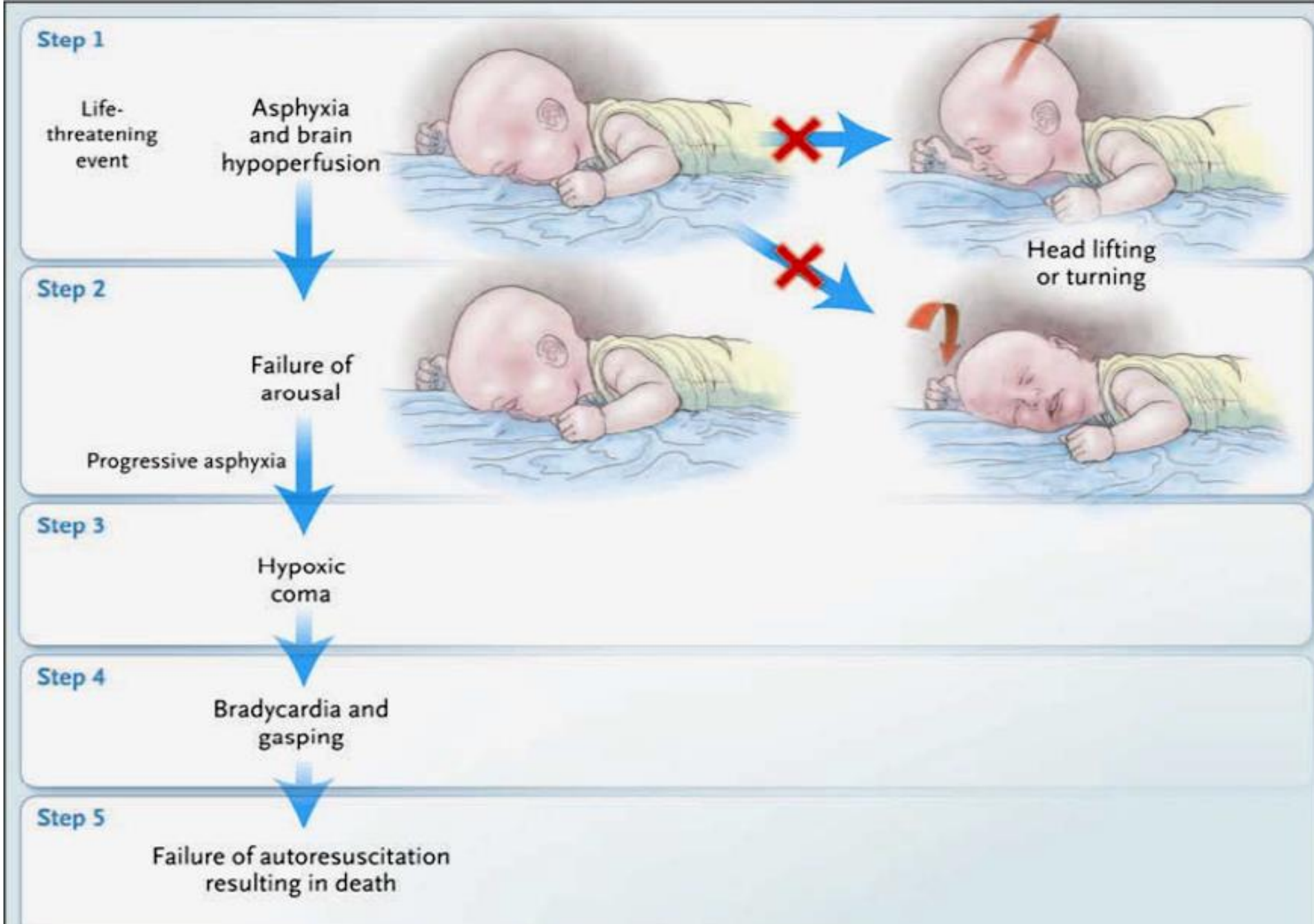
- **If normal infants do not precisely control breathing, heart rate, and oxygenation ...**
- **Then SIDS may not have to be a catastrophic physiological crisis.**
- **Maybe it just needs to be a small problem which nudges or pushes a vulnerable infant over the edge.**



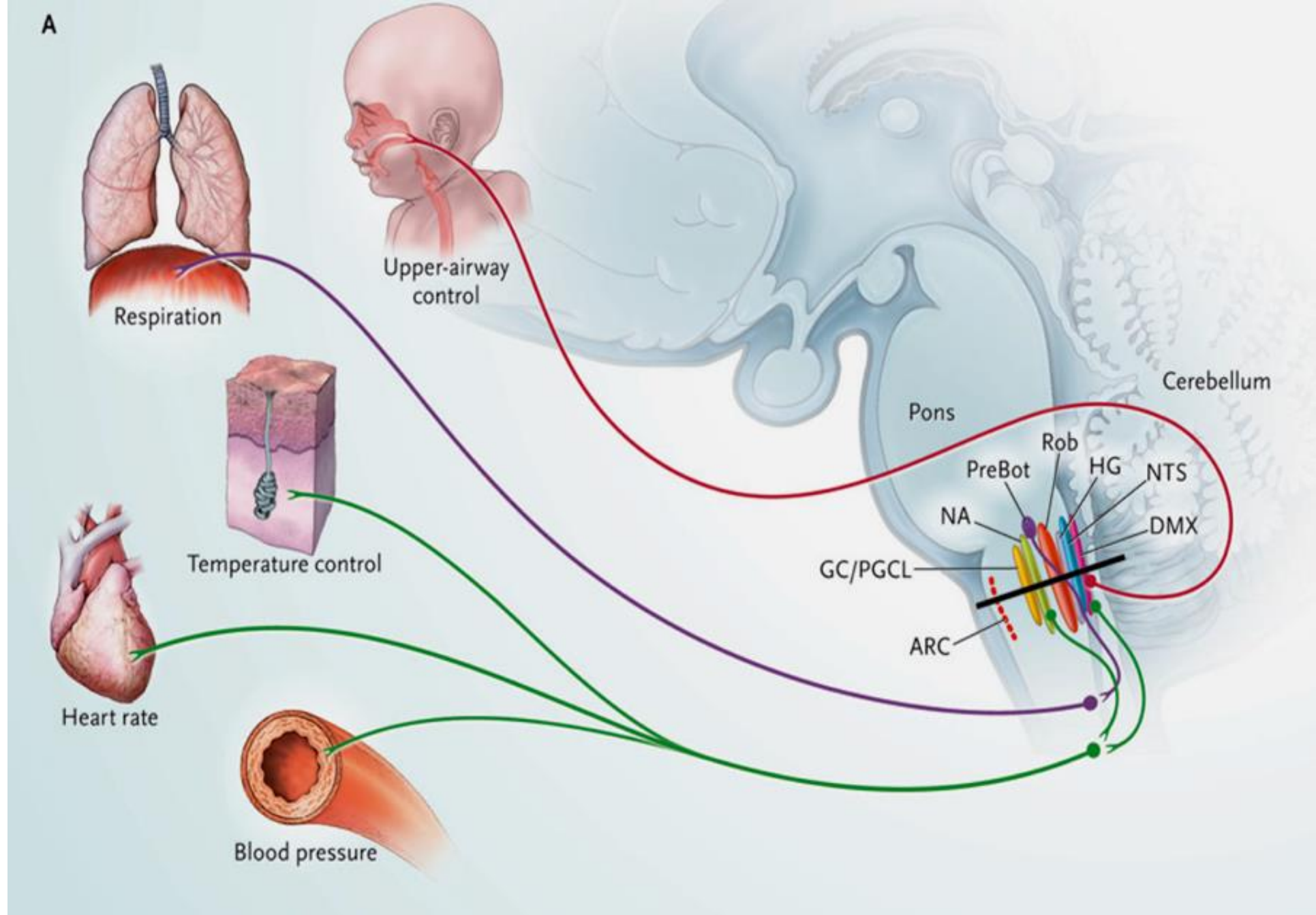
Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.



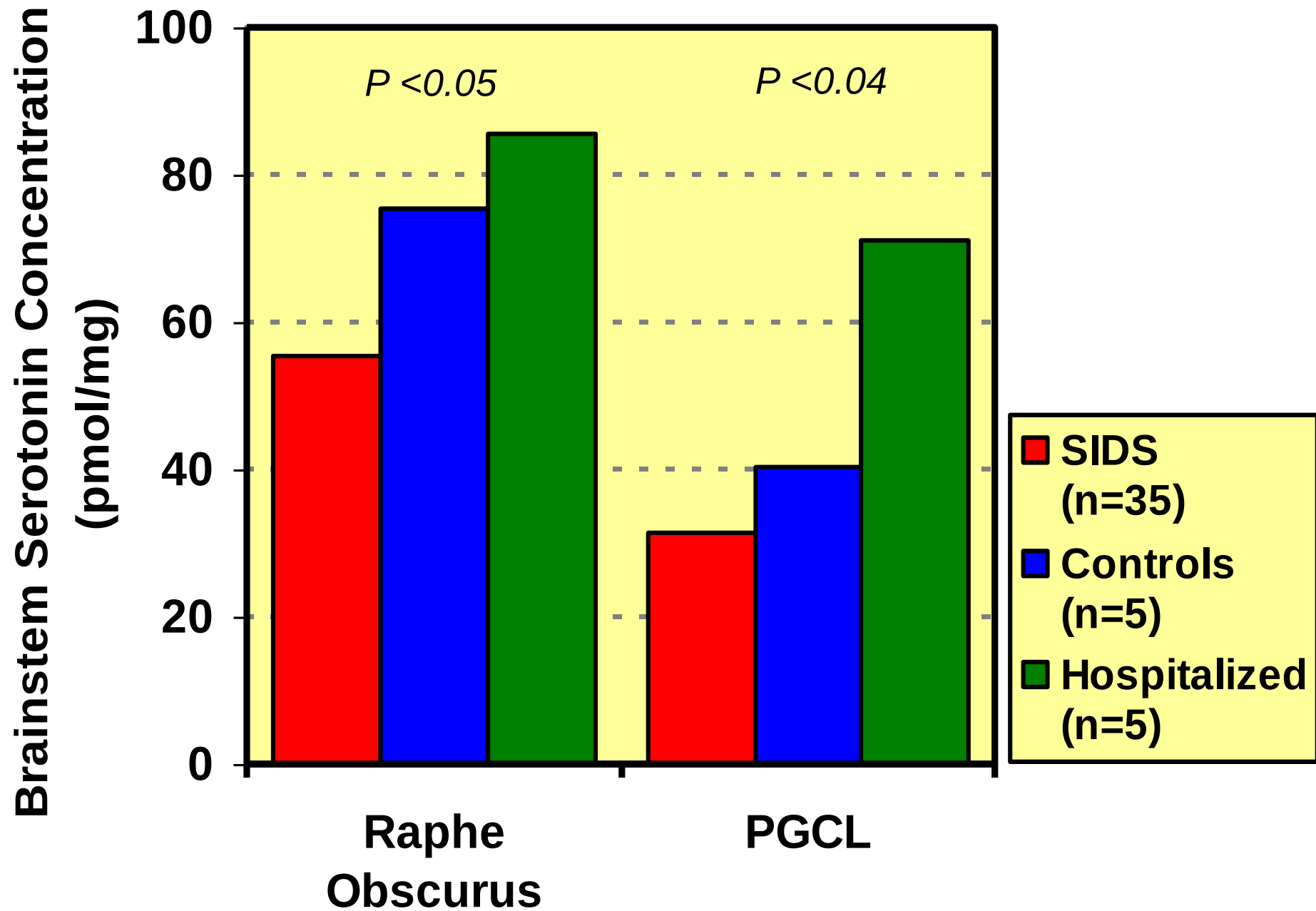
Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.



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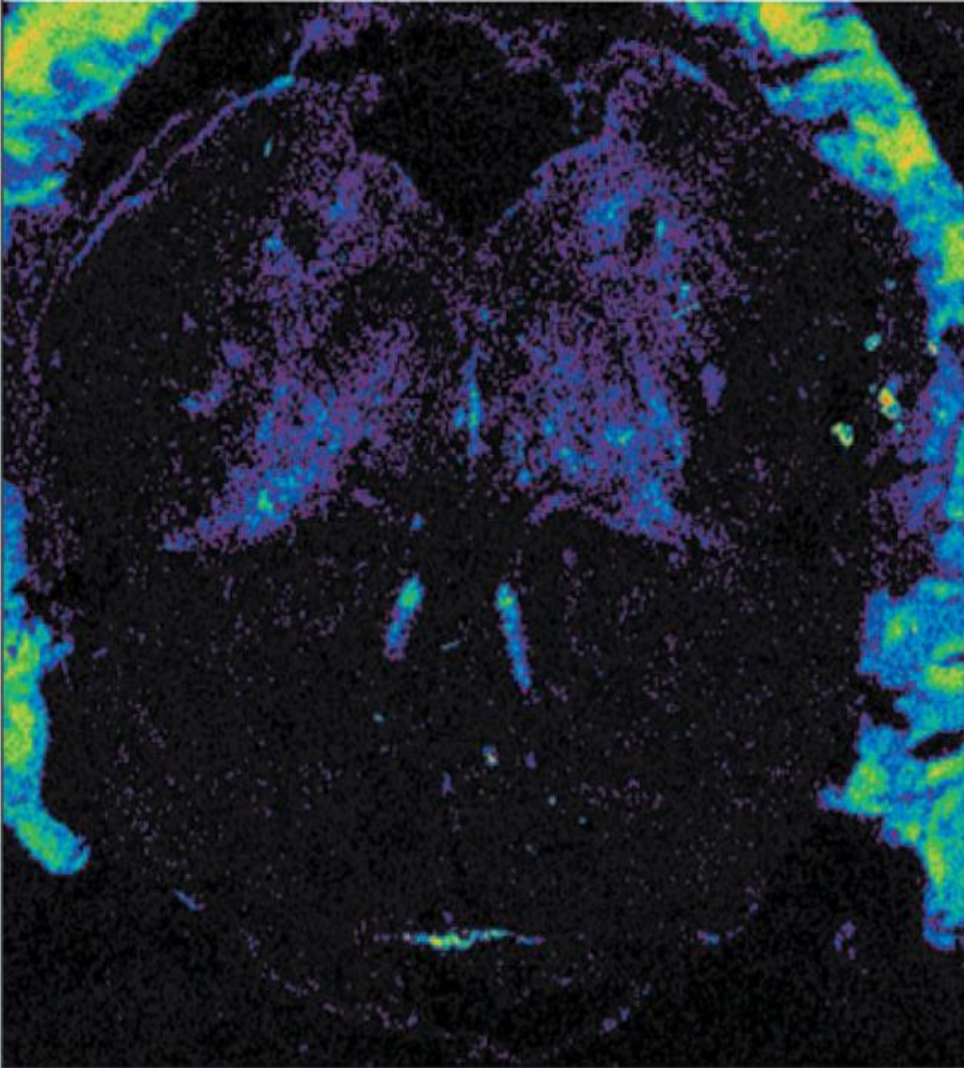




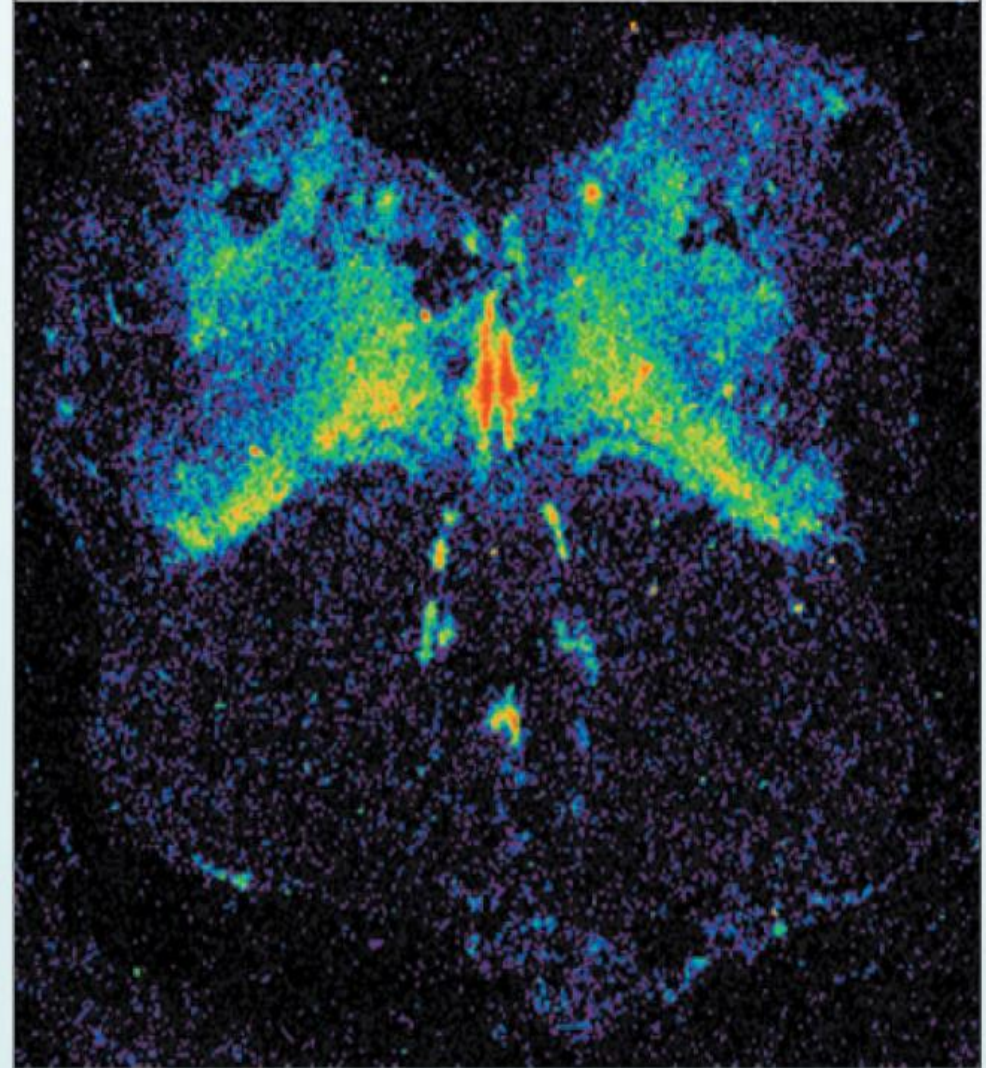
# 5-HT<sub>1A</sub> Receptor Binding Density in SIDS Brainstems



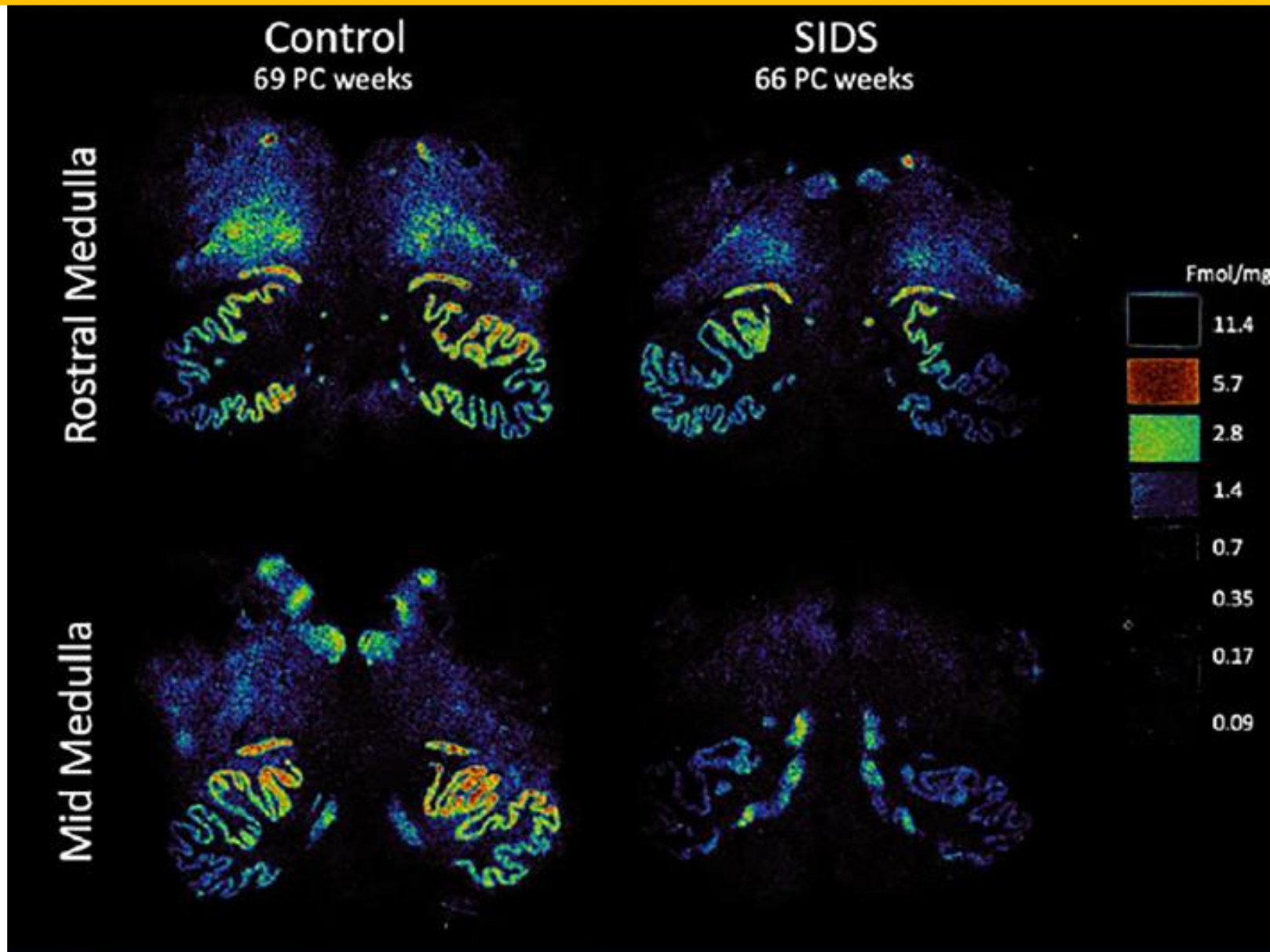
**B** Infant with Sudden Infant Death Syndrome



**C** Control Infant

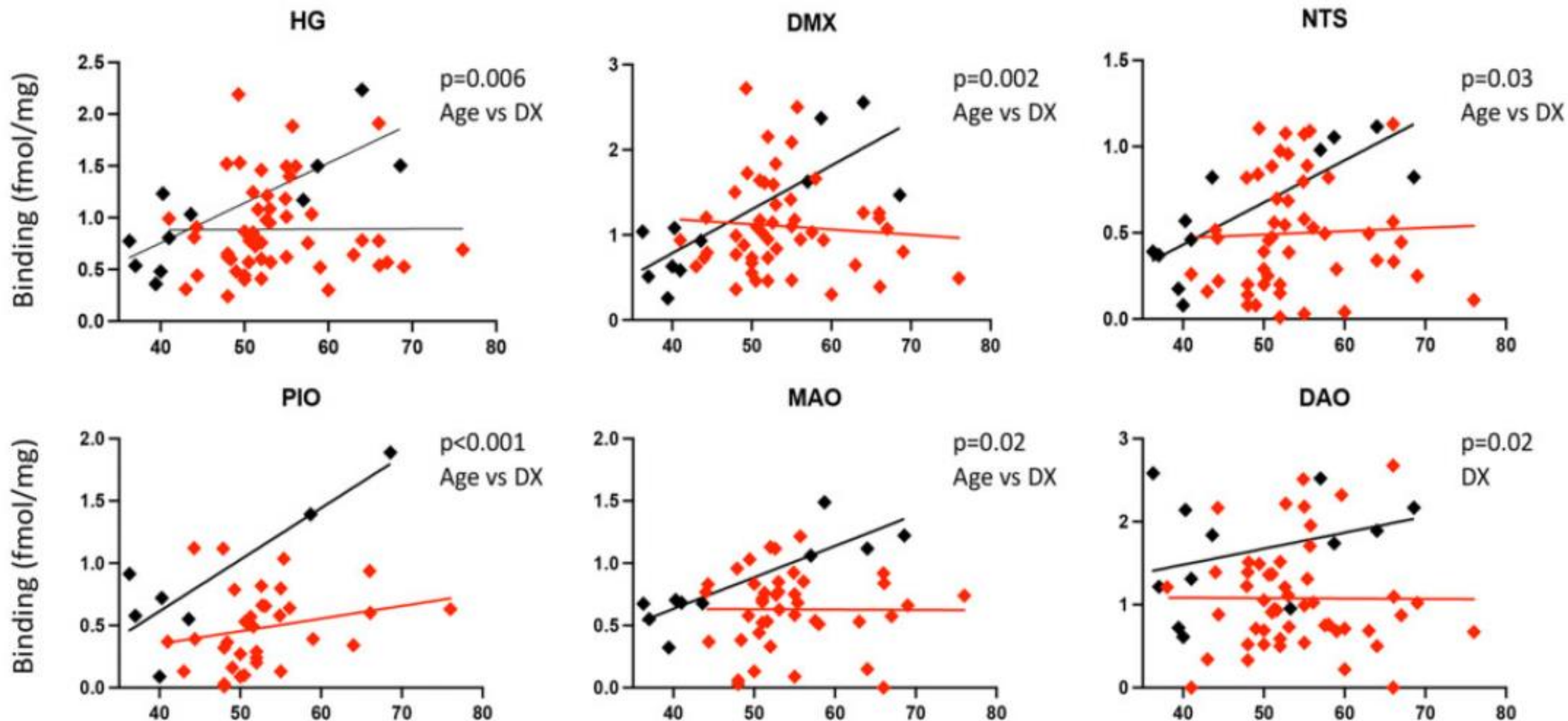


Paterson, D.S., et al. *J. Amer. Med. Assoc.*, 296: 2124-2132, 2006.

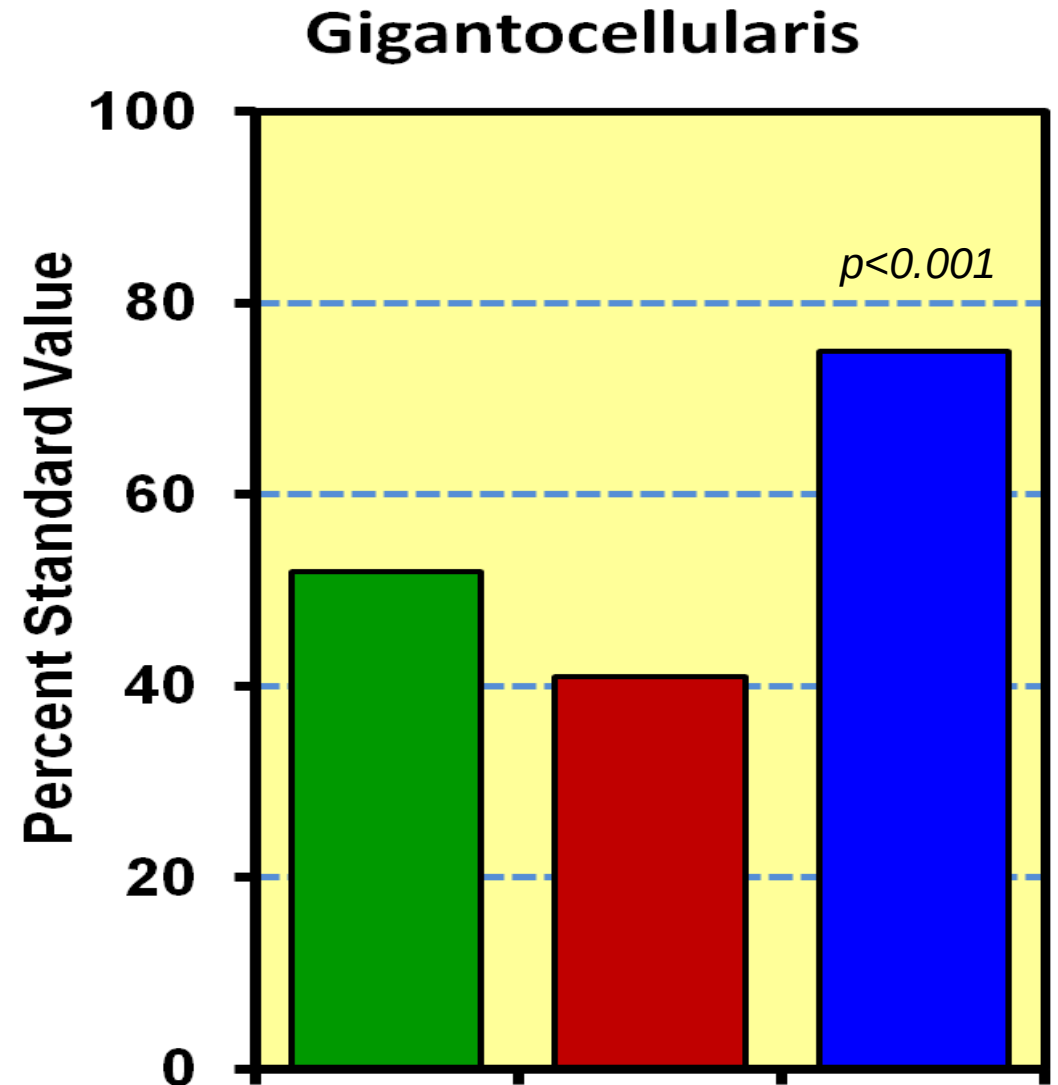
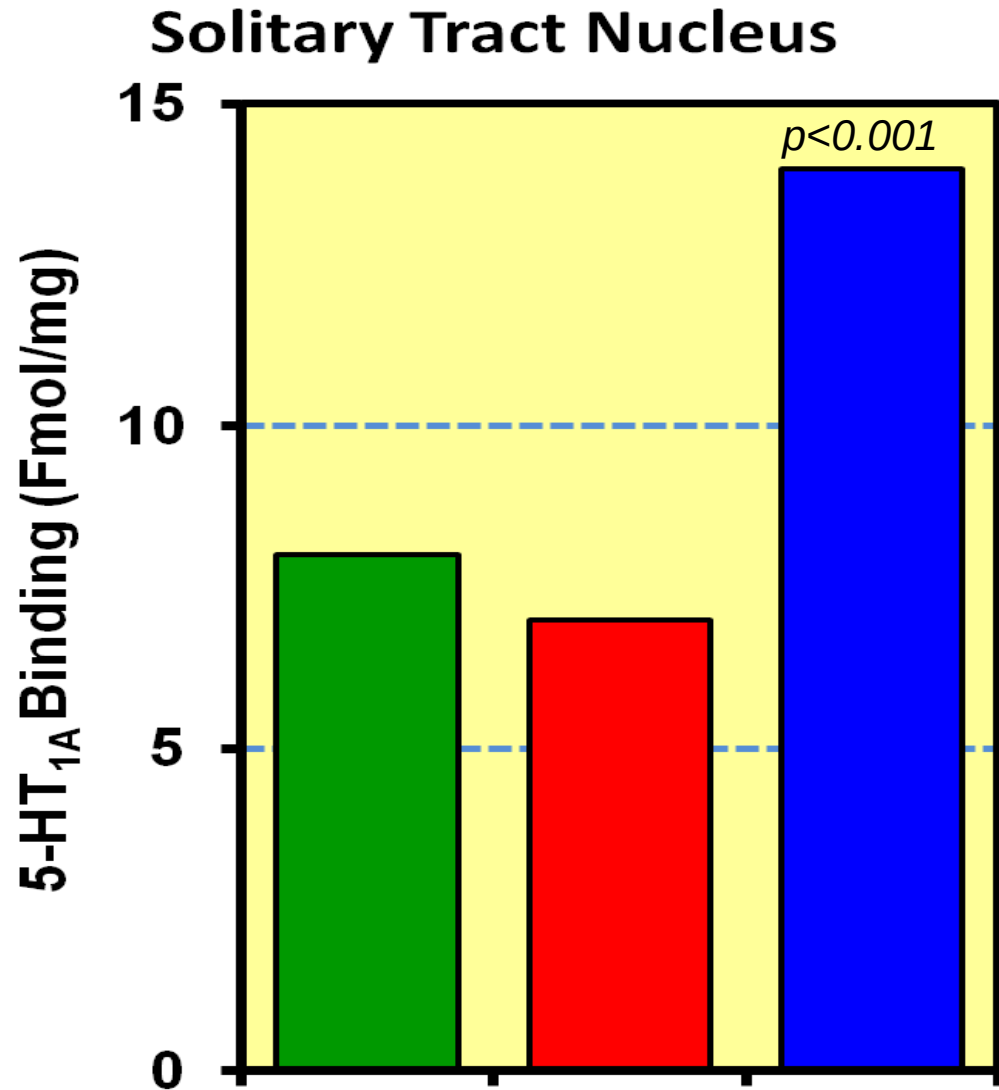




# 5-HT<sub>1A</sub> Receptor Binding Density in SIDS Brainstems



- Sudden death without Asphyxia
- Sudden death with Asphyxia
- Known Cause of Death





**Accidental  
Asphyxia or  
Suffocation**

**Sudden  
Death with  
Asphyxia**

**Sudden Death  
without  
Asphyxia**

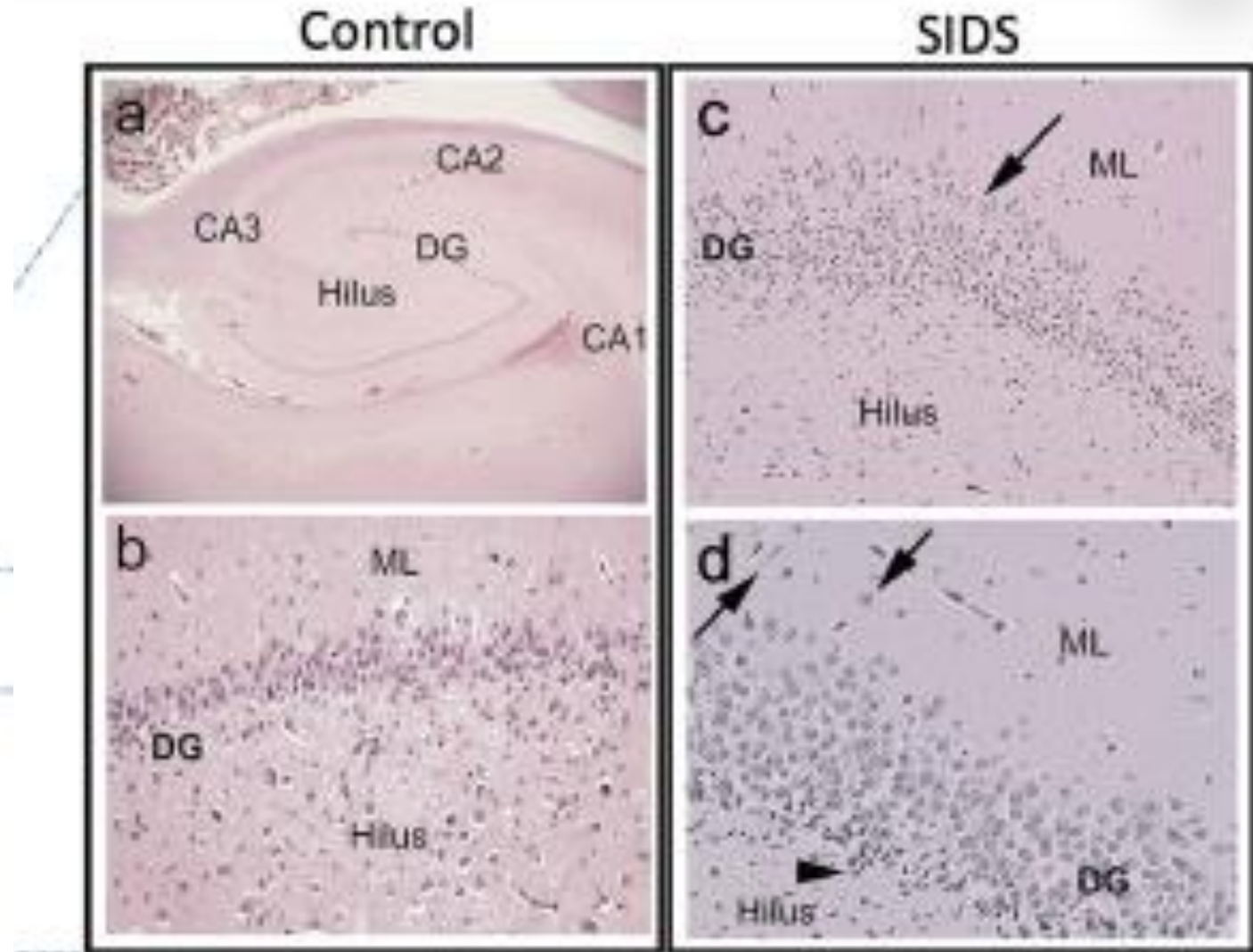
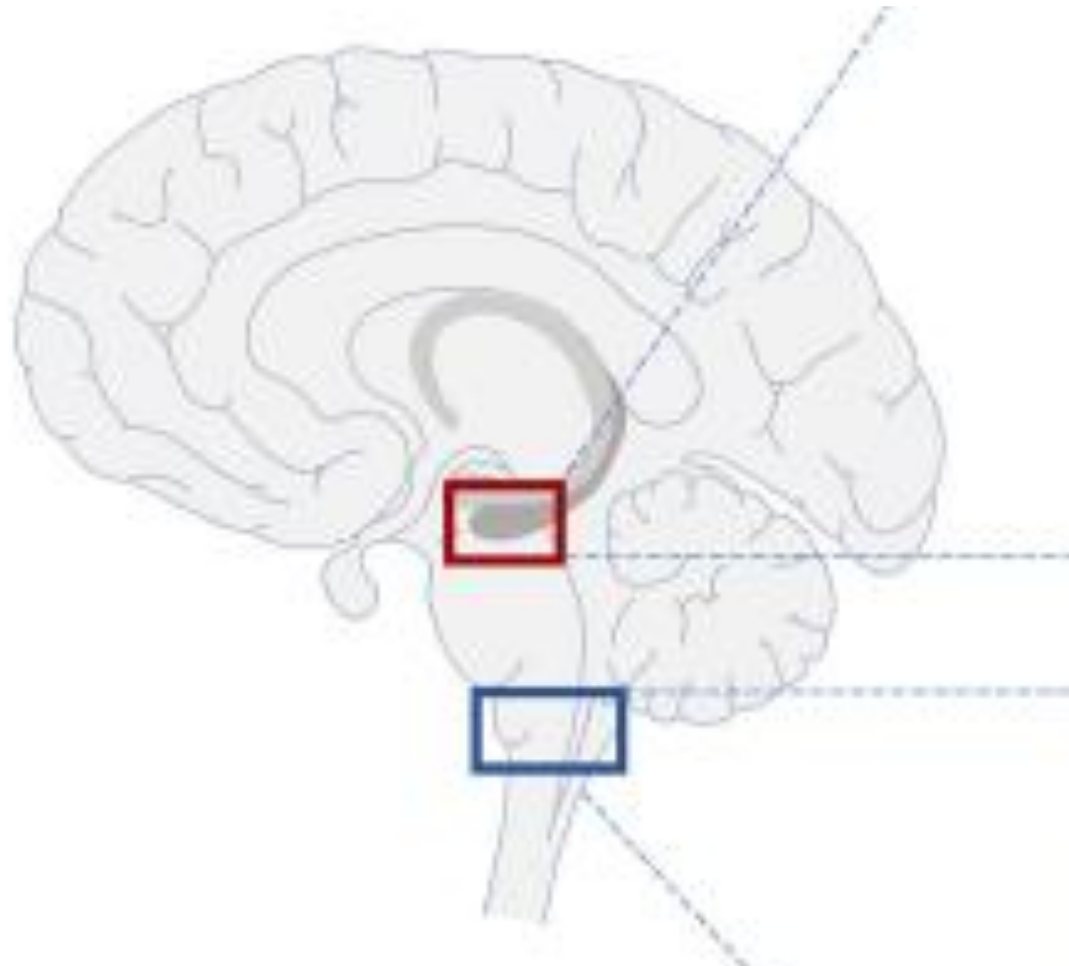


Randall, B.B., et al. *Pediatrics*, doi: 10.1542/peds.2013-0700. 2013.  
Goldstein, R.D., et al. *Pediatrics*, 137: e20154661, 2016.



# SUDDEN UNEXPLAINED DEATH IN CHILDHOOD

# Hippocampal Abnormalities Found in Febrile Convulsions, SUDC, and some SIDS





Hannah Kinney.  
Neuropathologist.  
Harvard Medical School.

- SUDC have a high incidence of febrile convulsions and hippocampal abnormalities.
- Similar findings observed in some SIDS.

Kinney, H.C., et al. *Pediatr. Dev. Pathol.*, 12: 455–463, 2009.

Rodriguez, M.L., et al. *Forensic Sci. Med. Pathol.*, 8: 441–446, 2012.

Kinney, H.C., et al. *Acta Neuropathol.*, 129: 65–80, 2015.

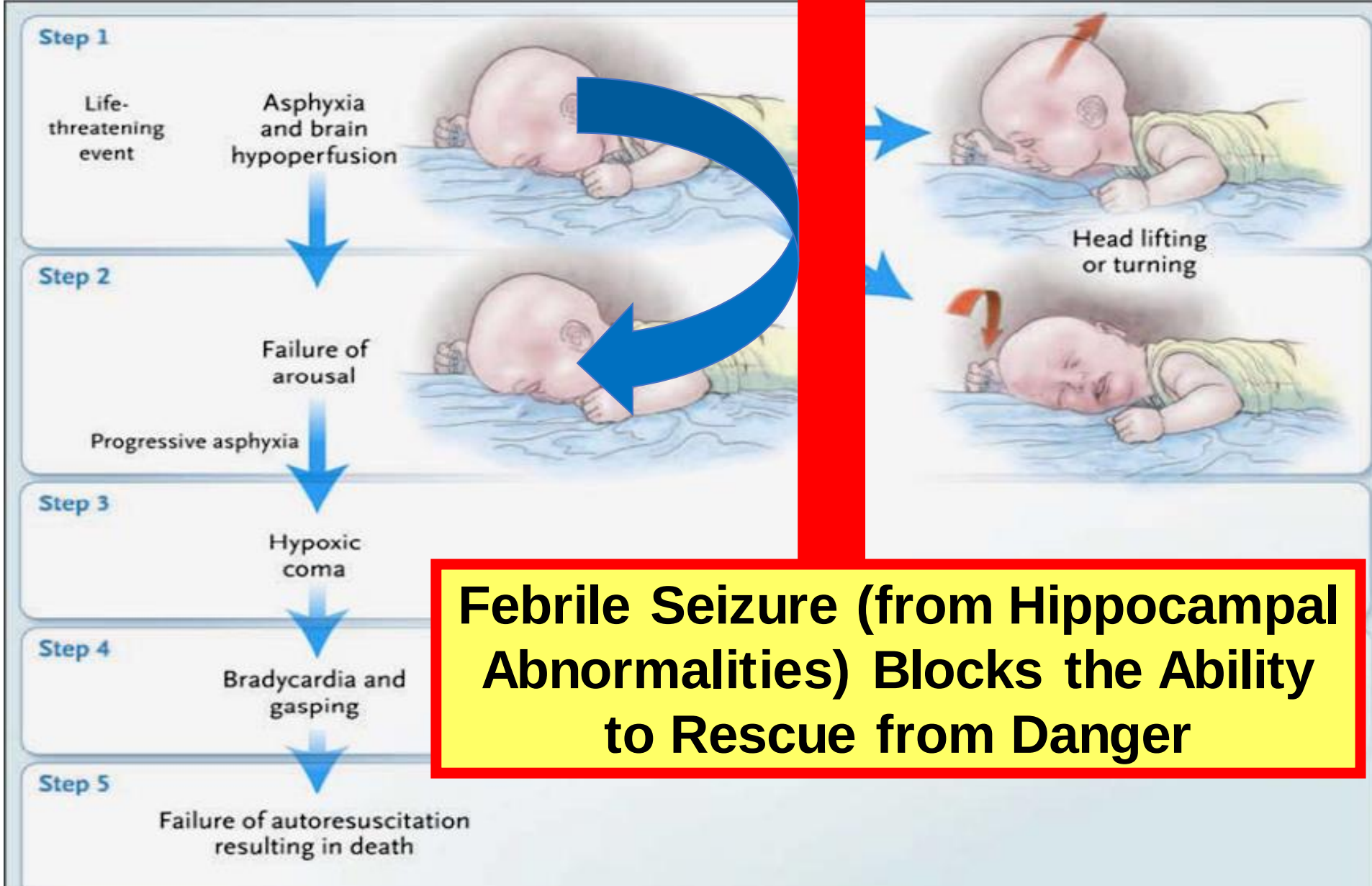
Hoppenbrouwers, T. *J. Child Neurol.*, 30: 904-911, 2015

Hefti, M.M., et al. *Forensic Sci. Med. Pathol.*, 12: 4-13, 2016.

Hefti, M.M., et al. *Forensic Sci. Med. Pathol.*, DOI 10.1007/s12024-015-9731-3, 2016.

Smith, C. *Forensic Sci. Med. Pathol.*, 12: 202–203, 2016.

Goldstein, R.D., et al. *Pediatrics*, 137: e20154661, 2016.

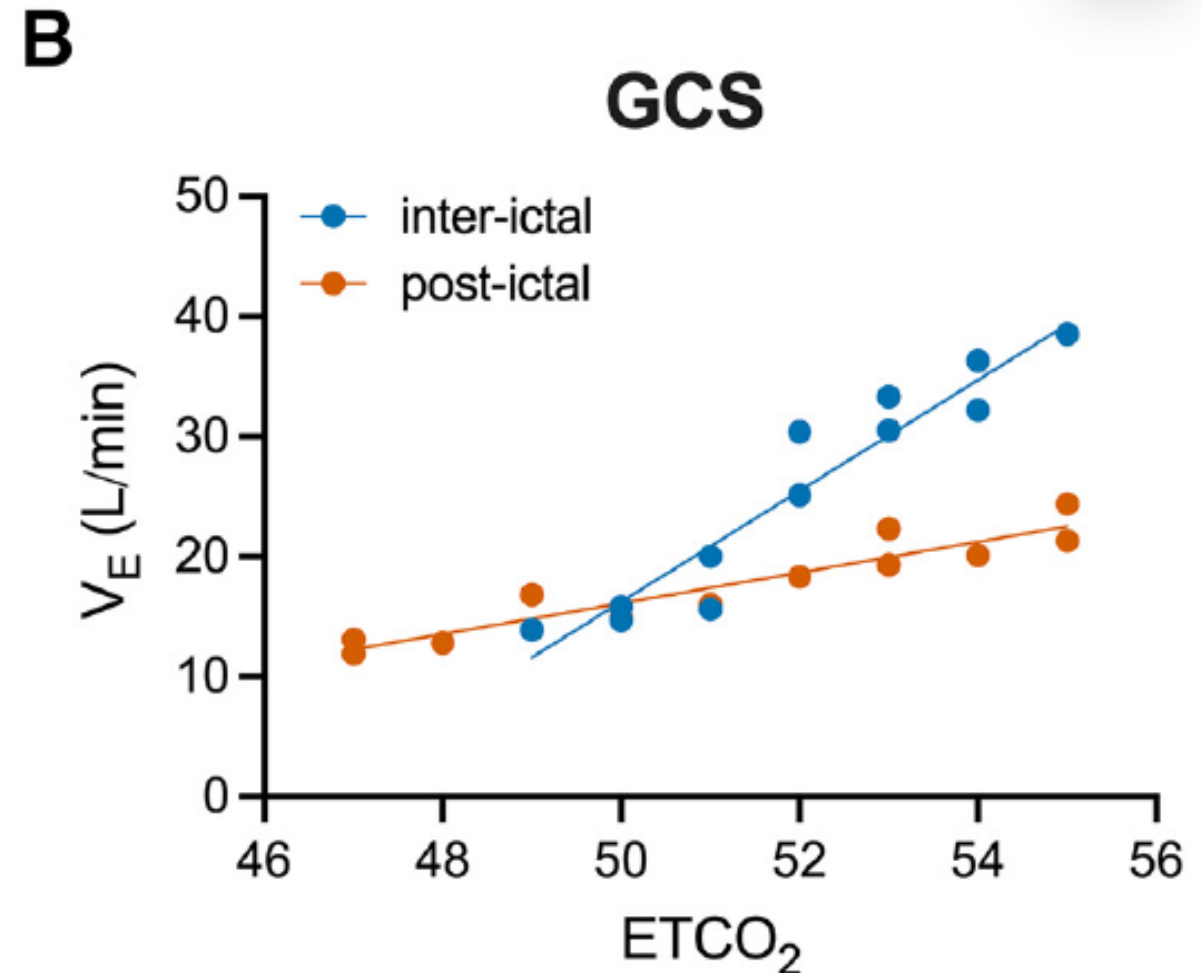
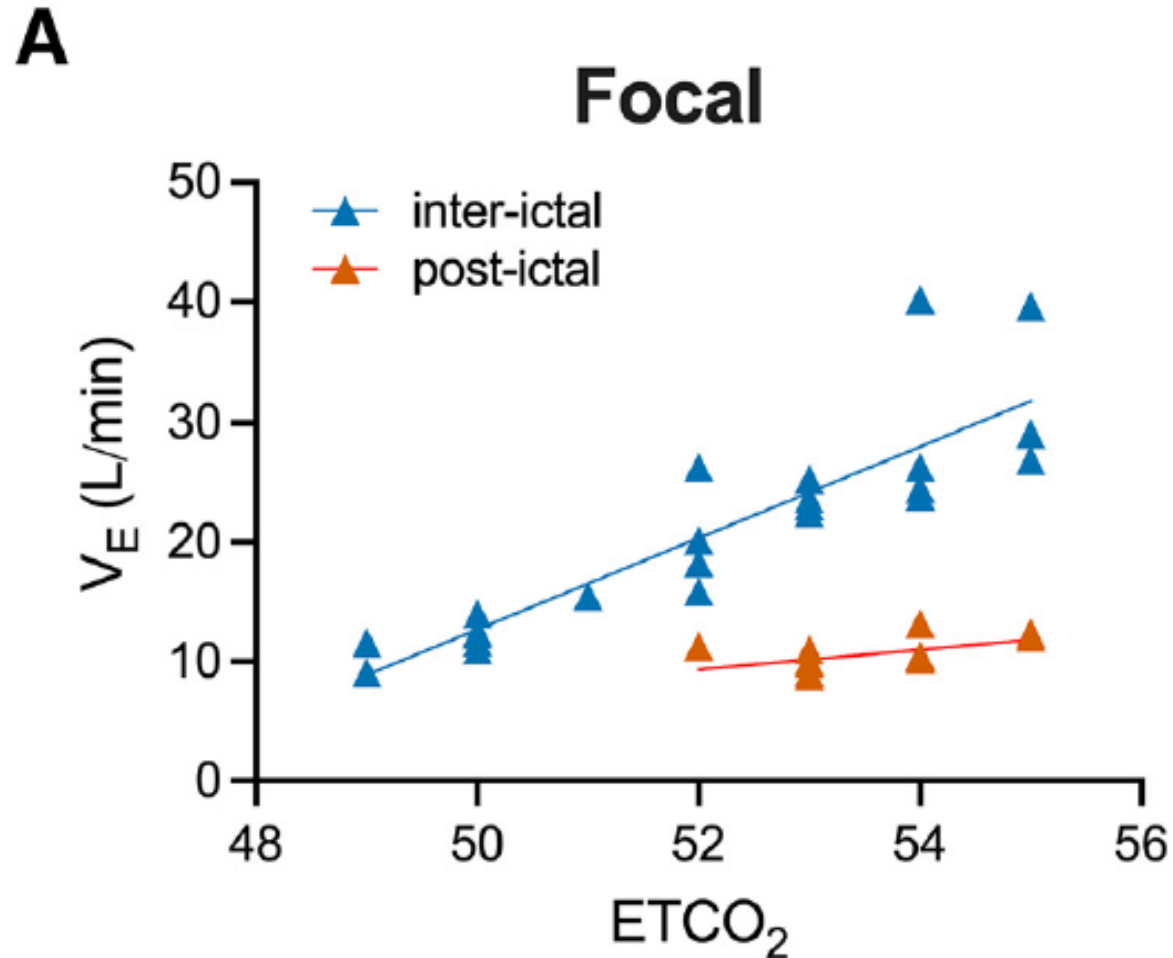


Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.

Kinney, H.C., et al. *Pediatr. Dev. Pathol.*, 12: 455–463, 2009.

Smith, C. *Forensic Sci. Med. Pathol.*, 12: 202–203, 2016.

# Hypercapnic Ventilatory Response Decreased in Post-Ictal State



Teran, F.A., et al. *J. Neurosci.*, 43: 4959-4971, 2023.

# Video Recordings of SUDC



- **Video recordings from baby monitors of death in seven toddlers age 13-27 months.**
- **Six of the seven recordings showed a terminal convulsive event lasting 8-50 seconds.**
- **Four of the seven children survived for over 2½-minutes after the convulsive event.**
- **Only one child in this study had a personal or family history of febrile convulsions.**
- **Speculate that many unexplained sleep-related deaths may result from seizures.**

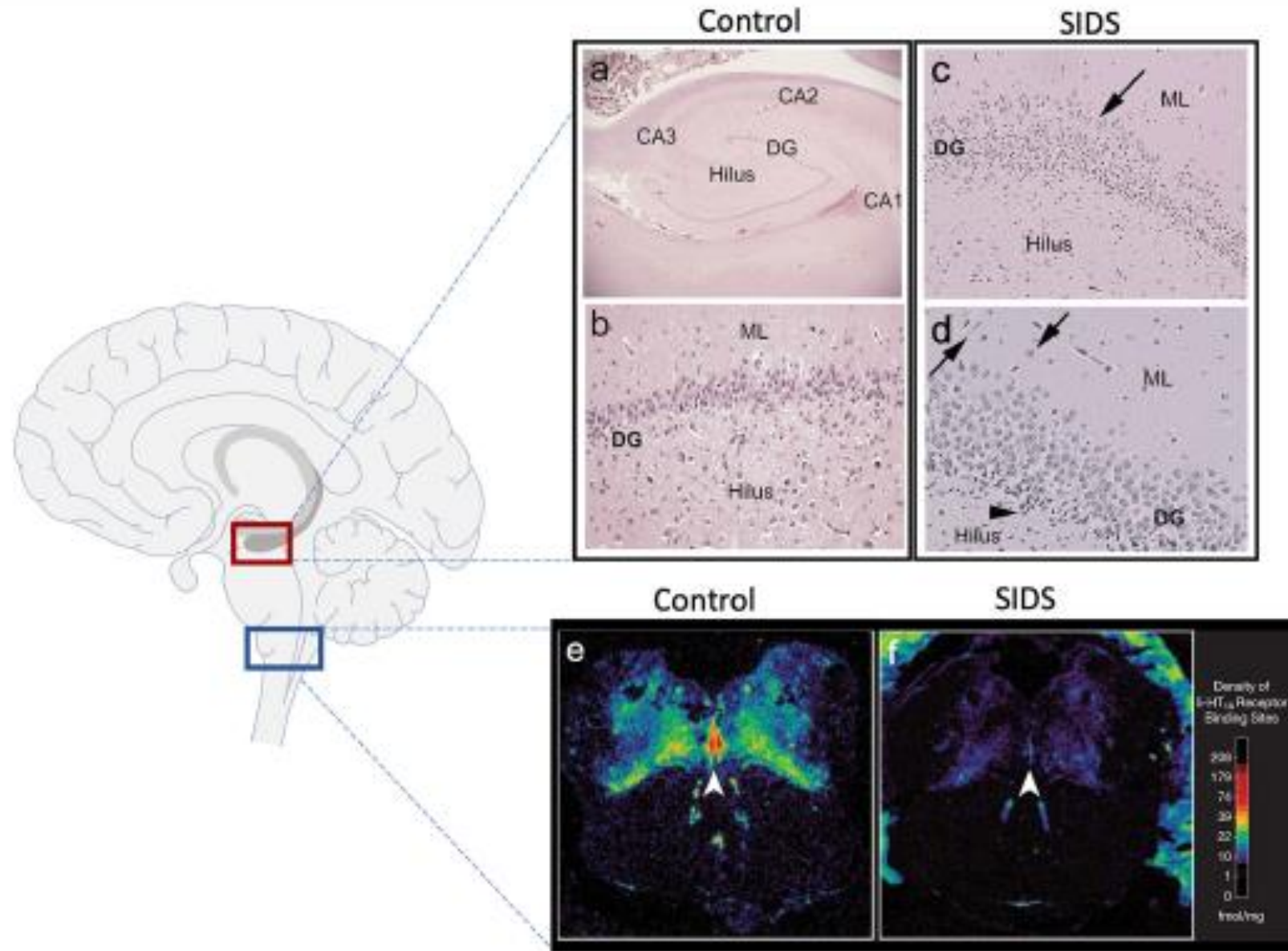


- **SUDC Video recordings suggest seizures are an etiology of SUDC and some SIDS.**
- **There are unanswered questions.**
- **Do most or all SUDC die from seizures?**
- **How does this relate to SIDS?**
- **How many SIDS may die from seizures?**
- **Research should pursue seizures as a cause of death in at least some SIDS.**

**Hoppenbrouwers, T. *J. Child Neurol.*, 30: 904-911, 2015.**

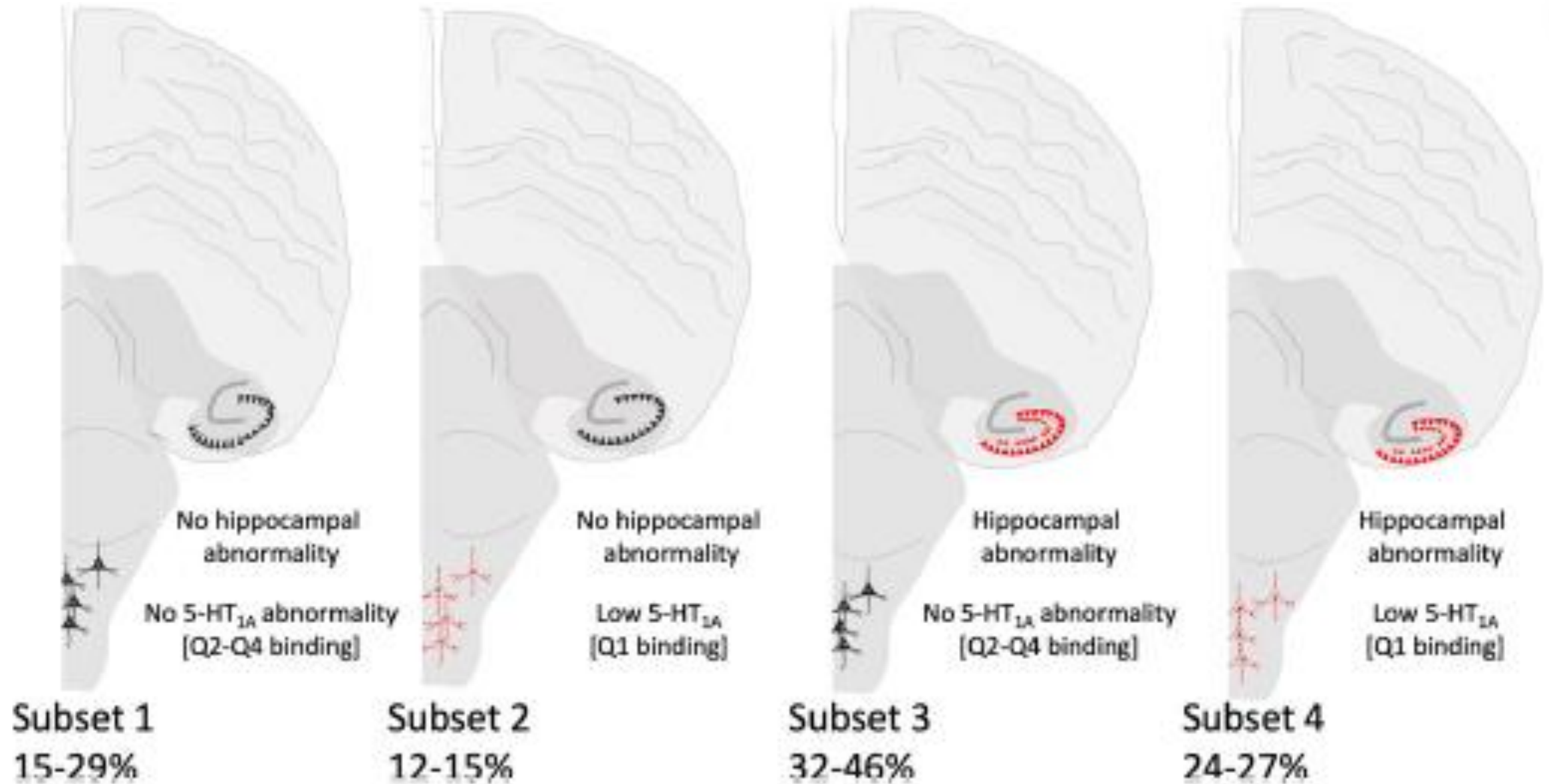
**Gould, L. et al. *Neurology*, 102: e208038, 2024.**

# Are These One Abnormality or Two?

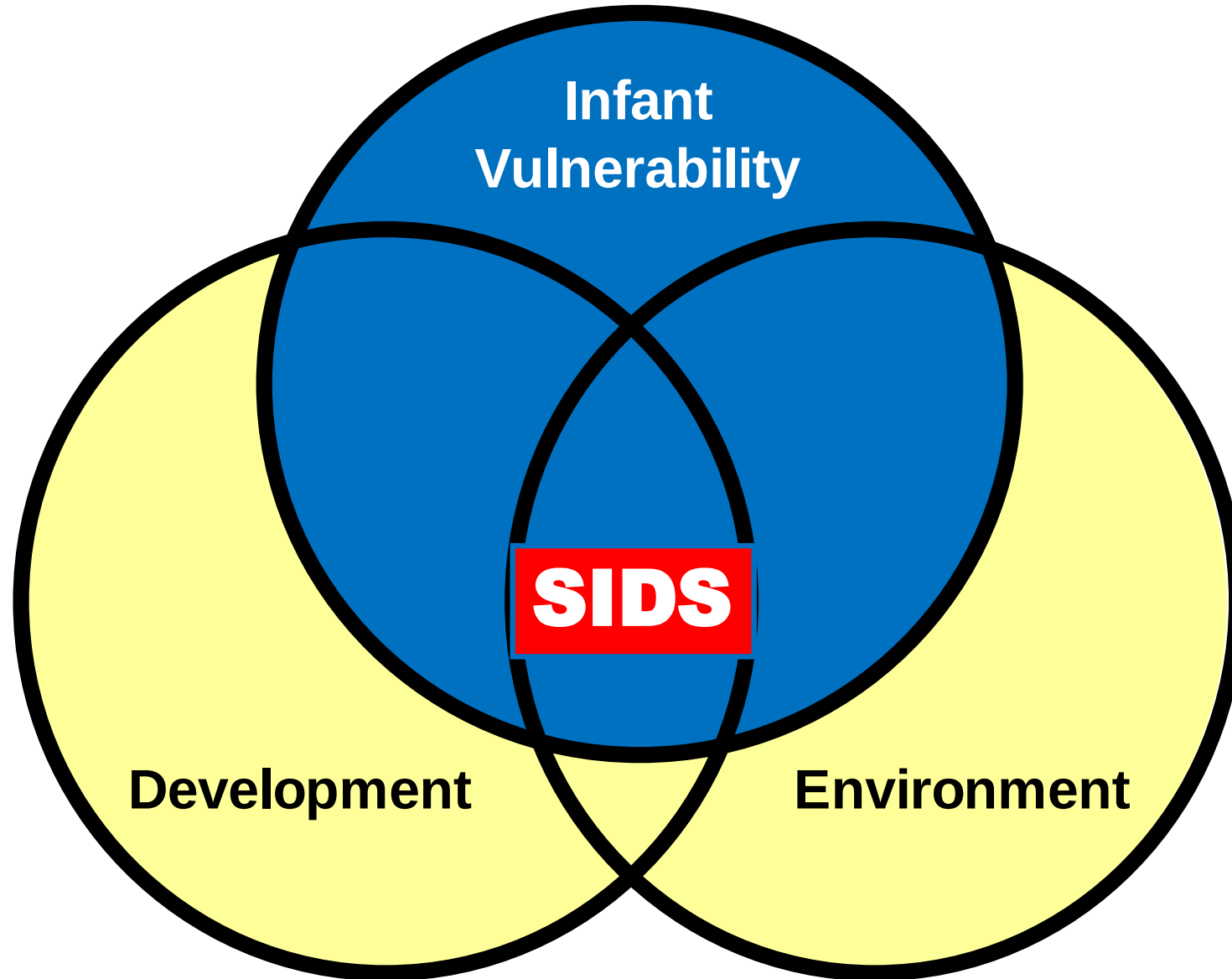


Haynes, R.L., et al. *Front. Pediatr.* 9: 762017, 2021.

# Are These One Abnormality or Two?



# Infant Vulnerability may have Many Causes



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

# How Are We to Understand SIDS?



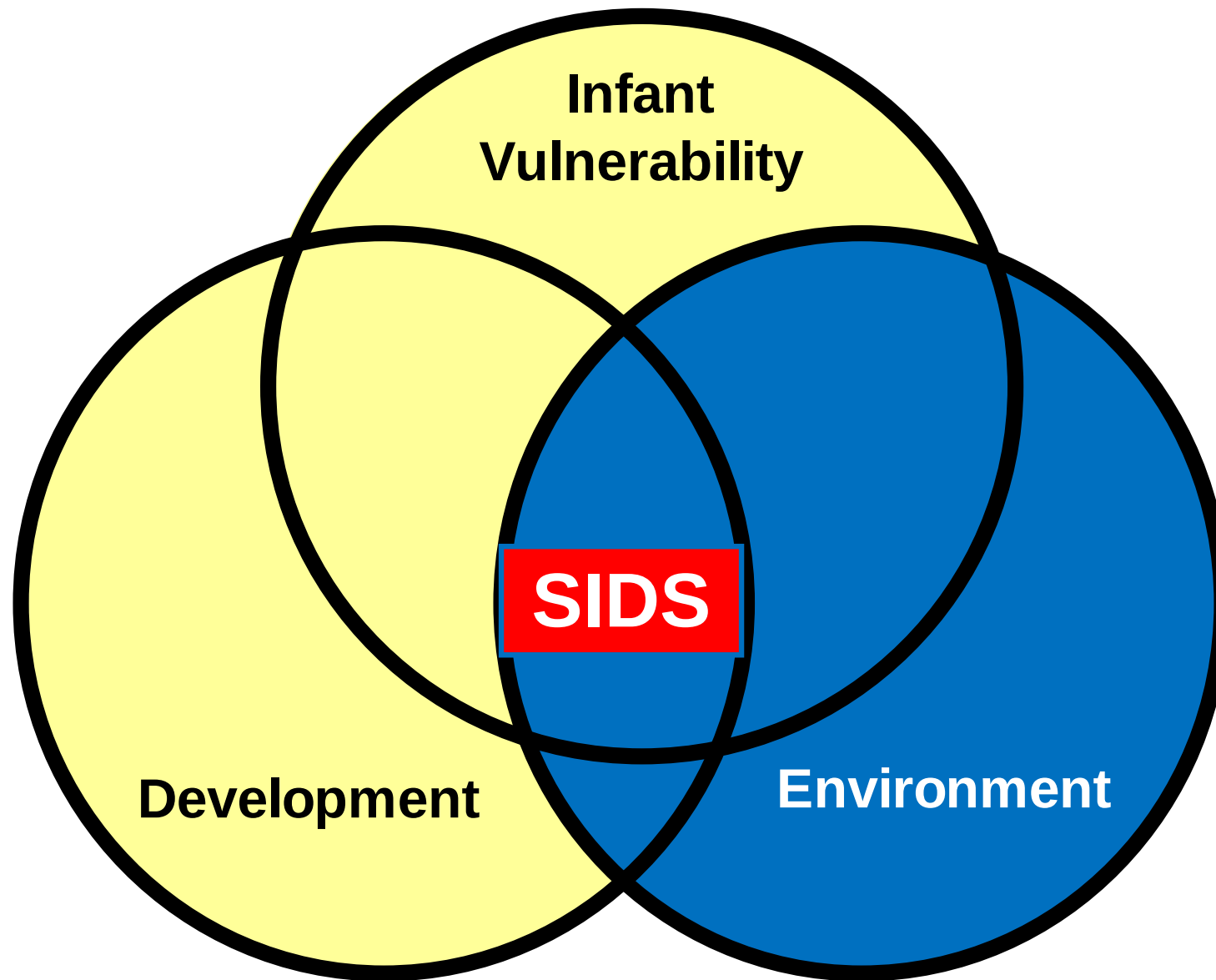
Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

## A New Way of Thinking:

- Some cars are Ferrari's.
- Some cars are Jeep's.

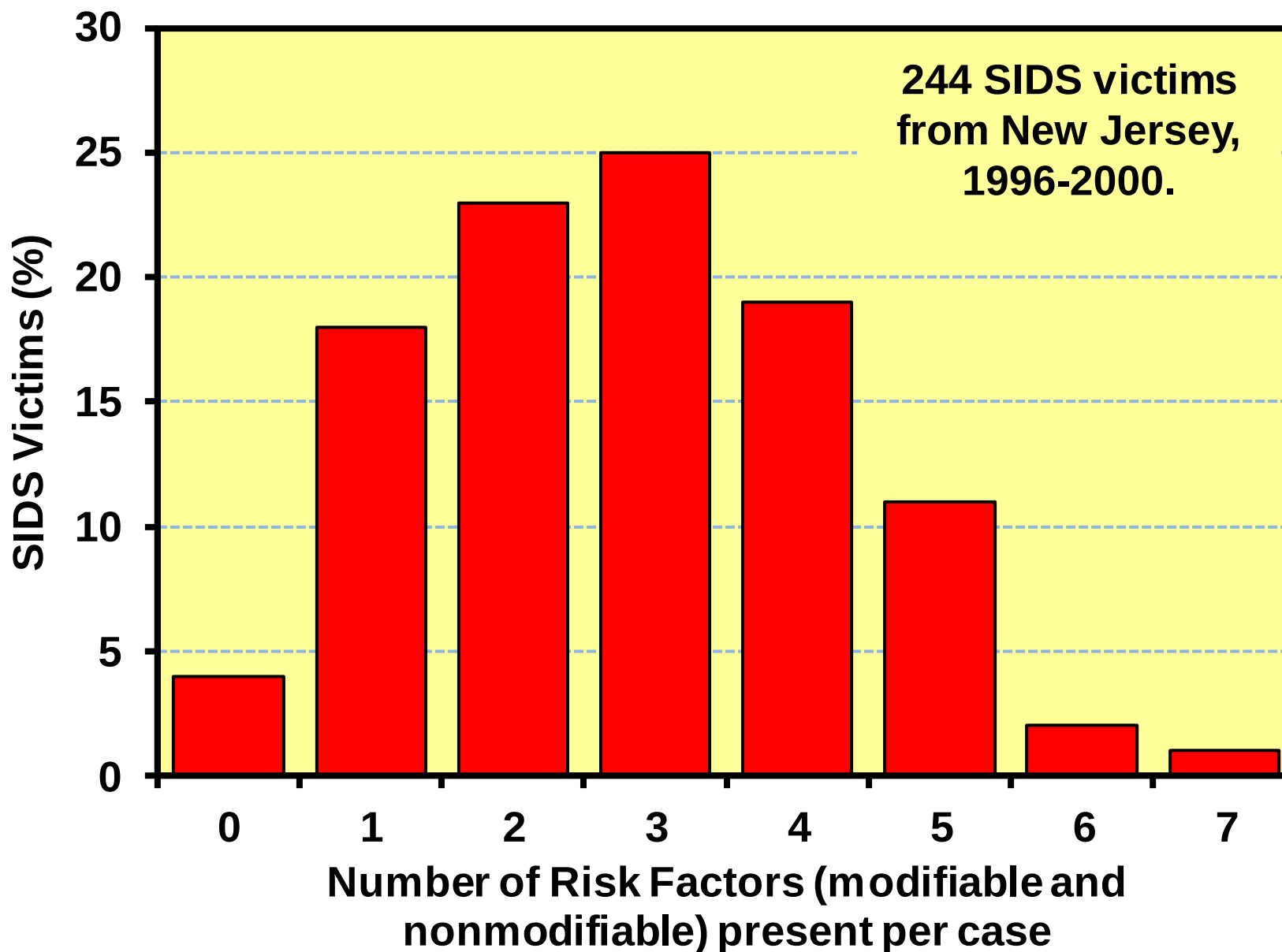


Modified after Professor Jacopo P. Mortola. McGill University.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

# Most SIDS Victims Have $\geq 1$ Risk Factor



Ostfeld, B.M., et al. *Pediatrics*, 125: 447-453, 2010.

# How can we, as a population, reduce the risk of SIDS?



# **Risk Factors $\neq$ Causes**

- **Most infants with risk factors will not die from SIDS.**
- **Some infants without risk factors will die from SIDS.**
- **However, infants with risk factors are at increased risk of dying from SIDS.**

## POLICY STATEMENT

Organizational Principles to Guide and Define the Child Health  
Care System and/or Improve the Health of all Children

American Academy  
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

# Sleep-Related Infant Deaths: Updated 2022 Recommendations for Reducing Infant Deaths in the Sleep Environment

Rachel Y. Moon, MD, FAAP,<sup>a</sup> Rebecca F. Carlin, MD, FAAP,<sup>b</sup> Ivan Hand, MD, FAAP,<sup>c</sup>

THE TASK FORCE ON SUDDEN INFANT DEATH SYNDROME AND THE COMMITTEE ON FETUS AND NEWBORN

Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



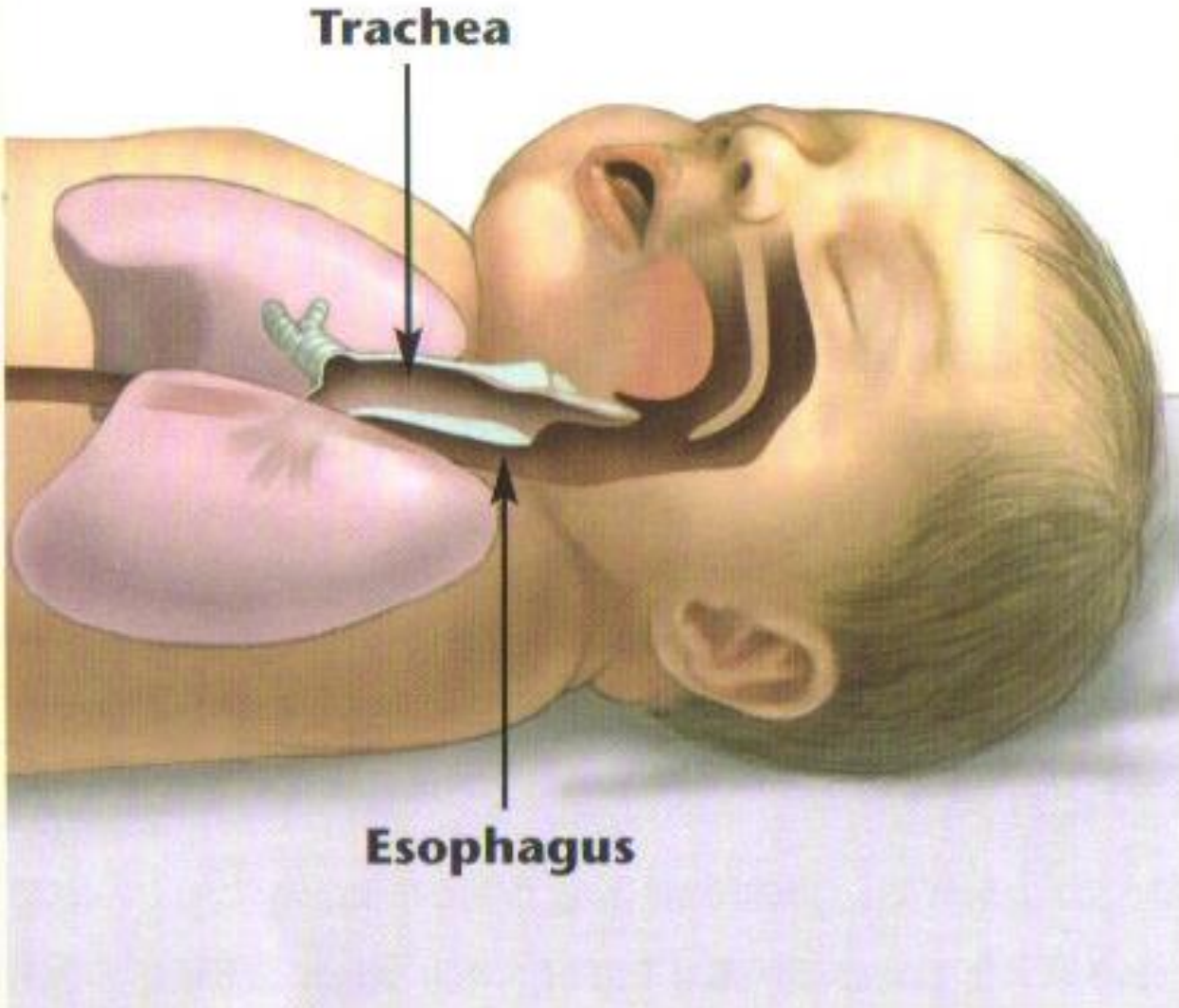
# Babies Should Sleep on their Backs for Every Sleep



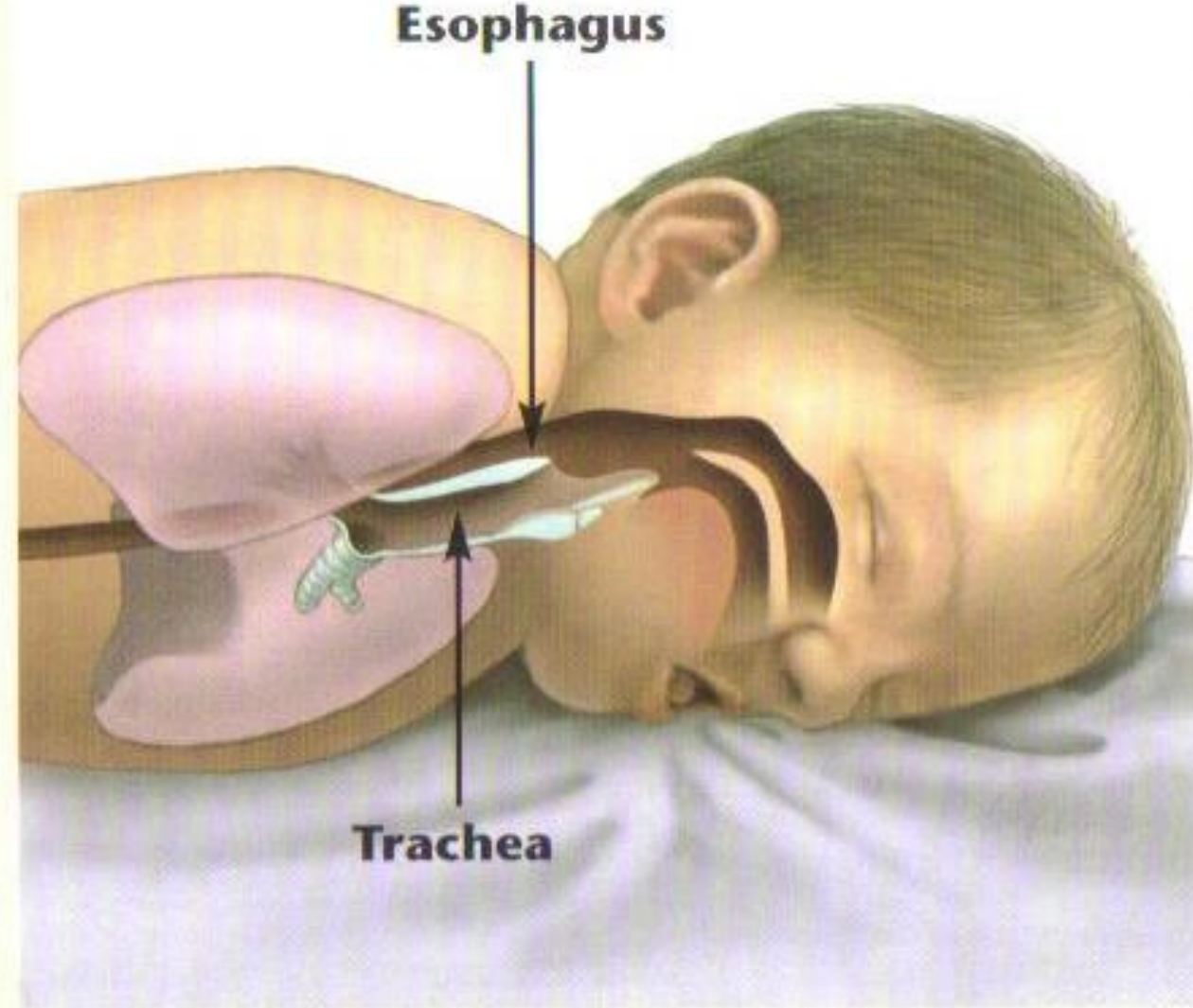
Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>

# Supine



# Prone





## New Emphasis in 2022:

- **Infants should sleep on a flat surface (<10° incline); including infants with GERD.**
- **Preterm infants should sleep supine as soon as medically stable; generally by 32-weeks PCA.**
- **Infants who roll may stay in their preferred position, but infant should be placed supine until 1-year of age.**
- **Skin-to-skin recommended at birth if the mother is alert, and if she is able to respond to her baby.**



# Use a Firm, Flat, Non-inclined Sleep Surface to Reduce the Risks of Suffocation, Wedging, and Entrapment



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# **Sitting Devices (Car Seats, Strollers, etc.) are Not Recommended for Routine Sleep**



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



# Feeding Human Milk is Recommended



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Roomsharing, Without Bedsharing, is Recommended



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

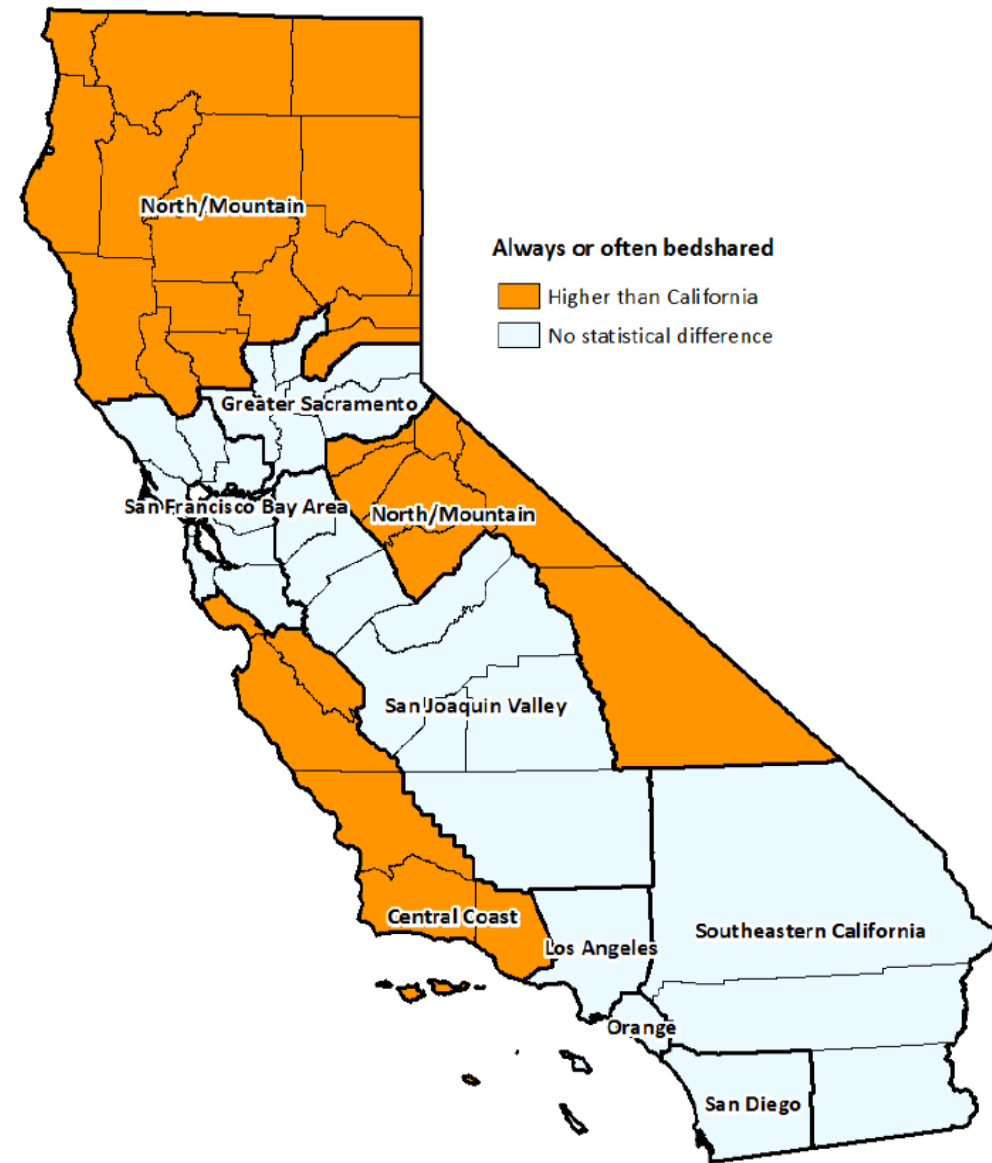
<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



## New Emphasis in 2022:

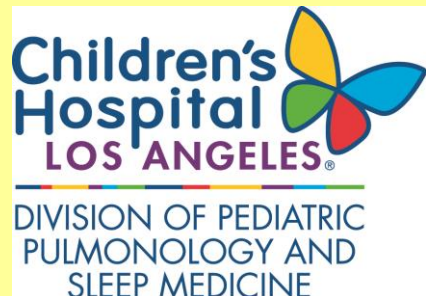
- **Couches, armchairs, and sofas are extremely dangerous.**
- **Inadvertent bedsharing may occur if a mother falls asleep while breastfeeding.**
- **Infants sleeping in a separate room from parents is associated with a 3-12 times increased risk of SIDS.**
- **Do not co-bed twins, triplets, etc.**

**California  
Infants Who  
Always or  
Often  
Bedshare:  
39.3%**



Data Source: Maternal and Infant Health Assessment Survey Prepared by: Maternal, Child and Adolescent Health Program, Center for Family Health, California Department of Public Health  
<http://www.cdph.ca.gov/data/surveys/MIHA/MIHAComparisonMaps/CompareRegBedshare2011.pdf>

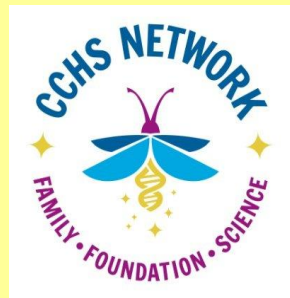
**“Nobody  
wants to do  
a bad job.”**



**Sheila S. Kun, R.N., M.S.**

**Nurse Care Manager**

**Division of Pediatric Pulmonology and Sleep Medicine  
Children's Hospital Los Angeles**





# Keep Soft Objects and Loose Bedding Out of the Crib



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>





# Consider Offering a Pacifier at Nap Time and at Bedtime



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



# Avoid Cigarette Smoke Exposure and Vaping During Pregnancy and After Birth



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Avoid Alcohol, Marijuana, and Illicit Drug Use During Pregnancy and After Birth



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Avoid Overheating and Head Covering: Infants Should Not Feel Hot to Touch



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



# Infants Should Be Immunized According to AAP and CDCP Advice



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://healthlevelup.com/vaccinations-and-children/>



# Avoid Use of Commercial Devices Inconsistent with Safe Infant Sleep



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# **SNOO: Recently FDA Approved to Increase Supine Sleep; Not Approved to Decrease SIDS**





# Do Not Use Cardiorespiratory Monitors to Reduce the Risk of SIDS in Healthy Infants



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



**Encourage *Tummy Time* when the Infant is Awake and Being Observed.**



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**  
<http://healthlevelup.com/vaccinations-and-children/>



# Avoid Swaddling if ...



- **Prone sleeping position.**
- **Thick blankets.**
- **Face covered.**
- **For infants older than 3-months.**  
There is a danger when infants begin to roll from supine to prone, the swaddled infant can not regain the supine position.

Ponsonby, A.L., et al. *N. Eng. J. Med.*, 329: 377-382, 1993.

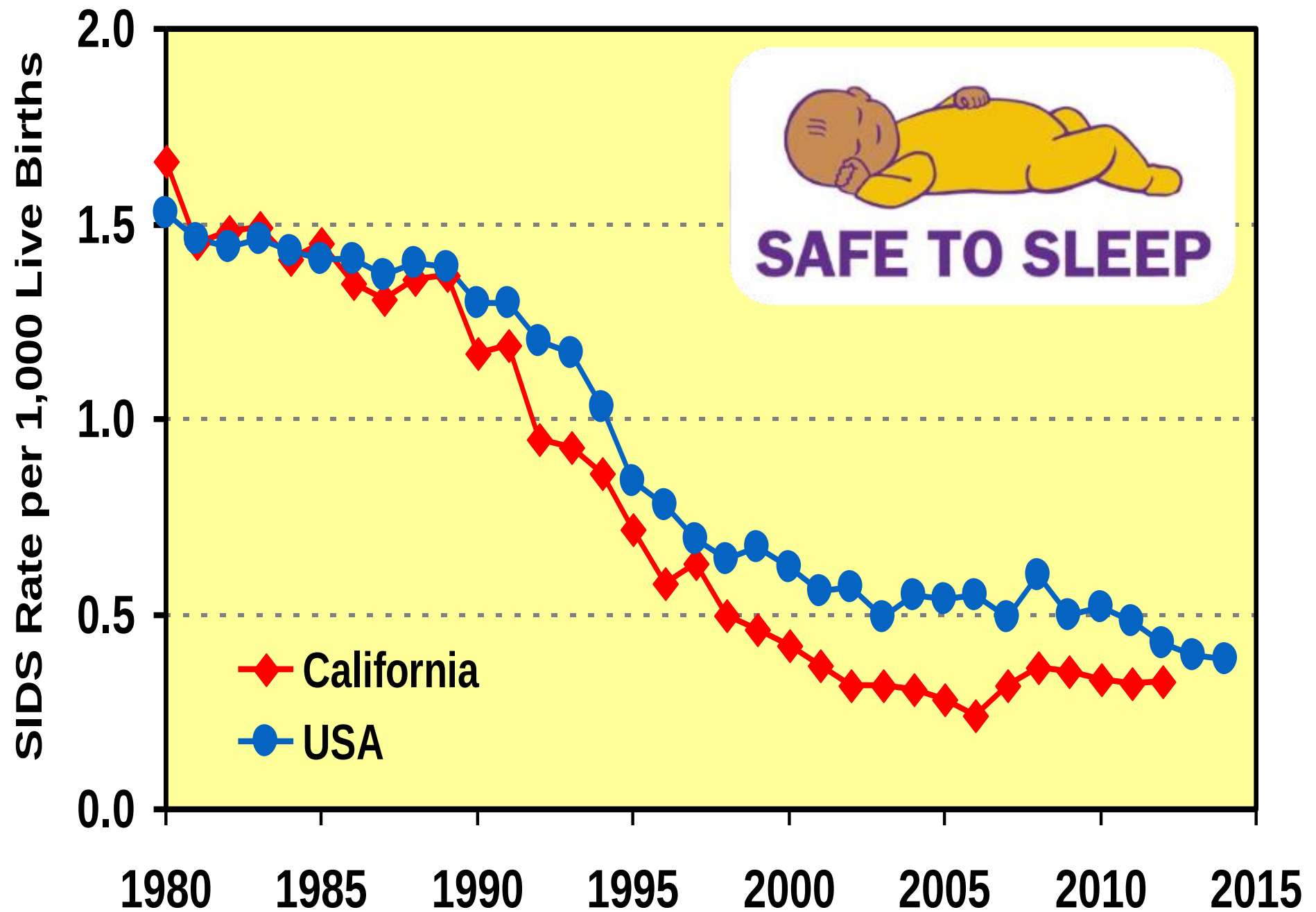
Wilson, C.A., et al. *J. Paed. Child Health*, 30: 506-512, 1994.

L'Hoir, M.P., et al. *Eur. J. Pediatr.*, 157: 681-688, 1998.

Van Sleuwen, B.E., et al. *Pediatrics*, 210: e1097-e1106, 2007.

Pease, A.S., et al. *Pediatrics*, 137: e20153275, 2016.

Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



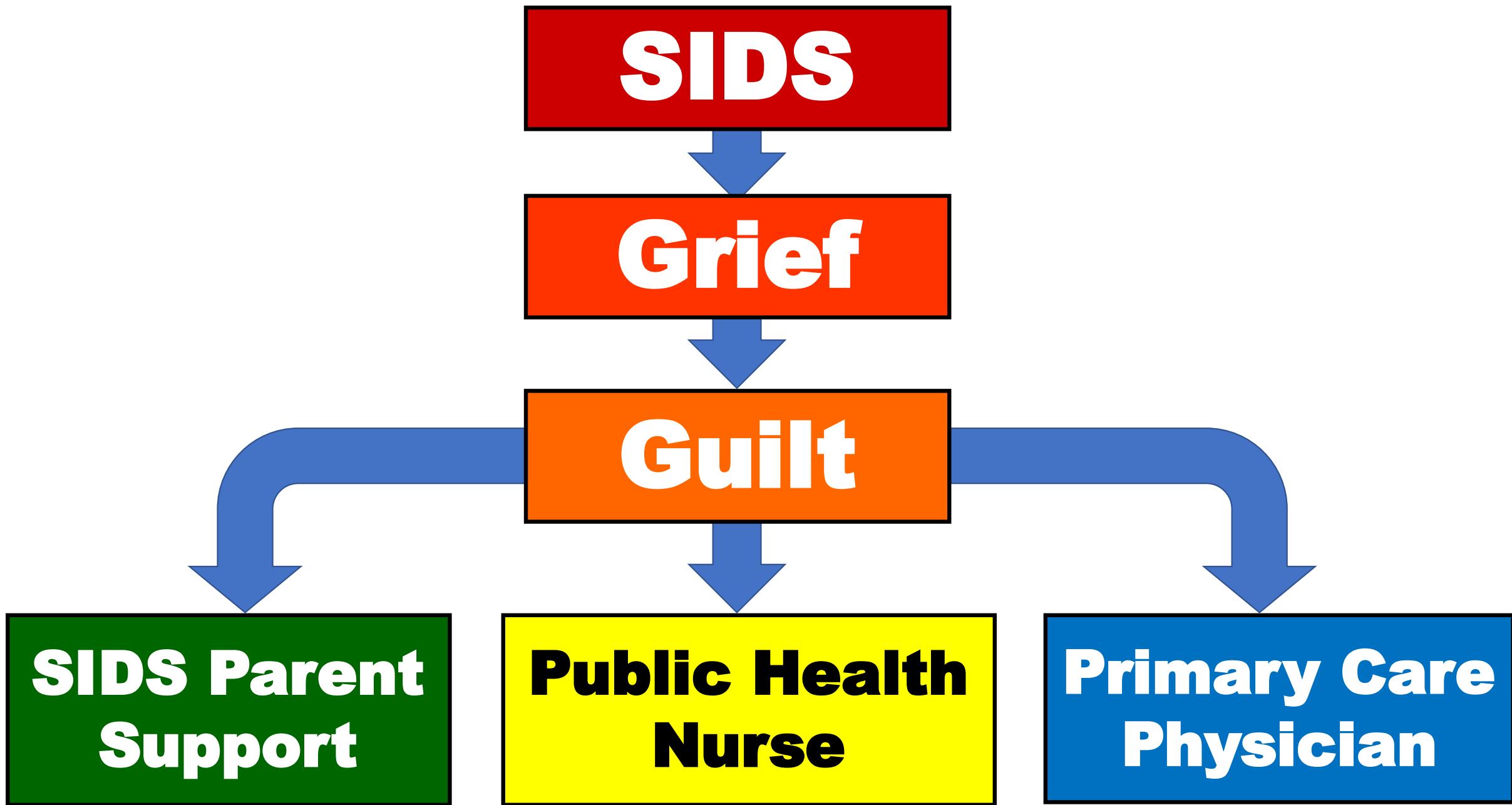
**S**upine

**A**lone

**F**irm mattress

**E**mpy crib





# If You Have a SIDS Baby in Your Practice



- **Meet with the parents.**
- **Refer them to a SIDS Parent Support group.**
- **As an authority on healthcare, tell them:**
  - **There is nothing they did to cause the death.**
  - **There is nothing they could have done to prevent the death.**
- **Recognize that health care professionals also feel guilty.**

**What does the Future hold for SIDS?**



**The problem  
with predicting  
the future is  
that it hasn't  
happened yet.**



**Yogi Berra**  
**1925-2015**



**The Holy Grail of  
SIDS Research is to  
be able to identify  
infants, near birth,  
who will die, before  
death occurs, in  
order to intervene  
and prevent death.**



# Predicting Infants at Birth Who Will Later Die from SIDS



- Is there a way to identify infants at or near birth, who will later die from SIDS?
- Butyrylcholinesterase (BChE), which correlates with arousal, was decreased in blood of SIDS vs controls.
- Newborn screen metabolites plus epidemiologic SIDS risk factors identified infant at 14.4 times increased risk of SIDS.
- Both of these studies attempt to do the above.

Harrington, C.T., et al. *eBiomedicine*; 80: 104041, 2022.

Oltman, S.P., et al. *AMA Pediatr*. doi:10. 1001/jamapediatrics.2024.3033, 2024.

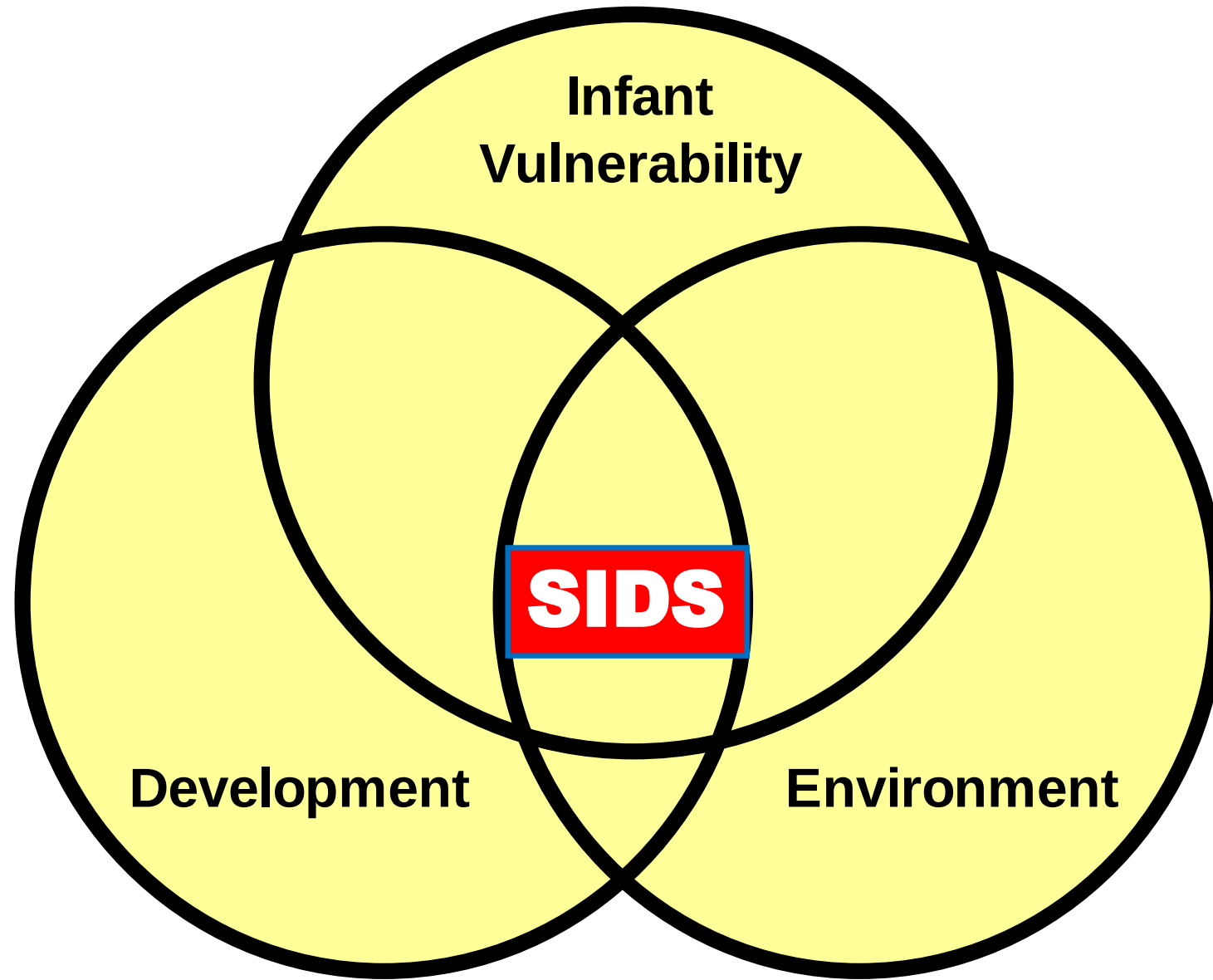
# Predicting Infants at Birth Who Will Later Die from SIDS



- The prediction in these studies is not precise.
- Many infants would be identified who are not at risk and who will not die.
- Even if we could identify infants who will die, we have no idea what intervention to implement in order to prevent their death.
- We are still not able to identify at birth infants who will die from SIDS.

Harrington, C.T., et al. *eBiomedicine*; 80: 104041, 2022.

Oltman, S.P., et al. *AMA Pediatr*. doi:10. 1001/jamapediatrics.2024.3033, 2024.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

- **Most common cause of sudden infant death between the ages of 1-month and 1-year.**
- **Cause remains unknown.**
- **Can not be predicted in infants prior to death.**
- **Reduction in SIDS in populations through public health intervention.**
- **SIDS has not been eliminated.**



