

The Final Diagnosis

Brain Death /
Death by Neurologic Criteria

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Agenda

1. Introduction
2. Pathophysiology
3. Prerequisites
4. The exam
5. Apnea testing
6. Ancillary testing

Landmark Article

Aug 5, 1968
(*JAMA* 1968;205:337-340)

A Definition of
Irreversible Coma

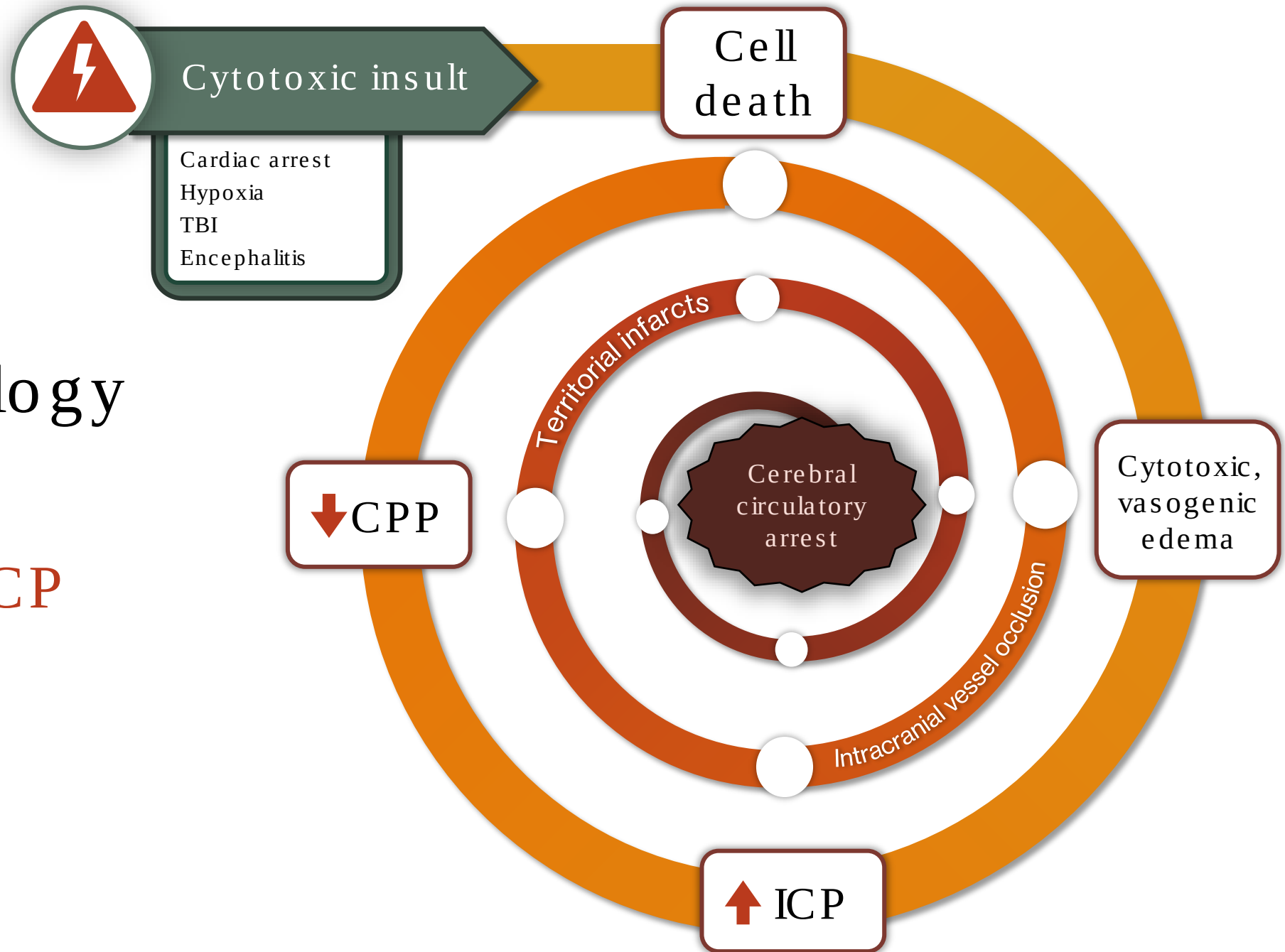
Report of the Ad Hoc Committee of the
Harvard Medical School to
Examine the Definition of Brain Death

“Our primary purpose is
to define irreversible
coma as a new criterion
for death.”

Harvard Ad Hoc Report, 1968

Pathophysiology of BD/DNC

$$CPP = MAP - ICP$$



Elements of BD/DNC

1



Prerequisites



Correct
Confounders

2



Neurologic
Exam

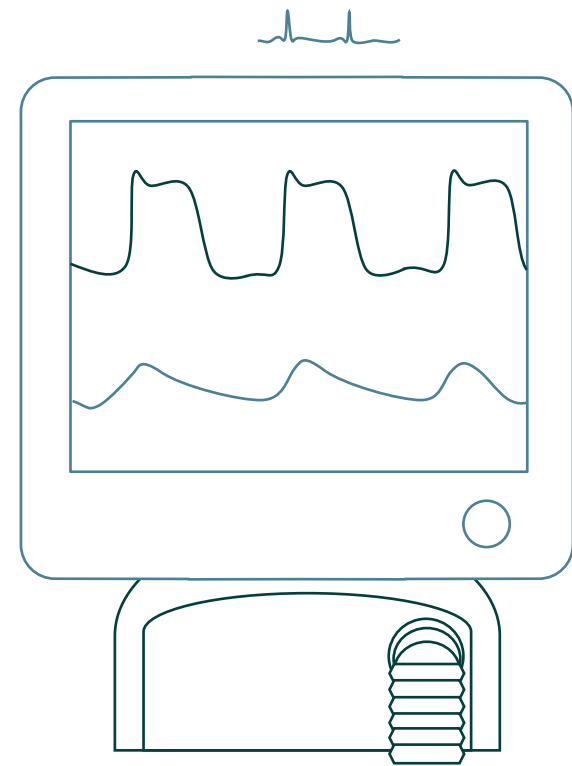


Apnea Test

3



Ancillary
Testing
If necessary



Pediatric and Adult Brain Death/Death by Neurologic Criteria Consensus Guideline

Report of the AAN Guidelines Subcommittee, AAP, CNS, and SCCM

David M. Greer, MD, MA,* Matthew P. Kirschen, MD, PhD,* Ariane Lewis, MD,* Gary S. Gronseth, MD, Alexander Rae-Grant, MD, Stephen Ashwal, MD, Maya A. Babu, MD, MBA, David F. Bauer, MD, MPH, Lori Billingham, MD, MSc, Amanda Corey, MD, Sonia Partap, MD, MS, Michael A. Rubin, MD, MA, Lori Shutter, MD, Courtney Takahashi, MD, Robert C. Tasker, MBBS, MD, Panayiotis Nicolaou Varelas, MD, PhD, Eelco Wijdicks, MD, PhD, Amy Bennett, JD, Scott R. Wessels, MPS, ELS, and John J. Halperin, MD

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American Academy of
Neurology
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Neurology® 2023;101:1112-1132. doi:10.1212/WNL.0000000000207740

2023 AAN consensus statement

Guidance for standardized assessment of BD/DNC



Prerequisites

1. **Known mechanism** for irreversible, catastrophic brain injury
2. Appropriate **observation period** for mechanism and age
3. Correction of **confounders**
 - Hypothermia
 - Hypotension
 - Pharmacology
 - Metabolics



Target normothermia

$\geq 36^{\circ}\text{C}$

If hypothermic or TTM to $\leq 35.5^{\circ}\text{C}$, rewarm to $\geq 36^{\circ}\text{C}$ for 24h prior to exam

No specific guidance for fever



Target normotension



Adult: SBP ≥ 100 mmHg, MAP ≥ 75 mmHg



Pediatric: SBP and MAP $\geq 5^{\text{th}}$ percentile for age

Adjust to individualized patient normal range

Inotropes / vasopressors if needed

Negative toxicology serum / urine
(if warranted)

CNS depressants therapeutic /
subtherapeutic

EtOH
 ≤ 80 mg/dL

Pentobarbital
 < 5 $\mu\text{g/mL}$



≥ 5 half-lives of
known intoxicants



Adjust for hepatic/renal
dysfunction



Extreme overdose delays
clearance



Consider toxicology consult
if unknown ingestion

Correct severe
acid-base,
electrolyte,
metabolic
derangements

Insufficient evidence for specific thresholds
(2023 AAN suggested targets)

Na < 160
mmol/L

pH > 7.3 ,
 < 7.5

BUN < 75
 $\mu\text{mol/L}$

NH3 < 75
 $\mu\text{mol/L}$



Correct gross
endocrine
abnormalities

Neurologic Exam



1. Coma
2. Pupillary reflex
3. Corneal reflex
4. Oculocephalic reflex
5. Vestibulo-ocular reflex
6. Cough reflex
7. Gag reflex
8. Root / suck reflexes

Coma

Absence of any spontaneous, patient-initiated movements

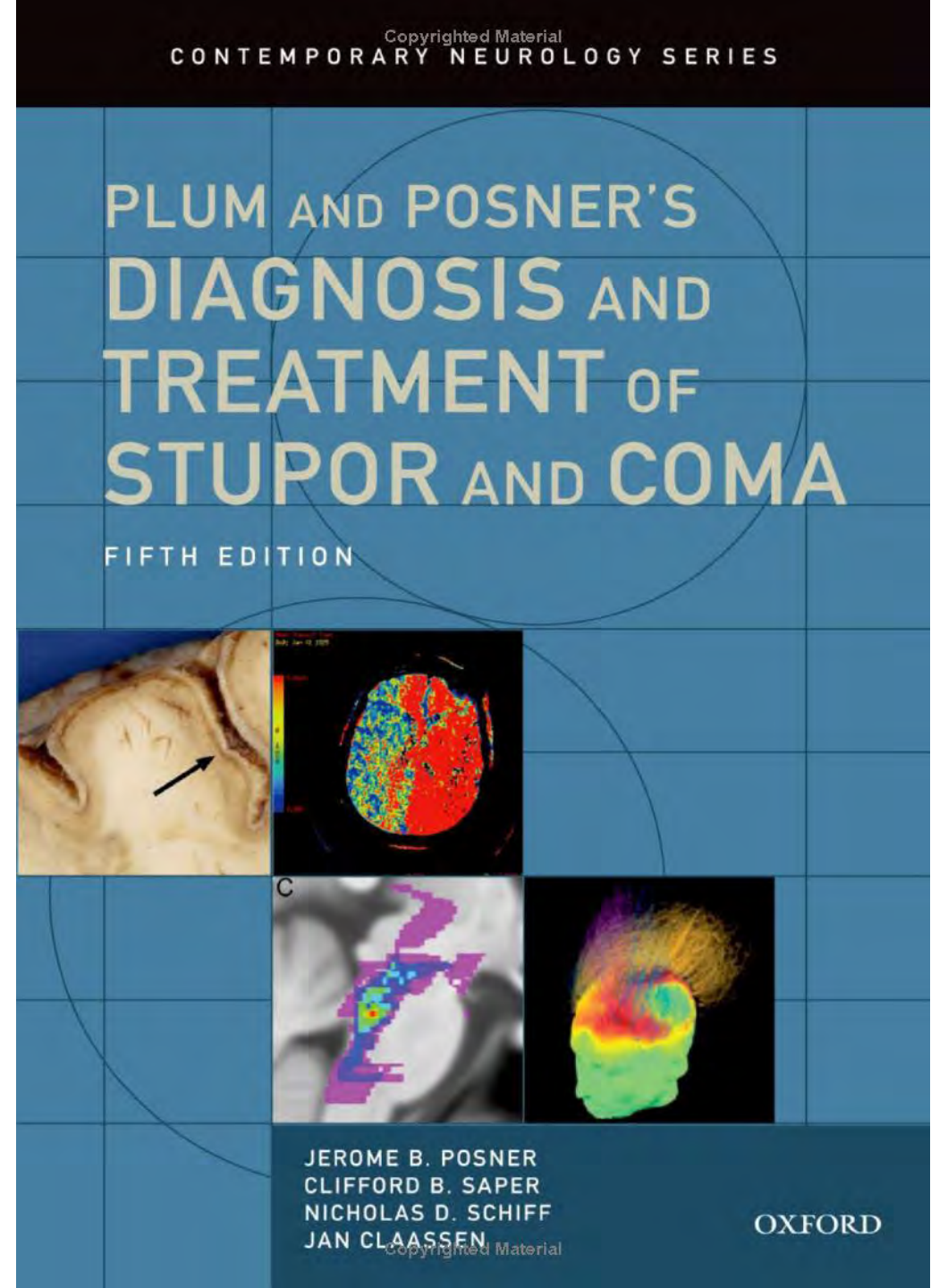
Absence of motor response to cranial, axial, appendicular noxious stimulus

Spinal reflexes are permitted

Unclear movements

Neuro consult

Consider ancillary testing



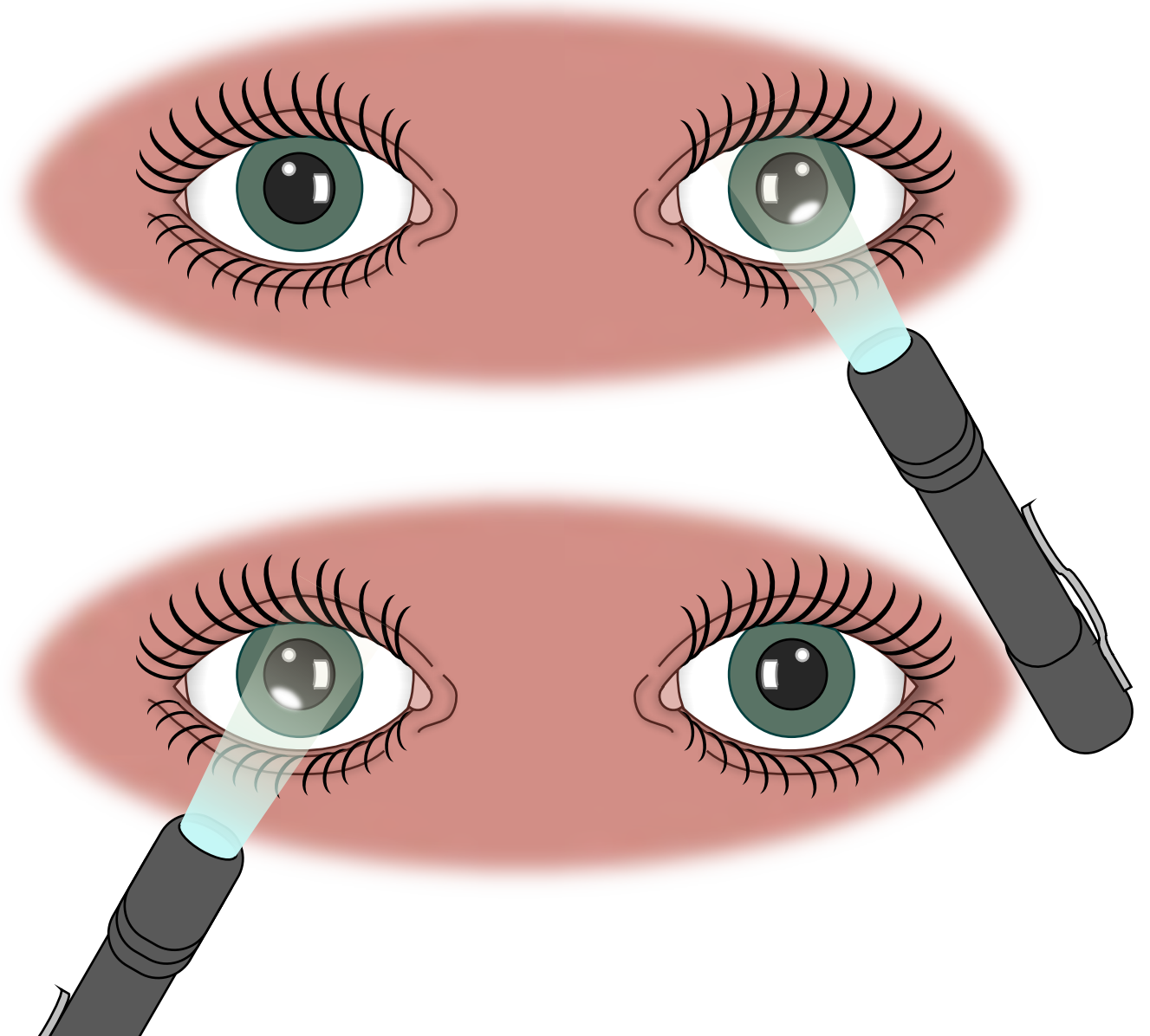
No pupillary change to penlight

Pupillary reflex

Afferent: CN2

Efferent: CN3

Pupillometry: not formally validated, but case series where quantitative pupillometry revealed pupillary reactivity that traditional flashlight technique missed



No blink reflex to corneal contact

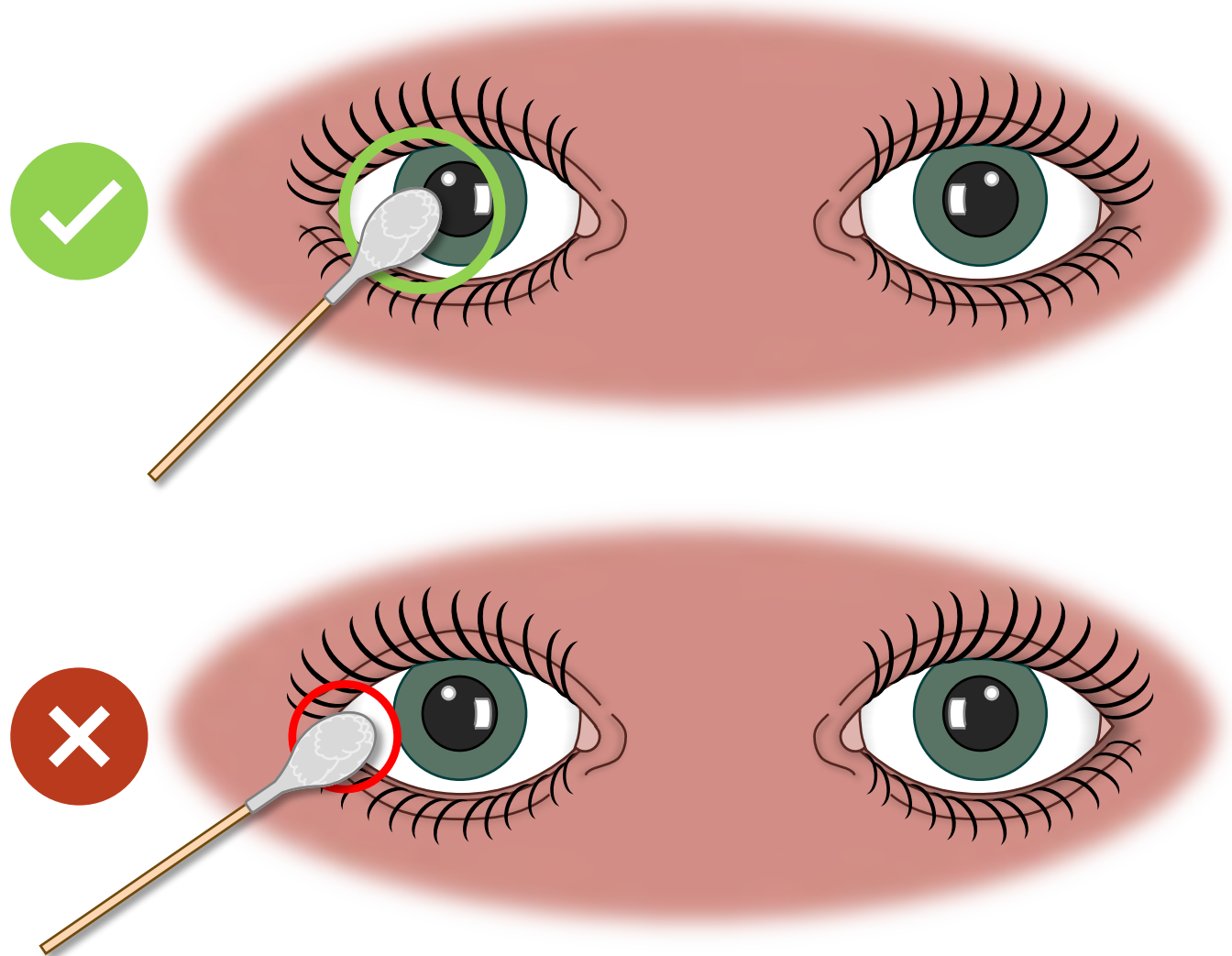
Corneal reflex

Afferent: CN5(V1)

Efferent: CN7

- Pressure over the cornea with cotton-tipped applicator or soft gauze

Contact cornea not sclera



Oculocephalic reflex

Afferent: CN8

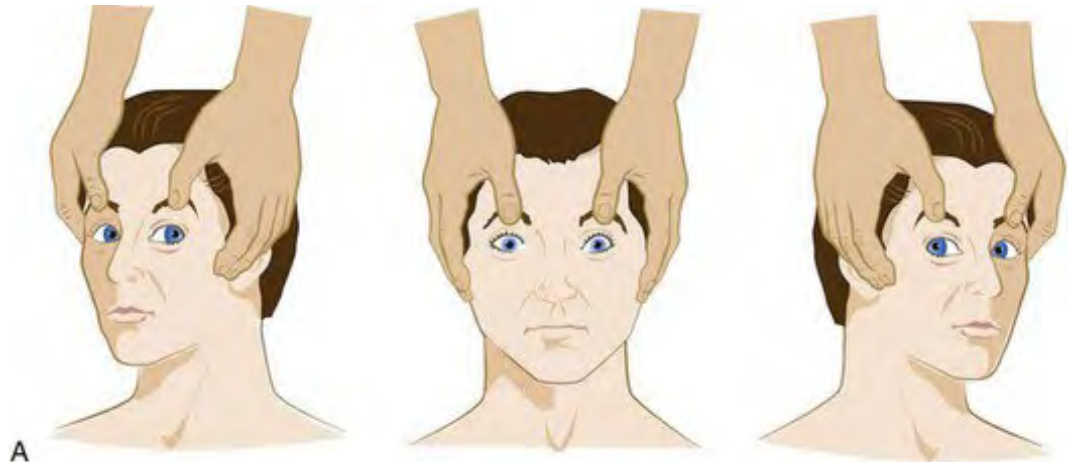
Efferent: CN3, 4, 6

Hold eyes open and firmly
rotate head to either side
with moderate speed

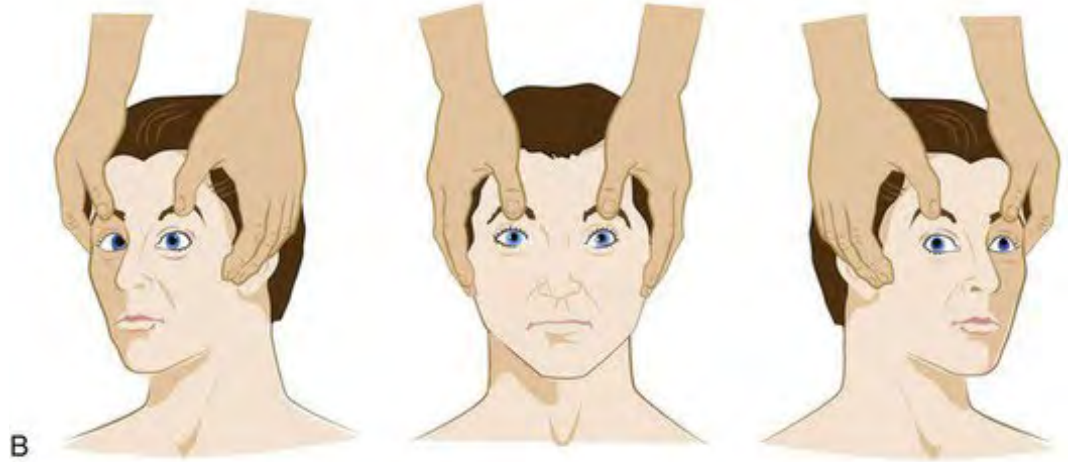
Reflex absent or
can't be performed

Proceed to
VOR

No extraocular movement on head turn



A: Normal reflex



B: Absent reflex

Vestibulo-Ocular reflex

Afferent: CN8

Efferent: CN3, 4, 6

60-second instillation of ice-cold water to the tympanic membrane bilaterally

5min between sides to allow prior stimulus to subside

No extraocular movement on irrigation

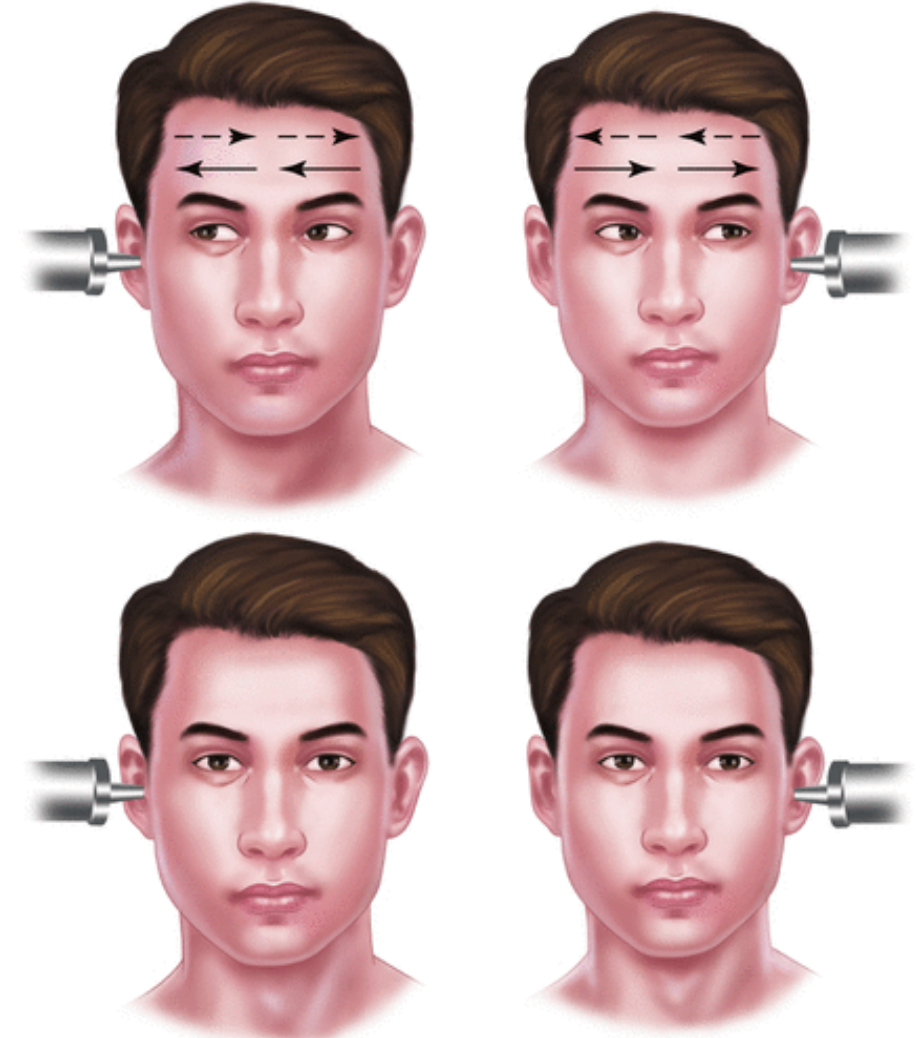
Unilateral cold water irrigation

Caloric response

Right ear

Left ear

Normal, awake patient
(Fast phase nystagmus
----->
(Slow phase nystagmus
----->



Adapted from: Nguyen et al. Reflex Eye Movements (Doll's Eyes and Caloric Testing).

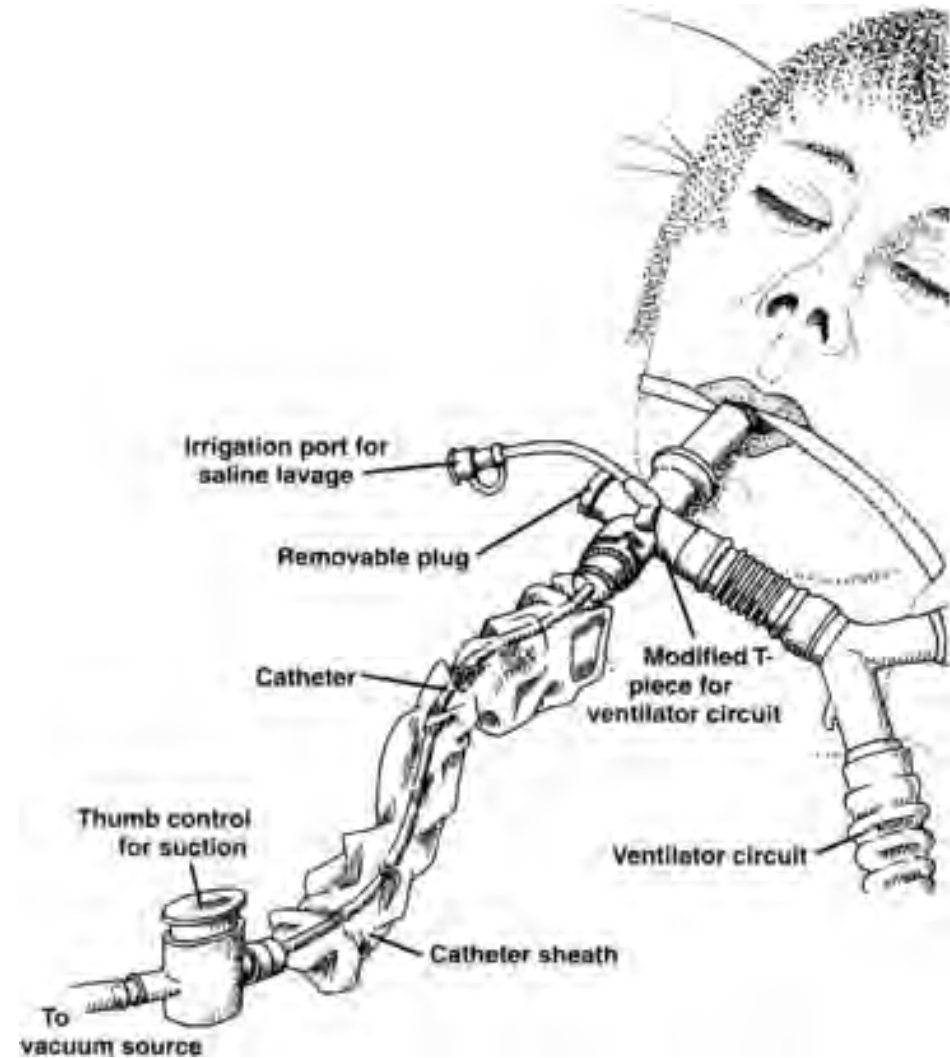
Absence of cough to tracheal stimulation

Cough reflex

Afferent: CN10

Efferent: larynx, respiratory muscles,
pelvic floor muscles

Stimulate trachea with endotracheal
tube in-line suction



Chulay M, Seckel MA. Suctioning: endotracheal or tracheostomy tube.

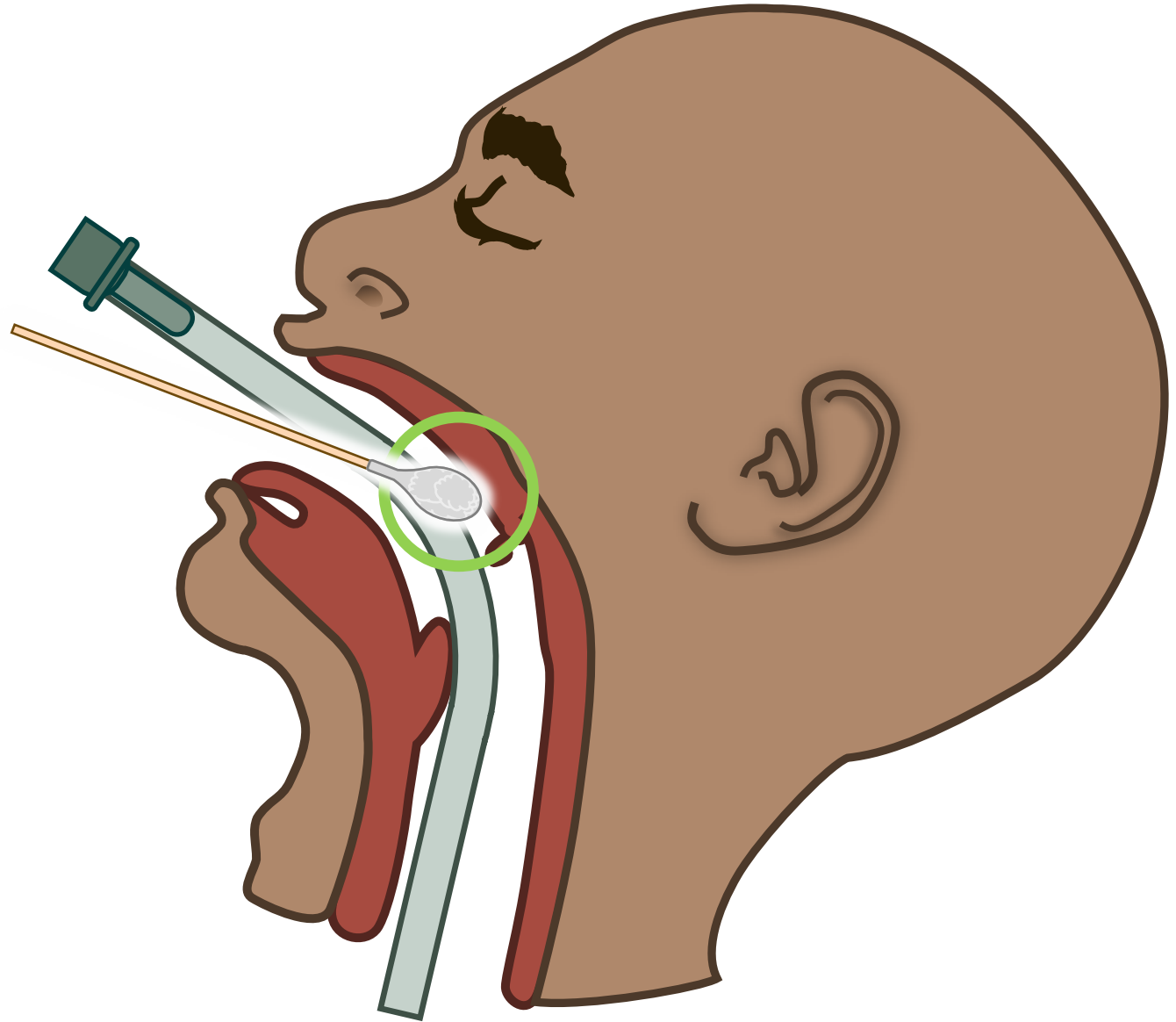
Absence of gag to palatal stimulation

Gag reflex

Afferent: CN9

Efferent: CN10, extended
to CN12, diaphragm,
emetic reflex

Contact both sides of the
posterior pharynx



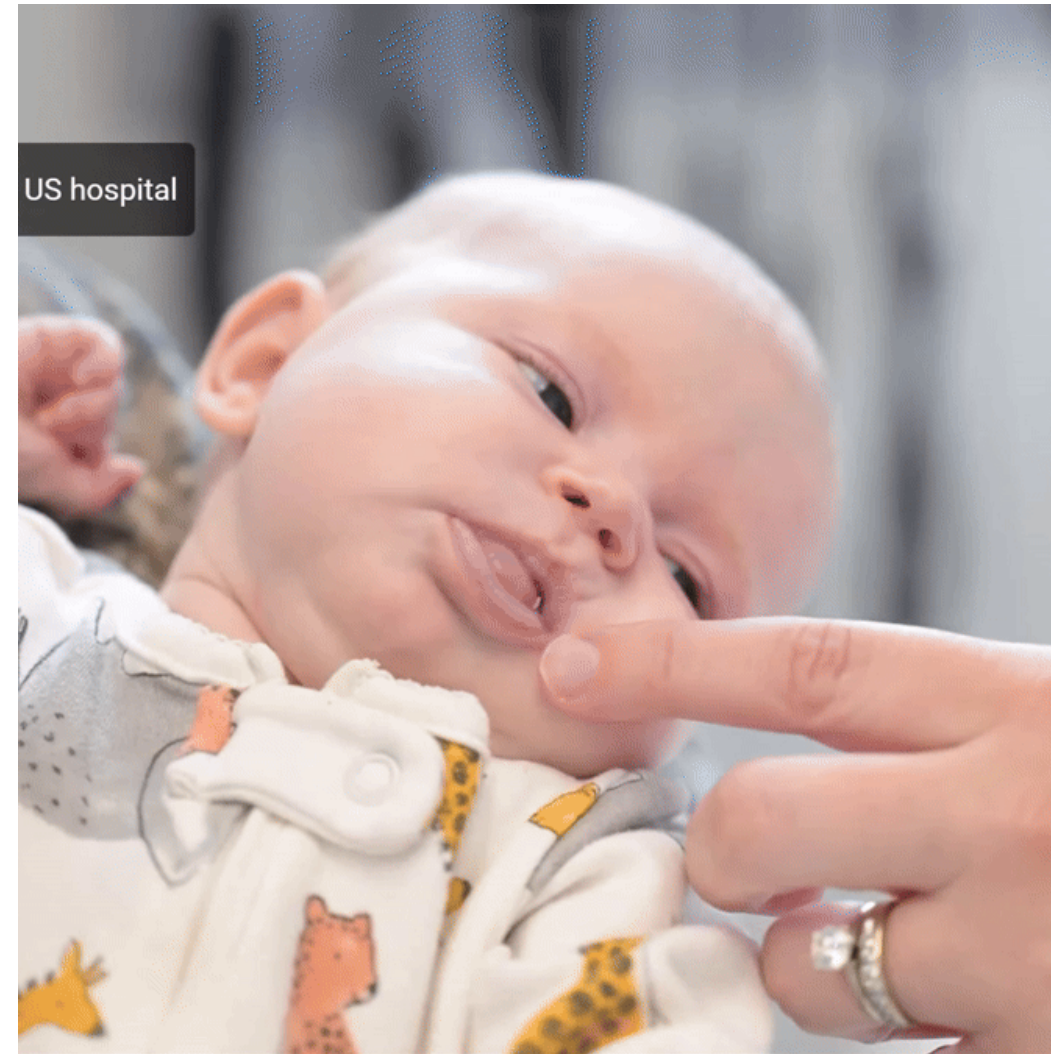
Root reflex (<6 mos)

Afferent: CN5

Efferent: CN7, neck muscles

Stroke each cheek

Absence of head turn towards stimulus



Normal root reflex

Cleveland Clinic. What Are Newborn Reflexes? (2025)

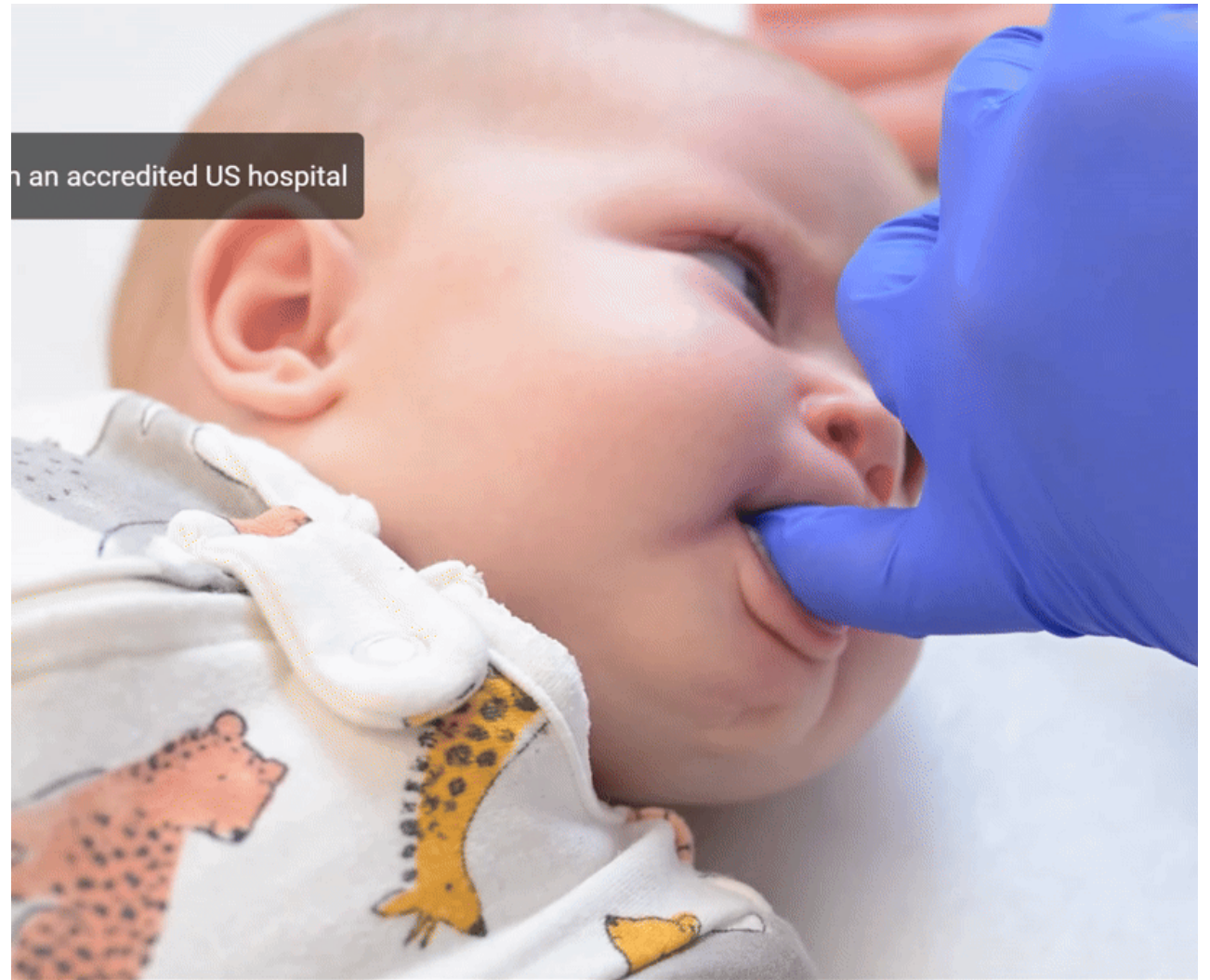
Absence of sucking to oral stimulus

Suck reflex (<6 mos)

Afferent: CN5

Efferent: CN5, 7, 9, 10, 12

Place gloved finger in mouth



Normal suck reflex

Cleveland Clinic. What Are Newborn Reflexes? (2025)

Apnea Test



1. Prerequisites
2. Technique
3. Early discontinuation
4. Findings consistent with BD/DNC
5. ECMO

Apnea Test Prerequisites

No patient-triggered breaths on ventilator!

Hemodynamically stable (pressors / inotropes ok)

Preoxygenate
100% FiO₂

PaO₂
>200 mmHg

Acid/base

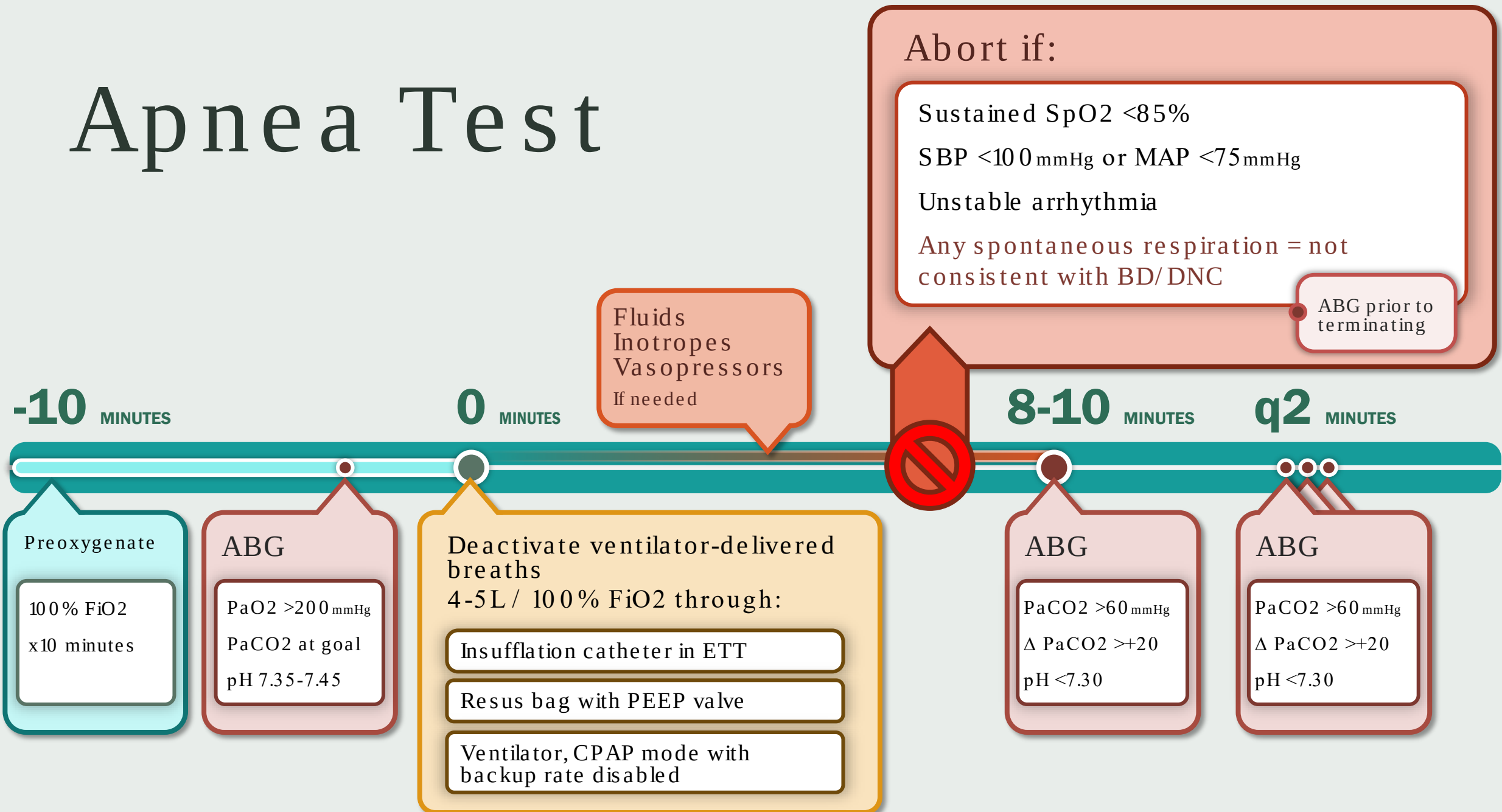
pH
7.35-7.45

PaCO₂
35-45 mmHg
or Pt baseline
or Est. baseline

Unknown baseline,
suspected hypercarbic

Ancillary testing
after apnea test

Apnea Test



Consistent with BD/DNC



No respirations



pH < 7.30



PaCO₂ > 60 mmHg



Δ PaCO₂ > +20 mmHg

ECMO

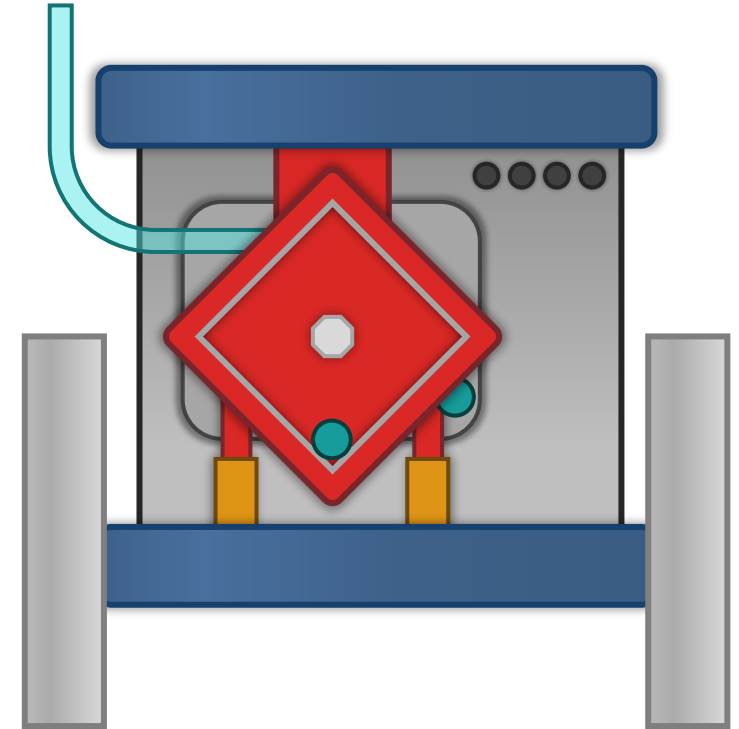
ABG should approximate PaO_2 ,
 PaCO_2 seen by cerebral circulation

Sampling site matters!

Circuit removal of PaCO_2 interferes
with intended rise

Decrease sweep

Introduce CO_2 into gas blender

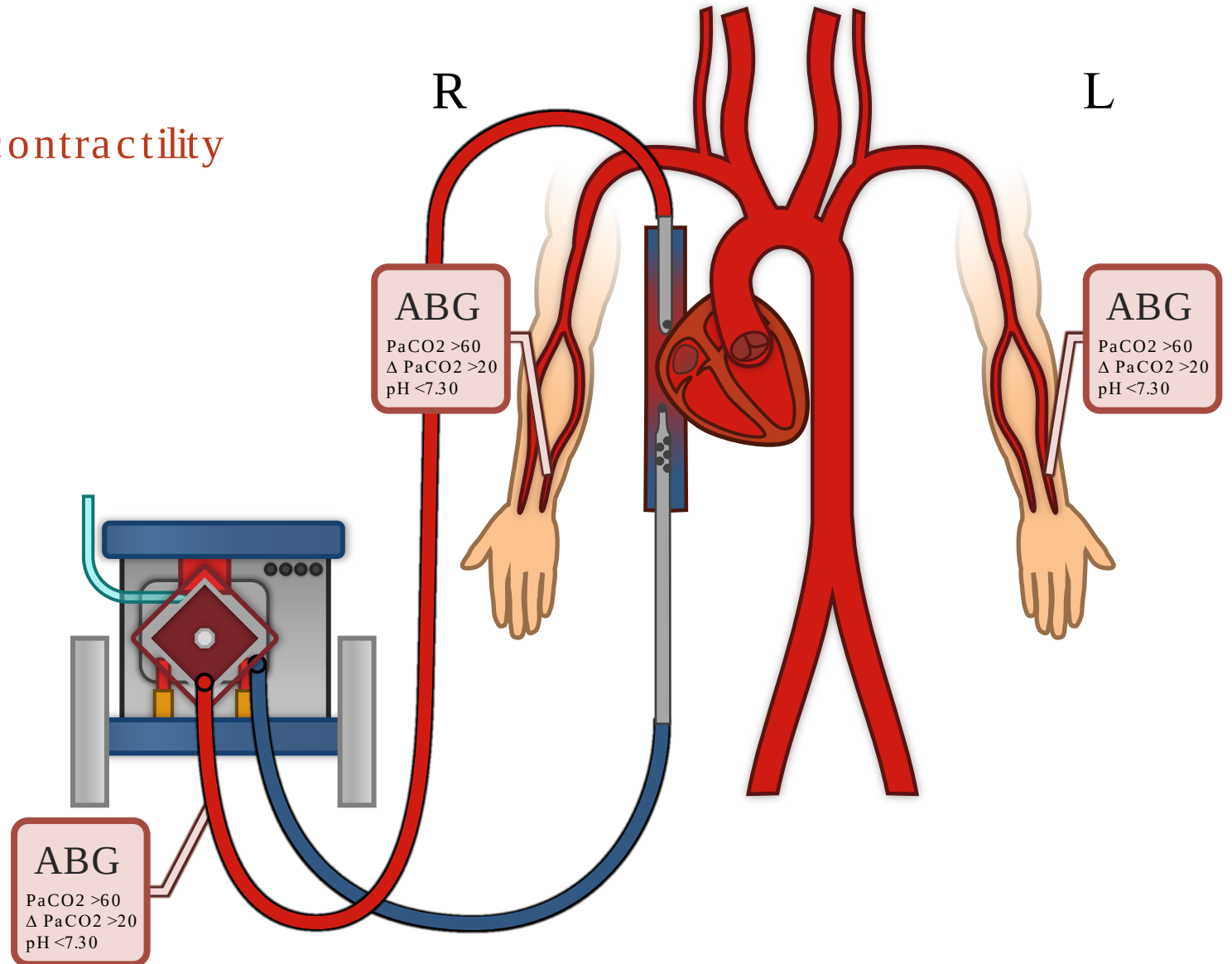


V-V ECMO

V-A ECMO without cardiac contractility

All distal limb gases
approximate cerebral
circulation

No technique adjustments



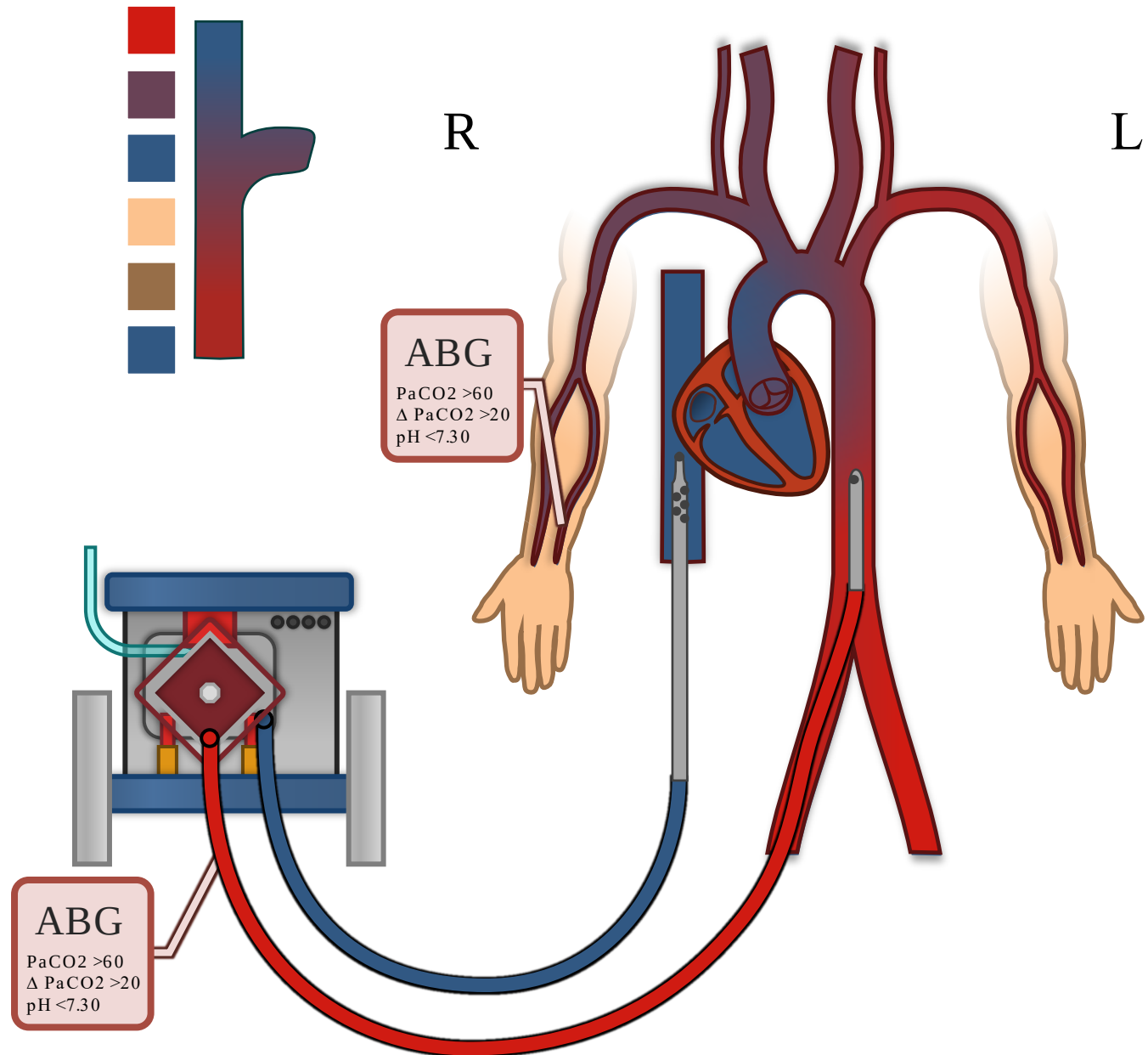
V-A ECMO

Femoral cannulation

Native cardiac function mixes native circulation (pre-ECMO) and ECMO outflow blood

Measure ABG from most distal limb

Right arm



V-A ECMO

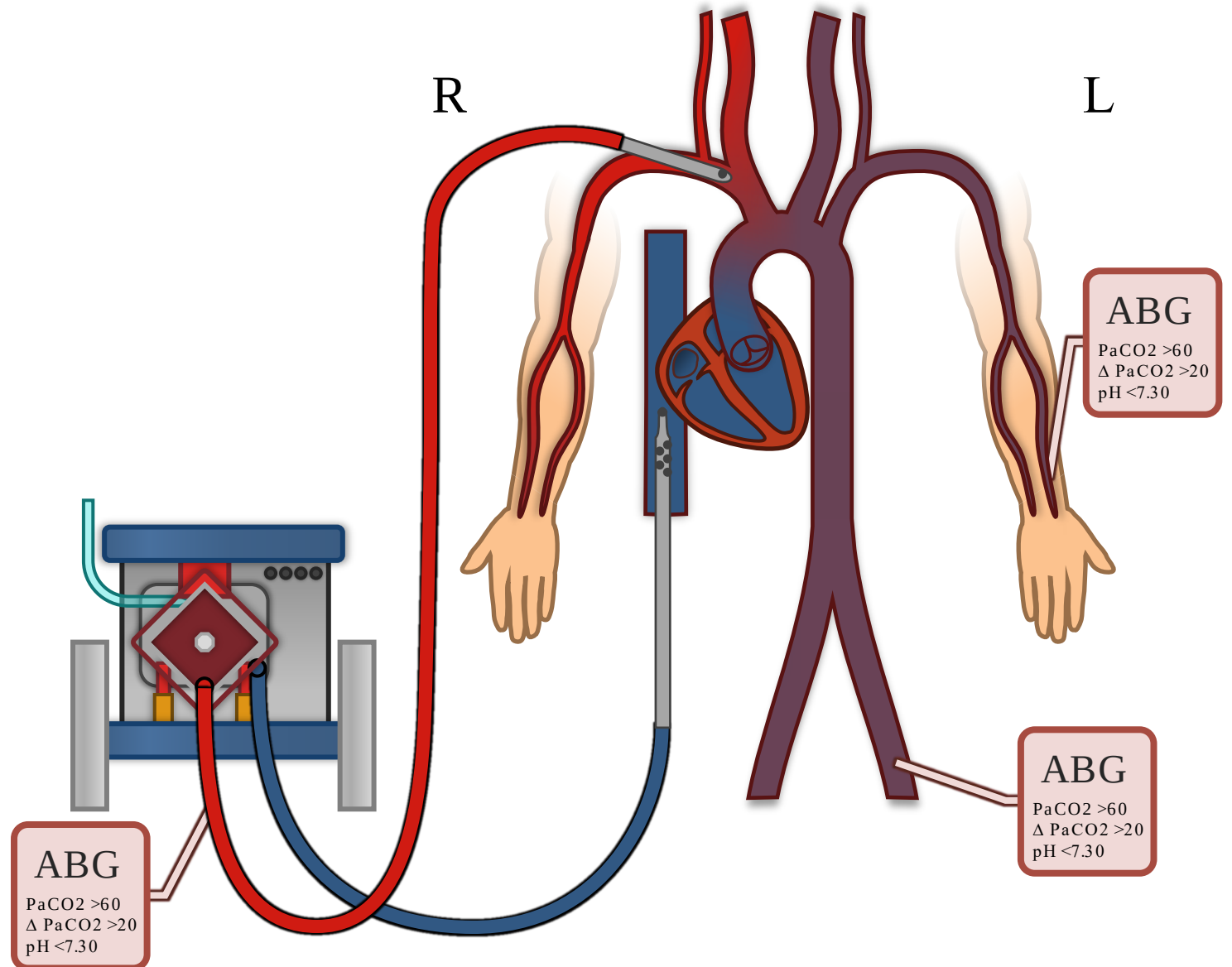
Right upper cannulation

Native cardiac function mixes native circulation (pre-ECMO) and ECMO outflow blood

Measure ABG from most distal limb

Left arm

Left leg



When do we need ancillary testing?



Can't perform full cranial nerve exam

- C-collar, C-spine fusion
- Known prior CN palsies
- Orbital fractures interfering with EOMs
- Other bony defect preventing exam maneuver



Can't complete apnea test

- Terminated for instability, ABG thresholds not met
- Cannot preoxygenate to $\text{PaO}_2 > 200 \text{ mmHg}$
- ECMO sweep can't be lowered to PaCO_2 threshold



Suspect hypercarbic at baseline but can't confirm



Can't correct metabolic derangements



Movements during exam, unclear if reflex

Presuming remainder of exam is consistent with BD/DNC,

When do we **not** need ancillary testing?



Can't perform oculoccephalic reflex, but vestibulo-ocular (cold calorics) is consistent with BD/DNC



Apnea test aborted early, but pre-termination ABG met BD/DNC criteria



Hypothermia



Sedating medications



Skull defect relieving intracranial pressure

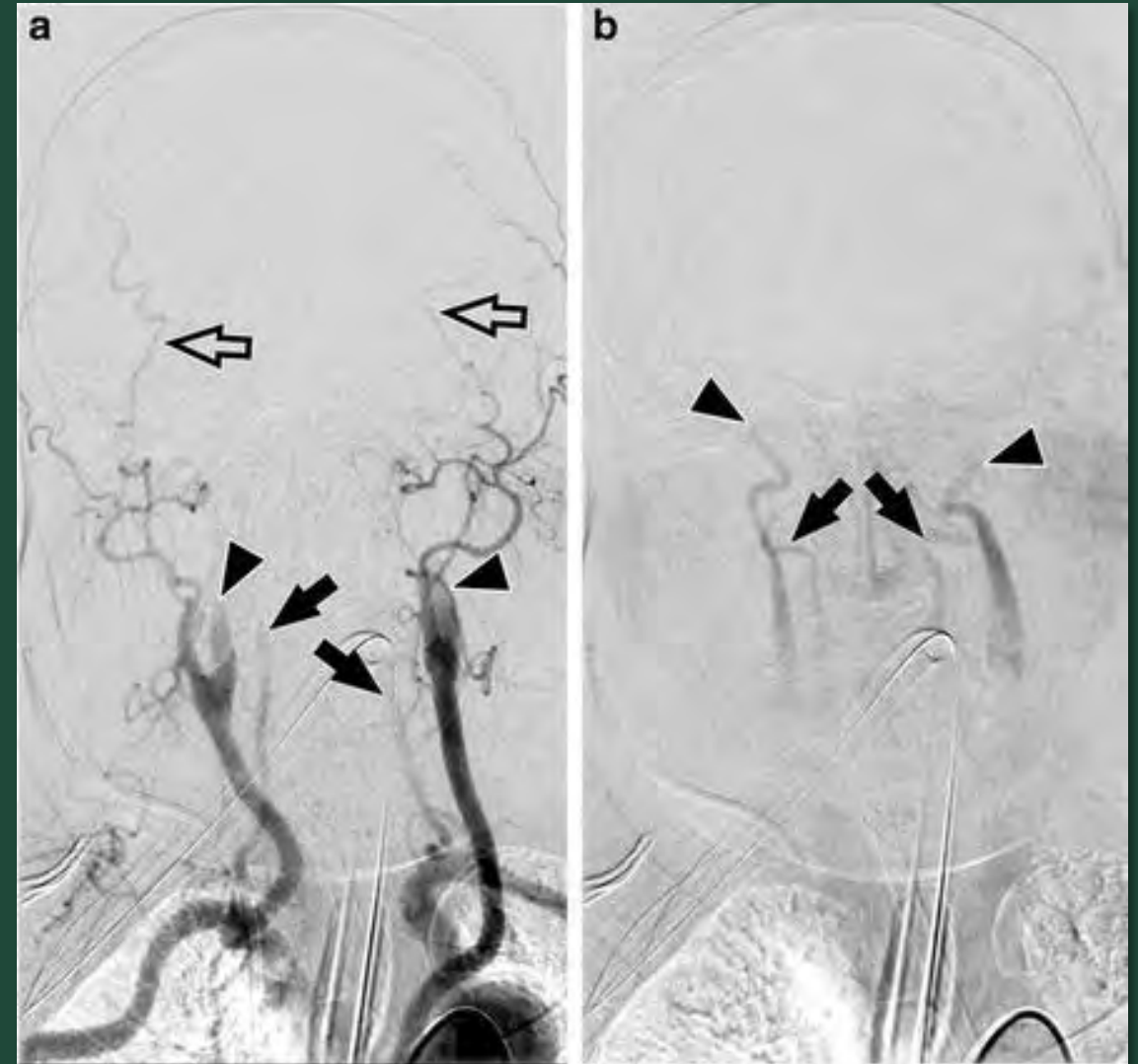
- Open fontanelle
- Decompressive hemicraniectomy
- CSF diversion device
- Open skull fracture



Substitute for otherwise performable neurologic exam maneuver

Conventional Angiography (DSA)

Absence of filling of intracranial vessels is consistent with BD/DNC



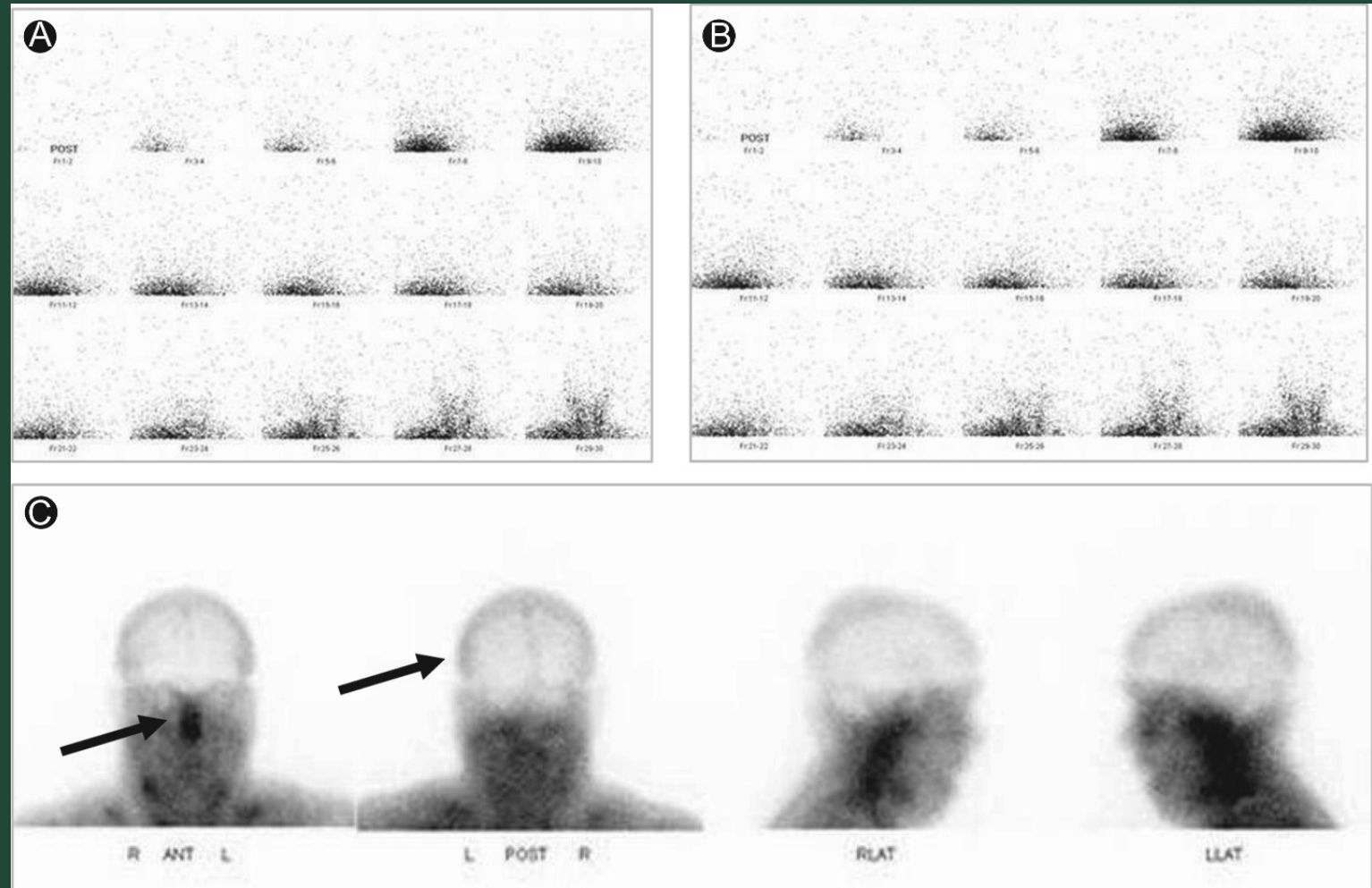
Radiology KeyFastest Radiology Insight Engine, 2016 <https://radiologykey.com/brain-death-imaging/>

- ⇨ External carotid branches
- ➡ Extracranial vertebral portion
- ▶ Extracranial internal carotid absence

Radionuclide Perfusion (SPECT)

Absence of brain tracer uptake is consistent with BD/DNC

Use brain-specific / lipid-soluble Tc99 agents



Rizvi T, Batchala P, Mukherjee S. Brain death: diagnosis and imaging techniques. In Seminars in Ultrasound, CT and MRI 2018 Oct 1 (Vol. 39, No. 5, pp. 515-529). WB Saunders.

A, B: absence of intracranial tracer uptake

C: "Light bulb" sign of absent intracranial, present scalp tracer uptake

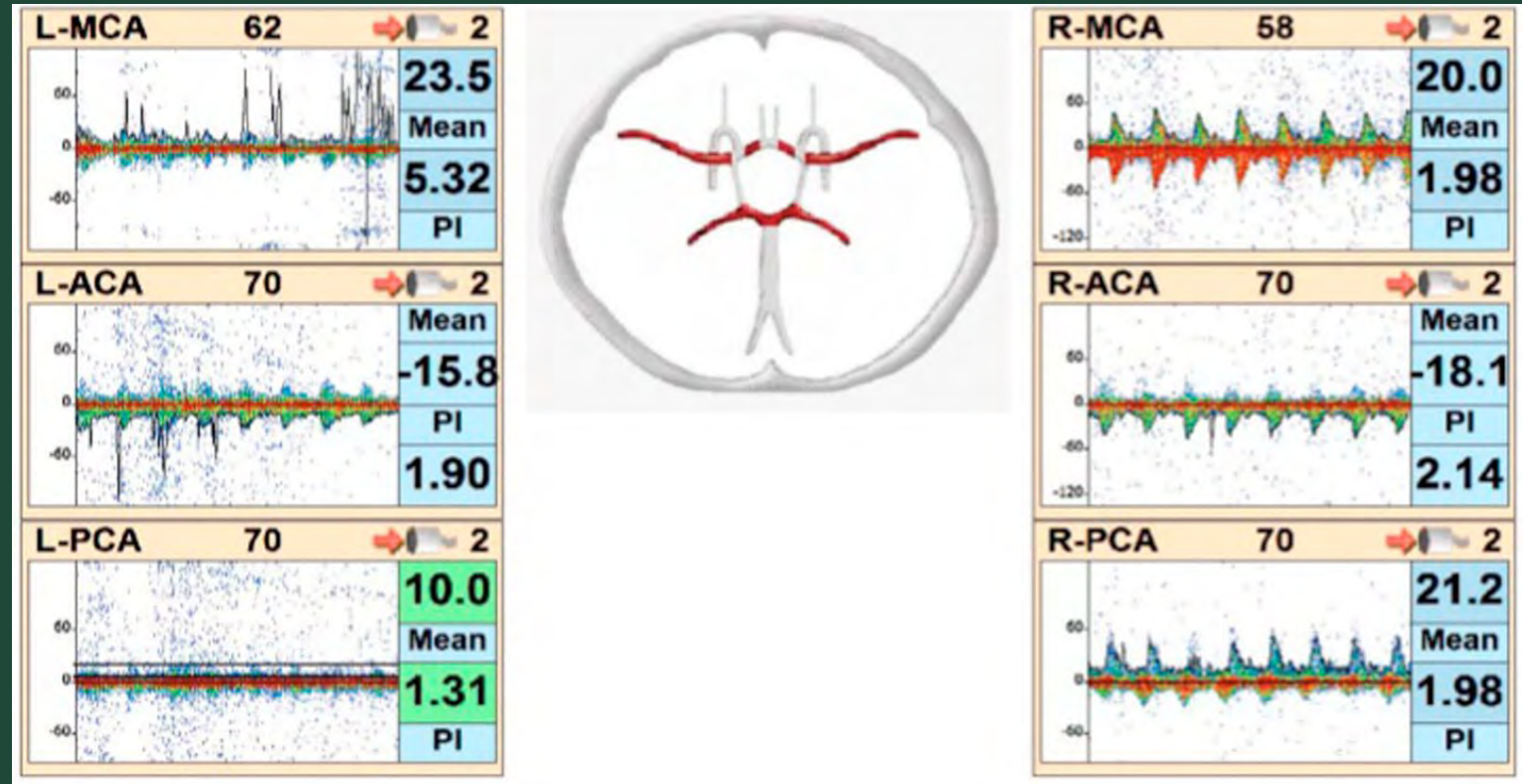
C (anterior): "Hot nose" sign

Transcranial Dopplers (TCDs)

Oscillating flow is consistent with BD/DNC

Systolic spike of antegrade flow

Retrograde flow in diastole



Rizvi T, Batchala P, Mukherjee S. Brain death: diagnosis and imaging techniques. In Seminars in Ultrasound, CT and MRI 2018 Oct 1 (Vol. 39, No. 5, pp. 515-529). WB Saunders.

Oscillating flow in intracranial vessels

Not appropriate for BD/DNC

EEG

Does not evaluate
brainstem

Susceptible to
metabolic artifact

CTA/MRA

Not validated

Contrast injection
variability

Potential for false
positives

Low sensitivity

CT/MR Perfusion

Not validated

Contrast injection
variability

Low sensitivity and/or
specificity

Time of Death

By apnea test

Time ABG is reported by lab

or

Time point of care ABG results

By ancillary test

Time final radiologist attestation is published

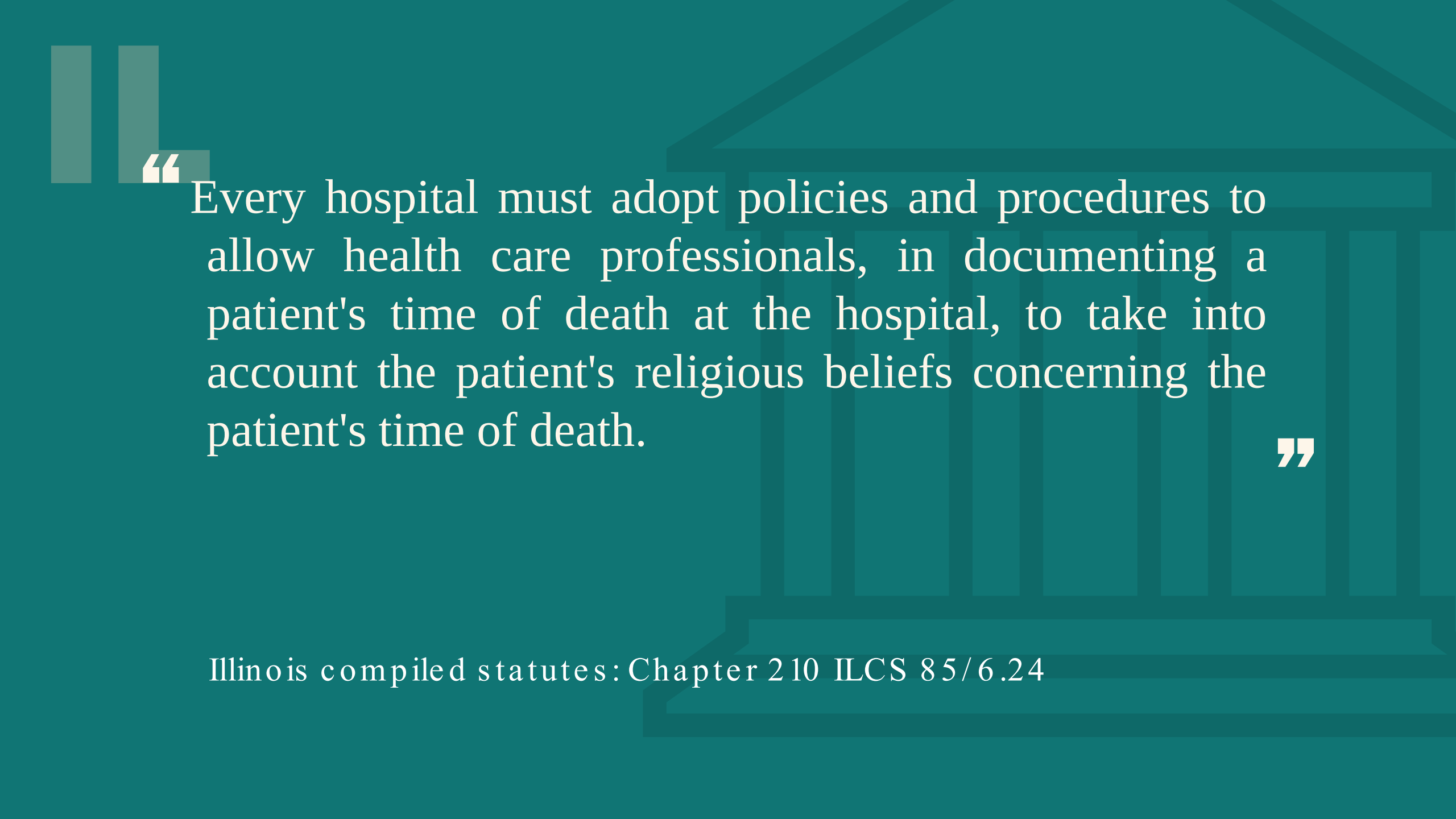
NJ

“

The death of an individual shall not be declared upon the basis of neurological criteria... when the licensed physician authorized to declare death, has reason to believe... that such a declaration would violate the personal religious beliefs of the individual. In these cases, death shall be declared... solely upon the basis of cardio-respiratory criteria....

”

NJ Administrative Code § 13:35-6A.6: Exemption to accommodate personal religious beliefs



“

Every hospital must adopt policies and procedures to allow health care professionals, in documenting a patient's time of death at the hospital, to take into account the patient's religious beliefs concerning the patient's time of death.

”

Illinois compiled statutes: Chapter 210 ILCS 85/6.24

CA

“

...[A] reasonably brief period of accommodation... from the time that a patient is declared dead by [neurological criteria].... During this reasonably brief period of accommodation, a hospital is required to continue only previously ordered cardiopulmonary support. No other medical intervention is required.

...[A] “reasonably brief period” means an amount of time afforded to gather family or next of kin at the patient’s bedside.

...[T]he hospital shall make reasonable efforts to accommodate... religious and cultural practices....

...For purposes of this section, in determining what is reasonable, a hospital shall consider the needs of other patients and prospective patients in urgent need of care.

”

California Health and Safety Code § 1254.4

Neurocritical Care Society Brain Death Toolkit



<https://www.neurocriticalcare.org/NCS-Learning-Center/Learning-Center/Results/Details/brain-death-toolkit>

eAppendix 5. Brain Death/Death by Neurologic Criteria Checklist

Last Name	First name	DOB	MRN
PREREQUISITES FOR CLINICAL EXAMINATION			
1. Ascertainment that the patient has sustained a catastrophic, permanent brain injury caused by an identified mechanism that is known to lead to brain death/death by neurologic criteria (BD/DNC) (7a and 13a)			☐ Yes ☐ No Etiology:
2. Neuroimaging consistent with mechanism and severity of brain injury (in patients with primary posterior fossa injury, neuroimaging should demonstrate catastrophic supratentorial injury) (7c and 40)			☐ Yes ☐ No
3. Observation for permanency a) ≥48 hours after acute brain injury (particularly hypoxic ischemic brain injury) for patients ≤2-years-old (8) b) ≥24 hours after hypoxic ischemic brain injury for patients ≥2-years-old (9b) c) A sufficient amount of time after brain injury to ensure there is no potential for recovery of brain function as determined by the evaluator based on the pathophysiology of the brain injury (9a)			☐ Yes ☐ No Observation period (hours)
4. Core body temperature ≥ 36°C (for ≥24 hours for patients whose core body temperature has been ≤35.5°C [10a and b])			☐ Yes ☐ No
5. Systolic blood pressure (SBP) ≥ 100 mm Hg and mean arterial pressure (MAP) ≥ 75 mm Hg for adults/SBP and MAP ≥ 5 th percentile for age in children (for patients on venoarterial ECMO: MAP ≥ 75 mm Hg for adults/MAP ≥ 5 th percentile for age in children) (11b and 11c)			☐ Yes ☐ No
6. Exclusion of pharmacologic paralysis (if administered or suspected) through use of train-of-four stimulator or demonstration of deep tendon reflexes (12a)			☐ Yes ☐ No ☐ Not
7. Drug levels for medications that may suppress central nervous system function are therapeutic/subtherapeutic (if available), pentobarbital level is <5 mcg/mL (if the patient received pentobarbital) and at least five half-lives for all other such drugs have passed (longer if there is renal/hepatic dysfunction or if the patient is obese or was hypothermic); (12a)			☐ Yes ☐ No
8. Alcohol blood level ≤ 80 mg/dL (if clinically indicated) (12a)			☐ Yes ☐ No ☐ Not
9. Toxicology screen (urine and blood) is negative (if clinically indicated) (12a)			☐ Yes ☐ No ☐ Not
10. Exclusion of severe metabolic, acid-base, and endocrine derangements; (12a)			☐ Yes ☐ No
11. A reasonable attempt has been made to inform the patient's family of the plan to perform a BD/DNC examination (35a)			☐ Yes ☐ No
Prerequisite Summary (check one):			
☐ All prerequisites were met			
☐ Unable to adequately correct metabolic derangements, but all other prerequisites were met, so will complete the neurologic examinations and apnea testing and if they are consistent with BD/DNC, will perform ancillary testing (12b)			
☐ One or more prerequisites were not met, so the evaluation was not completed			

Q&A





Only the cat

Thank you

Special thanks to Dr. Igor
Rybinnik for his slide style
guide

Ref

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