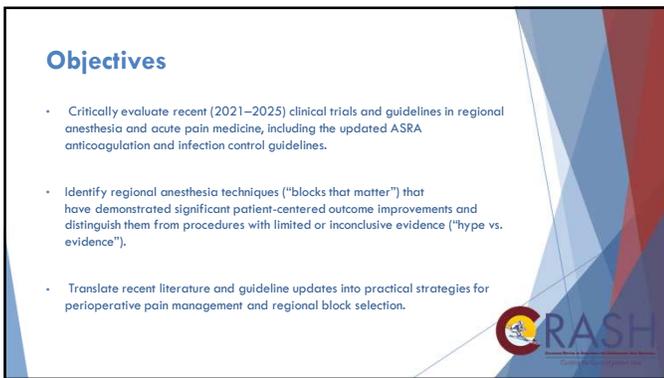


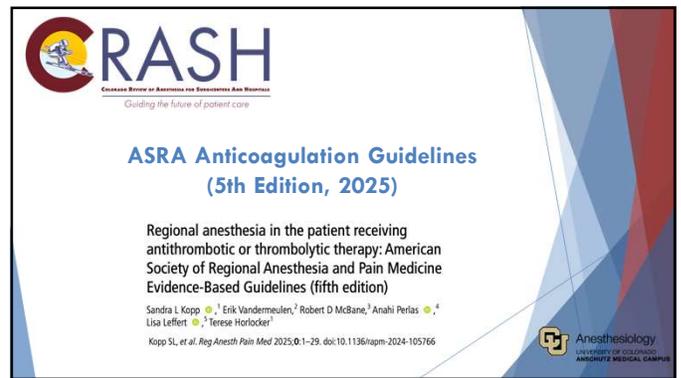
1



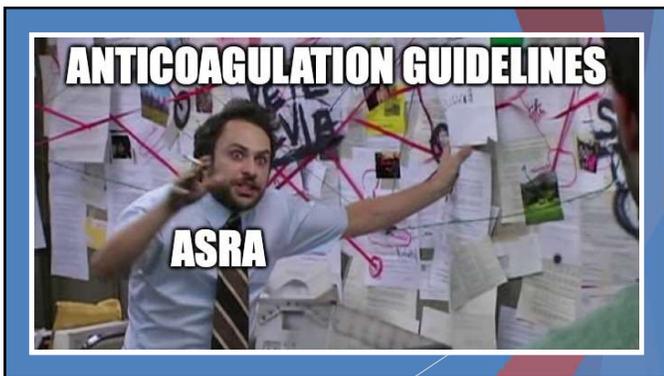
2



3



4



5



6

### Evolution of the Guidelines

- 1998 and 2003**
  - Original ASRA Guidelines.
  - In response to rise of hemorrhagic complications with rollout of enoxaparin.
  - Focused on neuraxial blocks and surgical patients
- 2010**
  - Added comments on deep plexus blocks and peripheral techniques
- 2018**
  - Described growing literature about VTE prevention and hemorrhagic risk in parturients.
  - Acknowledged differential risk for interventional pain procedures and pregnant population.
  - Great discussion of pharmacokinetics of anticoagulants.
- 2025**
  - Current published guidelines

7

### 10,000 ft View: Changes vs 2018 (4th Edition)

**BREAKING NEWS**

- Terminology shift:
  - "Prophylactic/therapeutic" → "low dose/high dose"
  - Aligns with other guidelines and accounts for patient characteristics
- Major expansion and clarification of DOAC sections
- Introduction of acceptable residual drug level thresholds for selected situations
  - New monitoring modalities with expansion of anti-Xa level testing
- More explicit renal-function-based pathways
- Deep plexus/deep peripheral blocks continue to follow neuraxial-style precautions (unchanged)

**CRASH**

8

### Lab Monitoring Changes:

### Drug-Level-Based "Off-Ramps"

- New concept: in selected situations, neuraxial/deep blocks may proceed based on measured residual anticoagulant activity
- For several DOACs, guideline now specifies acceptable residual levels
  - DOAC level < 30 ng/mL OR
  - Anti-Xa activity ≤ 0.1 IU/mL
- This is not a mandate to measure levels — it provides a safety target when levels are checked

9

Drug	Low Dose (Prophylaxis)	High Dose (Therapeutic)
Apixaban	2.5 mg BID • Post-THA/TKA prophylaxis • Extended VTE prevention	5 mg BID (or 2.5 mg BID if dose-reduced by criteria) • AF stroke prevention • DVT/PE treatment
Edoxaban	N/A	60 mg daily or 30 mg daily if: (1) CrCl 15–50 (2) wt ≤ 60 kg or (3) P-gp inhibitor
Rivaroxaban	10 mg daily (VTE prophylaxis) 2.5 mg BID + aspirin (CAD/PAD)	20 mg daily (CrCl >50) or 15 mg daily (CrCl 30–50)
Dabigatran	110 → 220 mg daily (THA prophylaxis)	150 mg BID or 75 mg BID if CrCl 15–30
Enoxaparin (Lovenox)	40 mg once daily or 30 mg q12h • VTE prophylaxis	1 mg/kg q12h or 1.5 mg/kg daily • Treatment dosing / bridging

Terminology: Low Dose vs High Dose

10

### Dabigatran: Clearer Low-Dose vs High-Dose Pathways

**Low-dose dabigatran:**

- Hold at least ~48h before neuraxial/deep block (or check level if shorter)
- Avoid neuraxial/deep block in CrCl <30 unless level confirms minimal activity

**High-dose dabigatran:**

- CrCl ≥50: hold ~72h (or check level if shorter)
- CrCl 30–49: hold ~120h (or check level if shorter)
- CrCl <30: generally avoid neuraxial/deep block unless level confirms minimal activity
- Postoperative restart timing is also more conservative for high-dose regimens

11

### Rivaroxaban: New Guidance for Unanticipated Dosing

- Addresses real-world problem: anticoagulant administered with neuraxial catheter in situ
- If low-dose rivaroxaban already given:
  - Delay catheter removal ≥24h (≥30h if CrCl <30) OR
  - Confirm residual level < ~30 ng/mL or anti-Xa ≤ ~0.1 IU/mL before removal
- More structured response to medication errors or communication failures

**CRASH**

12

### Low Molecular Weight Heparin (LMWH): What's Not Changed – And Why it's Discussed More

- ▶ Most core timing recommendations are unchanged from prior editions
  - ▶ Single-daily low-dose LMWH: similar catheter placement/removal intervals as before
  - ▶ High-dose LMWH: catheter out before first postoperative dose; delay first dose after placement
- ▶ What's expanded: discussion that anti-Xa activity may persist longer than expected in some patients

Implication: timing rules remain conservative by design



13



14

### Controversy #1: Conservative vs Thrombosis-Focused Guidelines

- ASRA explicitly states these are hemorrhage-avoidance guidelines
- This leads to more conservative timing than many thrombosis-prevention or perioperative medicine guidelines
- Core Tension:  
Delay of surgery / interruption of anticoagulation / VTE  
vs  
Extremely rare but catastrophic neuraxial bleeding

Practical takeaway: anticoagulation planning must include both bleeding and thrombosis perspectives



15

### Controversy #2: The "<30 ng/mL" and "anti-Xa ≤0.1 IU/mL" Thresholds

- Not all hospitals have rapid or reliable access to calibrated DOAC or anti-Xa assays
- Turnaround time may limit real-world usefulness
- Exact correlation between measured residual level and neuraxial bleeding risk is not definitively proven
- Guideline acknowledges uncertainty, especially after use of reversal agents
- Aligns with emerging European guidance and provides a rational safety target



16

### Controversy #3: Low Dose vs High Dose — Simpler, But Potentially Confusing

- Pros:
  - Better reflects that dose, indication, and patient factors change pharmacokinetics
  - Harmonizes with European (ESAIC/ESRA) approach
- Cons:
  - Clinicians may misclassify common "reduced dose" or renal-adjusted regimens

Practical solution: each institution should correlate common regimens to "low" vs "high" categories



17

### Controversy #4: Deep Blocks Treated Like Neuraxial

- ASRA continues to recommend neuraxial-style precautions for deep plexus/deep peripheral blocks
- Some clinicians argue ultrasound guidance and site compressibility should allow more flexibility
  - Other interventional societies (e.g. interventional radiology) have different guidelines for deep blocks or procedures
- Guideline remains conservative because bleeding in these sites can be occult and catastrophic
- This remains an area of practice variation and debate



18

January 2025

**Controversy #5:  
IV Heparin**

**Intravenous heparin**  
Discontinue heparin infusion for a minimum of 4-6 hours and coagulation status be assessed and normal prior to neuraxial block or deep plexus/peripheral block (grade 1A)

*Remarks: there is no change in this recommendation.*  
Delay intravenous heparin administration for a minimum of 1 hour after needle placement (grade 1A)

*Remarks: there is no change in this recommendation.*

**It is not recommended to maintain neuraxial or deep plexus catheters in the setting of continuous intravenous heparin administration. In the event of unanticipated heparinization, we recommend monitoring the patient with an indwelling catheter to allow for early detection of motor deficits and consider use of minimal concentration of local anesthetics to enhance early detection of a neuraxial hematoma (grade 1A)**

*Remarks: there is no change in this recommendation.*

Although the occurrence of a bloody or difficult neuraxial needle placement may increase the risk of hematomas, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is recommended (grade 1A)

*Remarks: there is no change in this recommendation.*

It is not suggested to maintain neuraxial or deep plexus/peripheral catheters in the setting of full anticoagulation during cardiac surgery. If unanticipated heparinization occurs, we suggest postoperative monitoring of neurological status and consider use of minimal concentration of local anesthetics to enhance early detection of neuraxial hematoma (grade 1C)

*Remarks: there is no change in this recommendation.*

19

September 2025

**Controversy #5:  
IV Heparin**

**Intravenous heparin**  
Discontinue heparin infusion for a minimum of 4-6 hours and coagulation status be assessed and normal prior to neuraxial block or deep plexus/peripheral block (grade 1A)

*Remarks: there is no change in this recommendation.*  
Delay intravenous heparin administration for a minimum of 1 hour after needle placement (grade 1A)

*Remarks: there is no change in this recommendation.*

**Monitor the patient postoperatively to provide early detection of motor blockade and consider use of minimal concentration of local anesthetics to enhance the early detection of a spinal hematoma (grade 1A).**

*Remarks: There is no change in this recommendation although it was inadvertently removed from this edition.*

Although the occurrence of a bloody or difficult neuraxial needle placement may increase the risk of hematomas, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is recommended (grade 1A)

*Remarks: there is no change in this recommendation.*

It is not suggested to maintain neuraxial or deep plexus/peripheral catheters in the setting of full anticoagulation during cardiac surgery. If unanticipated heparinization occurs, we suggest postoperative monitoring of neurological status and consider use of minimal concentration of local anesthetics to enhance early detection of neuraxial hematoma (grade 1C)

*Remarks: this suggestion reflects a change to avoid the use of neuraxial or deep plexus catheters in cardiac surgery patients with full anticoagulation, due to the increased risk of hematomas and the availability of less invasive alternatives.*

20

“ Deviation from suggestions or recommendations contained in this document may be acceptable based on the judgment of the responsible anesthesiologist. The recommendations are designed to encourage safe and quality patient care but cannot guarantee a specific outcome. They are also subject to timely revision as justified by evolution of information and practice. ”

Special article

**Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (fifth edition)**

Sandra L Kopp Erik Vandermeulen,<sup>2</sup> Robert D McBane,<sup>3</sup> Anahí Perlas ,<sup>4</sup> Lisa Jeffert ,<sup>5</sup> Tense Horlocker<sup>1</sup>

21

**CRASH**  
Critical Review of Anesthesia for Emergent Airway Resuscitation  
Guiding the future of patient care

**WHERE WERE GOING WE DON'T NEED ...ROADS**

22

**CRASH**  
Critical Review of Anesthesia for Emergent Airway Resuscitation  
Guiding the future of patient care

**Research**

**Common interventional procedures for chronic non-cancer spine pain: a systematic review and network meta-analysis of randomised trials**

BMJ 2025 ; 388 doi: <https://doi.org/10.1136/bmj-2024-079971> (Published 19 February 2025)  
Cite this as: BMJ 2025;388:e079971

Anesthesiology  
University of Colorado  
ANESTHESIOLOGY MEDICAL CAMPUS

23

**Strong recommendations AGAINST**

All or nearly all well-informed people would likely not want such interventions. Such interventions should therefore not be offered outside of a clinical trial

**Chronic axial spine pain**

- ✘ Epidural injection of local anesthetic, steroids, or their combination (1)
- ✘ Joint radiofrequency ablation (2)
- ✘ With or without joint targeted injection of local anesthetic and steroids (2)
- ✘ Joint targeted injection of local anesthetic, steroids, or their combination (2)
- ✘ Intramuscular injection of local anesthetic with or without steroids (3)

**Chronic radicular spine pain**

- ✘ Dorsal root ganglion radiofrequency with or without epidural injection of local anesthetic, or local anesthetic and steroids (1)
- ✘ Epidural injection of local anesthetic, steroids, or their combination (1)

These recommendations are based on the evidence that was reviewed in this systematic review and network meta-analysis.

Anesthesiology  
University of Colorado  
ANESTHESIOLOGY MEDICAL CAMPUS

24

“ [...] the substantial reimbursement associated with these procedures may act as a *perverse incentive* for their delivery as opposed to less well paying, and more time-consuming, interventions that have evidence of effectiveness (for example, cognitive functional therapy, exercise therapy, pain reprocessing therapy). ”

**RAPID RECOMMENDATIONS**

**Commonly used interventional procedures for non-cancer chronic spine pain: a clinical practice guideline**

Jason W Busse,<sup>1,2,3</sup> Stéphane Genevay,<sup>4</sup> Arnav Agarwal,<sup>5</sup> Christopher J Standaert,<sup>6</sup> Kevin Carneiro,<sup>6</sup> Jason Friedrich,<sup>7</sup> Manuela Ferreira,<sup>8</sup> Hilde Verbeke,<sup>9</sup> Jens Ivar Brox,<sup>10</sup> Hong Xiao,<sup>11</sup> Jasmeer Singh Virdee,<sup>12</sup> Janet Gunderson,<sup>13</sup> Gary Foster,<sup>14</sup> Conrad Heegoma,<sup>15</sup> Caroline F Samar,<sup>16,17</sup> Matteo Coen,<sup>18,19</sup> Gordon H Guyatt,<sup>20</sup> Xiaojin Wang,<sup>21</sup> Behnam Sadeghrad,<sup>2,3</sup> Faheem Malam,<sup>22</sup> Dena Zeraatkar,<sup>2,3</sup> Per O Vandvik,<sup>23</sup> Ting Zhou,<sup>24</sup> Feng Xie,<sup>25</sup> Reed A C Siemieniuk,<sup>26</sup> Thomas Agoritsas<sup>28,29</sup>

25

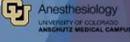


**BREAKING NEWS**

Pain Management > Back Pain

**Another Expert Group Throws Shade at Spinal Injections for Back Pain**  
— “No more effective than sham procedures,” evidence review finds

by John Geier, Contributing Writer, MedPage Today  
February 19, 2025 - 5 min read  
Last Updated March 5, 2025



26

**Multisociety Response to *The BMJ* Publications on Interventional Spine Procedures for Chronic Back and Neck Pain (March 18, 2025)**

- International Pain and Spine Intervention Society
- American Academy of Pain Medicine
- American College of Radiology
- American Society of Neuroradiology
- American Society of Pain and Neuroscience
- American Society of Regional Anesthesia and Pain Medicine
- American Society of Spine Radiology
- ANICA (Arbeitsgemeinschaft der Nicht-Operativen Orthopädischen)
- Association of Pain Program Directors
- Belgian Pain Society
- Boston Pain Society
- Dutch Society of Musculoskeletal Medicine
- Eastern Pain Association
- Flemish Anesthesiology Association for Pain Management
- GIIMDO (Gruppo Italiano Multidisciplinare Dolore Orofaciale)
- IGOST (Interdisziplinäre Gesellschaft für Orthopädische/Unfallchirurgische und Allgemeine Schmerztherapie)
- Indian Society for Study of Pain
- ISAL Foundation - Institute for Pain Research
- Italian Society of Pain Clinicians
- Korean Pain Society
- Latin American Pain Society
- North American Neuromodulation Society
- North American Spine Society
- Oregon Society of Interventional Pain Physicians
- PAIN, Dutch Chapter of the IASP
- Pacific Spine and Pain Society (PSPS)
- Pain Section of the Dutch Society of Anesthesiology
- SIAARTI (Società Italiana di Anestesia Analgesia Rilassazione e Terapia Intensiva)
- Sierra Spine Society
- Society of Interventional Radiology
- Spanish Pain Society
- Turkish Society of Physical Medicine and Rehabilitation Specialists
- World Academy of Pain Medicine United
- World Institute of Pain

27

- Balanced Authorship
- Enhanced Study Design and Execution
- Broader Evidence Inclusion When RC Data are Lacking
- Policy Implications Awareness
- The BMJ Clinical Practice Guideline Retraction




28

“ We agree with Rittenberg and Shanthanna that further research is warranted and acknowledged that *additional evidence may alter recommendations* [...] However, such claims are *not supported by the current best evidence*, which shows that all common interventional procedures supported by moderate or low certainty evidence provide little to no improvement in pain relief or physical functioning compared with sham procedures. ”



29

**The takeaway...**

We must publish what we are doing if we want recommendations/guidelines to reflect actual practice.



30



31

### Infection Control Guidelines First Edition (ASRA 2025)

ASRA Pain Medicine consensus practice infection control guidelines for regional anesthesia and pain medicine

David Anthony Provenzano<sup>1</sup>, Michael Hanes<sup>2</sup>, Christine Hunt<sup>3</sup>, Honorio T Benzon<sup>4,5</sup>, Jay S Grider<sup>6</sup>, Kelly Cawcutt<sup>7</sup>, Tina L Doshi<sup>8,9,10</sup>, Salim Hayek<sup>11,12</sup>, Bryan Hoelzer<sup>13</sup>, Rebecca L Johnson<sup>14</sup>, Hari Kalagara<sup>15</sup>, Sandra Kopp<sup>16</sup>, Randy W Loftus<sup>14</sup>, Alan James Robert Macfarlane<sup>17,18</sup>, Ameet S Nagpal<sup>19</sup>, Stephanie A Neuman<sup>20</sup>, Amit Pawa<sup>21,22</sup>, Amy C S Pearson<sup>23</sup>, Julie Pilitsis<sup>24</sup>, Eellan Sivasenan<sup>25</sup>, Rakesh V Sondekoppam<sup>26</sup>, Jan Van Zundert<sup>27,28</sup>, Samer Narouze<sup>29</sup>  
Provenzano DA, et al. *Reg Anesth Pain Med* 2025;0:1–50. doi:10.1136/rapm-2024-105651

32

## Big Picture

- Serious infectious complications after regional anesthesia are **rare but potentially catastrophic**
- Spectrum includes: insertion-site inflammation, local abscess, systemic infection, necrotizing fasciitis, and CNS infection
- Because events are rare, RCTs and databases often miss true risk factors; much evidence comes from case series
- Delayed diagnosis is associated with worse neurologic outcomes and death

**Low-probability, high-consequence events** → prevention and vigilance matter more than statistics

33

## Catheter Colonization vs True Infection

- Colonization is common:
  - Epidural/intrathecal catheter colonization ~4–29%; intrathecal anesthesia catheters ~7%
  - Peripheral nerve block (PNB) catheters: colonization ~6–46%
- Colonization ≠ infection; many positive cultures represent contamination during removal
- No reliable CFU threshold predicts clinical infection in RA catheters
- Colonization is influenced by: (1) duration, (2) patient risk factors, (3) tunneling, (4) dressing care, and (5) catheter manipulation

**Key concept:** colonization is common; true infection is rare; colonization is the gateway.

34

## Duration Matters (Major Modifiable Risk Factor)

- Insertion-site inflammation is more common than true infection (~5.3% vs 0.5%)
- Infection risk increases with **longer catheter duration**
  - Epidural catheters: ~40% increased risk per additional day in situ
  - Peripheral nerve catheters: risk rises after ~2–4 days
  - Large multicenter study (24,103 PNB catheters): ~2.9% infection rate with max duration 15 days

Simply: The longer a catheter stays in, the less likely it is to remain infection-free.

35

**German Network for Regional Anesthesia (25 centers)**

- 44,555 patients who had surgery between 2007 and 2014
- Examined the relationship between catheter duration and probability of infection-free catheter use

36

## Catheter related infection

- Peripheral catheter incidence: 0-7%; Epidural catheter incidence: 0.8-5%
- Rates of infection vary wildly based on placement technique and post-op duration
  - US max duration usually 1-4 days
  - Switzerland 1.5-5 days
  - Australia 1-13 days
  - Germany 1-36 days

37

## Prolonged Catheter Use and Infection in Regional Anesthesia

Retrospective Analysis of 44,555 Patients in 25 Centers in the German Network for Regional Anesthesia

Frequencies of Infection-free Catheters Decrease Over Time

	Peripheral	Epidural
Day 4	95%	95%
Day 7	96%	95%
Day 15	73%	73%

Rates of Infection

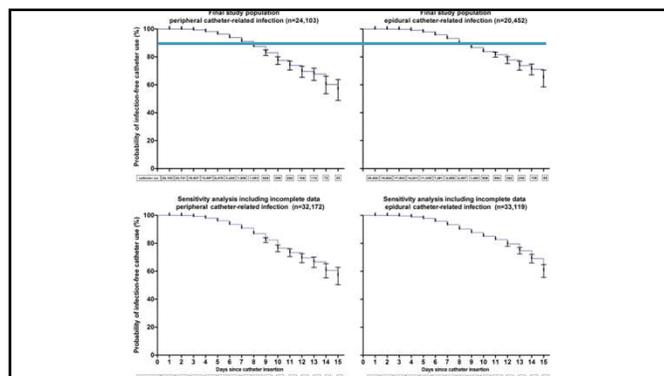
	Peripheral	Epidural
Mild	2.5%	3.3%
Moderate	0.5%	0.6%
Severe	0.07%	0.07%

1,497 Infected Catheters Were Identified, 38 Were Left In Situ  
Severe infections requiring surgical intervention developed in 207, 463 after catheter removal and in 536 left in situ

Infection risk for peripheral and epidural catheters increases over time, especially after 4 days.

Bombardieri H, et al. ANESTHESIOLOGY. April 2018.

38



39

## CNS Infections: Rare but Devastating

- Incidence after neuraxial block ~1-5 per 100,000 (≈8 per million spinals; ≈11 per million epidurals)
- Includes: epidural abscess, meningitis, discitis, osteomyelitis, sepsis, death
- Outcomes are worse with delayed diagnosis or neurologic deficits at presentation

Clinical pearl: fever + back pain + neurologic change after neuraxial = emergency until proven otherwise

40

## Tunneled vs Non-Tunneled Catheters

- Tunneled catheters are associated with lower infection risk
- Large series (22,411 thoracic epidurals): tunneling strongly associated with fewer catheter-related infections
- Subcutaneous ports: ~50% lower infection rate vs percutaneous exit; no infections before day 70 in one study
- Tunneled epidurals still have mechanical failures and infection risk in long-term use

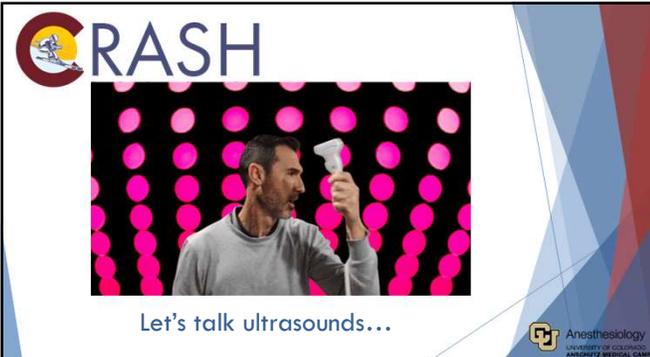
**Bottom line: if it must stay long (or placed in a site at risk for infection), tunnel the catheter.**

41

## Key Evidence-Based Recommendations (From This Section)

- Consider limiting duration of percutaneous tunneled catheters and placing a subcutaneous port to minimize infection risk (Grade B)
- Prolonged use of regional nerve block catheters (>4-5 days) should be **individualized** with close monitoring (Grade C)
- Avoid prolonged use (>2 weeks) of externalized intrathecal catheters due to meningitis risk (Grade B)

42



# CRASH

Let's talk ultrasounds...

Anesthesiology  
UNIVERSITY OF COLORADO  
ANSHUTZ MEDICAL CAMPUS

43

## How Contaminated Is Ultrasound Equipment?

- Multiple studies show frequent contamination of ultrasound probes and machines
- Reported contamination rates of ultrasound probes after clinical use:
  - 20–60% in various perioperative and ICU studies
  - Common organisms: coagulase-negative Staph, Staph aureus, Enterococcus, Gram-negative bacteria
- Contamination occurs even when probes appear visually clean
- Implication: the ultrasound machine is a major vector if not managed as part of the sterile field



44

## Probe, Cable, and Gel: Three potential problems

- The ultrasound **probe, cable, and gel** can all act as vectors for pathogen transmission
- Probe covers significantly reduce (but do not eliminate) contamination of the probe head
  - Microperforations in probe covers occur and increase with:
    - Longer procedures
    - Probe manipulation and needle contact
  - Therefore, **sterile gel inside the cover** and skin antiseptics remain critical
- Multiple outbreaks of bacterial infection have been linked to contaminated ultrasound gel
- Both multi-use and single-use gels have been implicated in outbreaks
- Gel can support bacterial growth and transmit organisms to the needle or catheter



45

## Probe, Cable, and Gel: Three potential problems

- Multiple outbreaks of bacterial infection have been linked to contaminated ultrasound gel
- Both multi-use and single-use gels have been implicated in outbreaks
- Gel can support bacterial growth and transmit organisms to the needle or catheter




46

## Probe, Cable, and Gel: Three potential problems



### Alert: Use Only Sterile Ultrasound Gel for Percutaneous Procedures

For Everyone  
MAY 13, 2025

**WHAT TO KNOW**

- CDC has received reports of *Paraburkholderia fungorum* (an environmental bacterium) associated with the use of ultrasound gel from multiple states from 2024–2025.
- Use of non-sterile ultrasound gel for percutaneous procedures (procedures that involve puncturing the skin) risks patient safety.
- CDC is assisting with an ongoing multistate investigation.



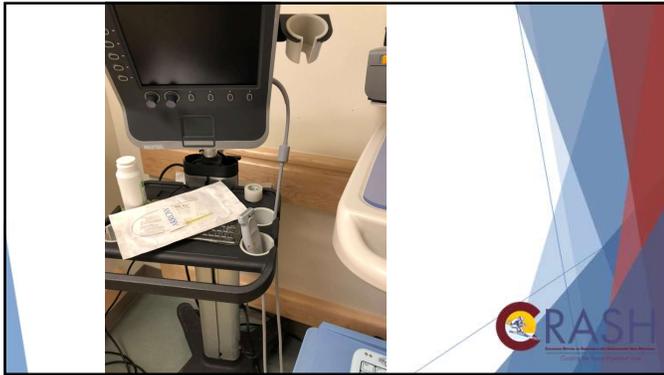
47

## Cleaning, Disinfection, and Sterilization: Not the Same Thing

- Cleaning: removes visible debris but does not reliably kill microorganisms
  - **Low-level disinfection:** kills some bacteria and viruses, not spores or mycobacteria
  - **High-level disinfection:** kills bacteria, viruses, mycobacteria, and most fungi
- Most ultrasound probes used for **regional anesthesia** require at least low- or intermediate-level disinfection between patients
- Probes used for **neuraxial or deep procedures** should follow institutional high-level disinfection policies when applicable



48



49



50

**ASRA Recommendations:**

- Use **sterile gel for neuraxial, deep blocks, and catheter procedures**
  - Never reuse gel packets between patients
- Use **sterile probe covers** for:
  - Neuraxial procedures
  - Deep plexus blocks
  - Continuous catheter techniques
- Use **sterile gel inside the cover**; non-sterile gel may be used on intact skin outside the sterile field only if it does not contact the needle path
- **Disinfect probe and cable** between patients per manufacturer and infection control policy
- Treat the probe, cable, and machine controls as part of the sterile field during the procedure



51

## Suzetrigine: A Novel Analgesic Approach

Slides adapted from Kenneth Hunt, MD

52

### Current State of Play

- ❖ Opioids
- ❖ NSAIDs
- ❖ Acetaminophen
- ❖ NMDA inhibitors
- ❖ Non-selective Sodium Channel Inhibitors
- ❖ Gabapentinoids
- ❖ Alpha 2 Agonists
- ❖ Antispasticity or Antispasmodic agents

Anesthesiology  
UNIVERSITY OF COLORADO  
ANIRVCHITZ MEDICAL CAMPUS

53

### Suzetrigine (Journavx) "suzzette-tre-gene" ("jor-na-vix")

- Approved Jan 2025 for use in adults with moderate to severe pain
  - 100 mg loading dose followed by 50 mg Q12 for up to 14 days
- First non-opioid analgesic approved in 25 years
- First in class
  - Highly selective NaV1.8 inhibitor (31,000:1 selectivity)
  - Stabilizes the closed state of Na channel
- NaV1.8 is Expressed in peripheral sensory neurons including dorsal root ganglion
  - Expressed in intracardiac ganglia in animals
- Does not appear to have addictive properties

54

## Suzetrigine - Pharmacology

### Pharmacokinetics

- Metabolized Via CYP3A and is **inducer** of CYP3A
- Has active but less potent metabolite (M6-SUZ)
- Excretion:**
  - Feces: 49.9%
  - Urine: 44.0%
- Half life elimination: 23.6 hours
  - 33 hr for M6-SUZ

### Contraindications and special considerations

- Avoid strong CYP3A4 inhibitors
  - Grapefruit juice, darifenpridine, azole antifungals
- May interact with hormonal contraceptives
  - Use **alternative contraceptives for 28 days after last dose**
- Dose adjustments needed for Child Pugh B
- No dose adjustments for eGFR >15ml/min

55

## Suzetrigine – Gimme the data

- Two phase 3 clinical trials
- Over 1000 patients in each trial Abdominoplasty and Bunionectomy
- Excluded patients that had painful physical conditions, sensory abnormalities, long term use of opioids or NSAIDs
- Randomization occurred post operatively
- Comparators:**
  - Suzetrigine vs. Hydrocodone/acetaminophen (5-325 q6) vs. Placebo
- Outcomes:** Reported pain on numeric rating scale at 19 time points (0.3-48 hours)

56

## Outcomes

### Primary outcome

- Time-weighted sum of the pain intensity difference for **suzetrigine compared to placebo** over 48 hours after first dose of study drug (SPID48)

### Secondary outcomes

- SPID48 for **suzetrigine compared to hydrocodone-acetaminophen**
- Time to 2 point or greater reduction in numeric pain rating scale from baseline
- AKA: time to clinically meaningful pain relief

57

## Results

- Suzetrigine vs. placebo
  - Abdominoplasty 48.4 (P <0.0001)
  - Bunionectomy 29.3 (P=0.0002)
- Suzetrigine vs. HB/APAP
  - Abdominoplasty 6.6 (p=0.278)
  - Bunionectomy -20.2 (P=0.0016)

**Table 2. Primary Endpoint: SPID48 Compared to Placebo**

	Abdominoplasty		Bunionectomy	
	Suzetrigine N = 447	Placebo N = 223	Suzetrigine N = 426	Placebo N = 216
Pre-specified analysis with rescue medication (propofol)				
LS mean ± SE	116.4 ± 4.3	70.7 ± 6.1	99.9 ± 4.5	70.6 ± 6.3
LS mean difference from placebo	45.6	—	29.3	—
95% CI	(33.0-48.1)	—	(14.5-44.0)	—
P value vs placebo	<0.0001	—	0.0002	—
Post hoc analysis without rescue medication (as treated)				
LS mean ± SE	153.0 ± 4.5	105.4 ± 6.4	128.8 ± 4.7	100.1 ± 6.6
LS mean difference from placebo	47.7	—	28.8	—
95% CI	(23.4-62.0)	—	(17.2-40.5)	—
Normal P value vs placebo*	<0.0001	—	0.0004	—

**Table 3. First Key Secondary Endpoint: SPID48 Compared to HB/APAP**

	Abdominoplasty		Bunionectomy	
	Suzetrigine N = 447	HB/APAP N = 446	Suzetrigine N = 426	HB/APAP N = 431
Pre-specified analysis with rescue medication (propofol)				
LS mean ± SE	116.4 ± 4.3	111.8 ± 4.3	99.9 ± 4.5	120.1 ± 4.5
LS mean difference from HB/APAP	4.6	—	-20.2	—
95% CI	(-5.4 to 16.7)	—	(-32.7 to -7.7)	—
P value vs HB/APAP	0.2781	—	0.0016	—
Post hoc analysis without rescue medication (as treated)				
LS mean ± SE	153.0 ± 4.5	141.0 ± 4.5	128.8 ± 4.7	140.8 ± 4.7
LS mean difference from HB/APAP	12.0	—	-11.8	—
95% CI	(-0.5 to 24.4)	—	(-24.8 to 11.2)	—
Normal P value vs HB/APAP*	0.0565	—	0.0752	—

58

## Results

### Secondary Outcome:

Time to 2-point or greater reduction in numeric pain rating scale

#### Abdominoplasty

- Suzetrigine 119 min
- Placebo 480 min

#### Bunionectomy

- Suzetrigine 240 min
- Placebo 480 min

**Table 4. Second Key Secondary Endpoint: Time to 2-Point or Greater Reduction in NPRS from Baseline Compared to Placebo**

	Abdominoplasty		Bunionectomy	
	Suzetrigine N = 447	Placebo N = 223	Suzetrigine N = 426	Placebo N = 216
Pre-specified analysis with rescue medication (propofol)				
Median time (min)	119	480	240	480
95% CI	(96-160)	(417-709)	(117-417)	(616-716)
Normal P value vs placebo* (log-rank test)	<0.0001	—	0.0016	—
Post hoc analysis without rescue medication (as treated)				
Median time (min)	91	180	132	180
95% CI	(69-116)	(115-235)	(115-177)	(120-240)
Normal P value vs placebo* (log-rank test)	<0.0001	—	0.0053	—

59

## Results

**Table 5. Mean NPRS over time**

**Fig 3. Mean NPRS over time** The figure includes participants who were randomized and received at least one dose of study drug. Participants were analyzed according to their randomization treatment at 0.3 h to 48 h. The y-axis represents the mean NPRS (0-10) and the x-axis represents time in hours. The lines represent the mean NPRS (± SE) for each treatment group. The lines represent the mean NPRS (± SE) for each treatment group. The lines represent the mean NPRS (± SE) for each treatment group.

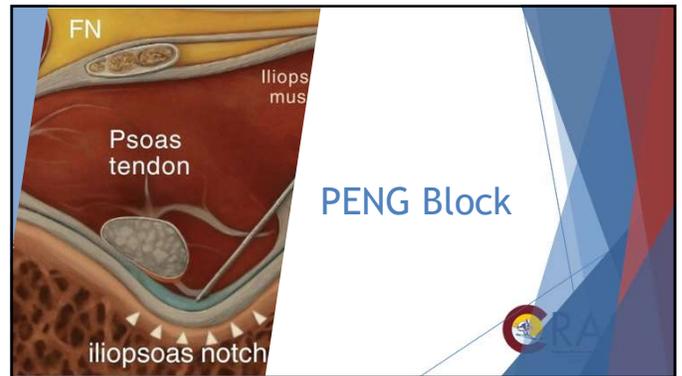
60

10

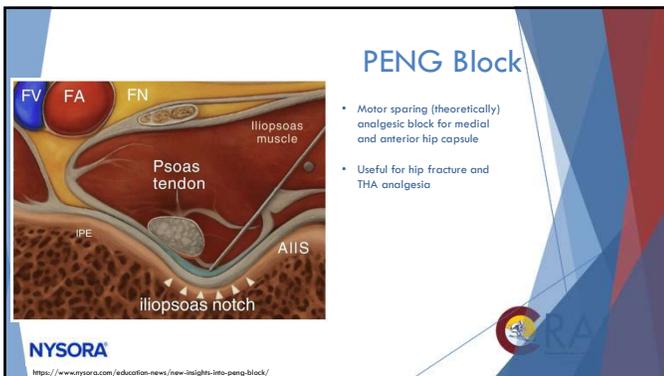




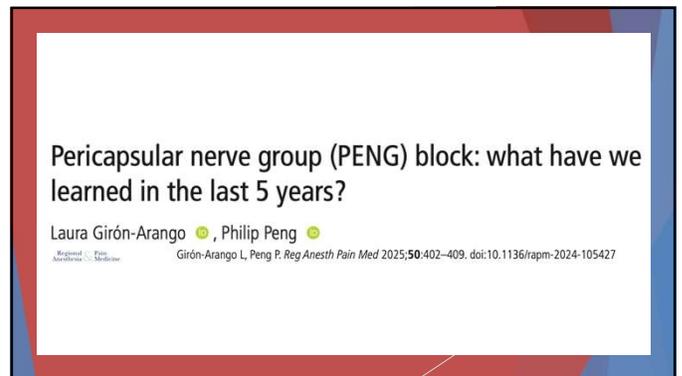
67



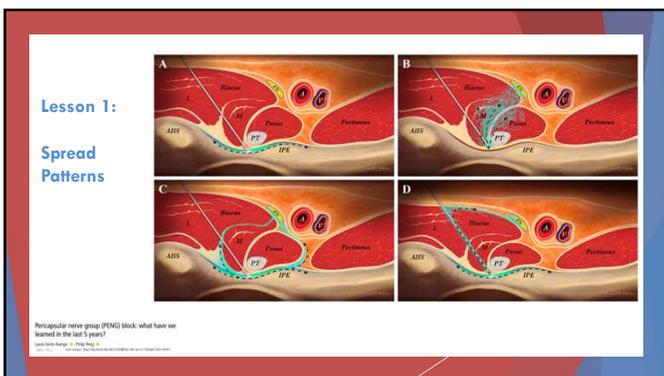
68



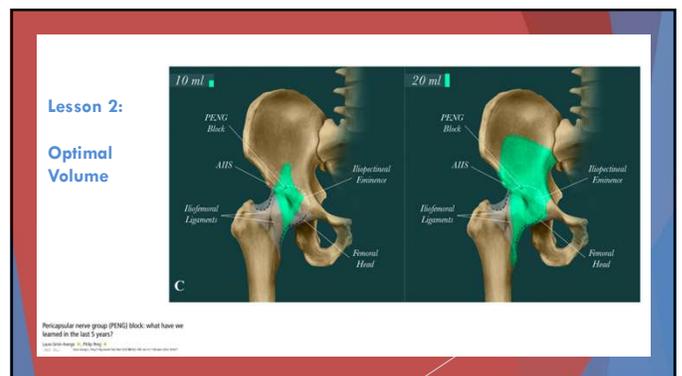
69



70



71



72

**Lesson 2:**  
**Optimal Volume**

Balocco et al. Reg Anesth Pain Med. 2024.

Pericapsular nerve group block: a 3D CT scan imaging study to determine the spread of ropivacaine

73

**Lesson 2b:**  
**What do we mean by "optimal"?**

74

**Lesson 2b:**  
**Balancing act between:**

- (1) analgesic efficacy and
- (2) motor sparing

75

**Lesson 2b:**  
**Optimal Volume**

Balocco et al. Reg Anesth Pain Med. 2024.

**20 mL volume (18 mL ropivacaine with 2 mL contrast)**

Pericapsular nerve group block: a 3D CT scan imaging study to determine the spread of ropivacaine

76

**Lesson 2b:**  
**Optimal Volume**

**• Pelvic and Intramuscular spread: possible femoral nerve or lumbar plexus involvement → motor block**

**• Hip capsule and Obturator spread: ideal (intended) spread pattern**

Pericapsular nerve group block: a 3D CT scan imaging study to determine the spread of ropivacaine

77

**Lesson 2b:**  
**Optimal Volume**

- 32 cadaver specimens – 45 randomized blocks
- Dye injected (0.1% methylene blue)
- Volumes 2-22 mL

**Cadaveric study investigating the femoral nerve-spreading volume for pericapsular nerve group (PENG) block:**

Pragathiweeranatharajah G, Prasad Karanika, Prithviraj Prasad, Venkatesh Madhavan, Venkatesh Madhavan, Pavan Ram, Madhavan Kishoregowd, Prasad Mahalingam, De G. Jay. J. Orthop. Res. 2024

78





