

Silencing the Storm: Anesthetic Approaches in Modulating Surgical Stress and Inflammation

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“Postoperative morbidity and mortality are largely the product of the *preoperative condition* of the patient, the *quality of surgical care* provided, and the *degree of surgical stress elicited*.” (Gillis, et al., 2022)

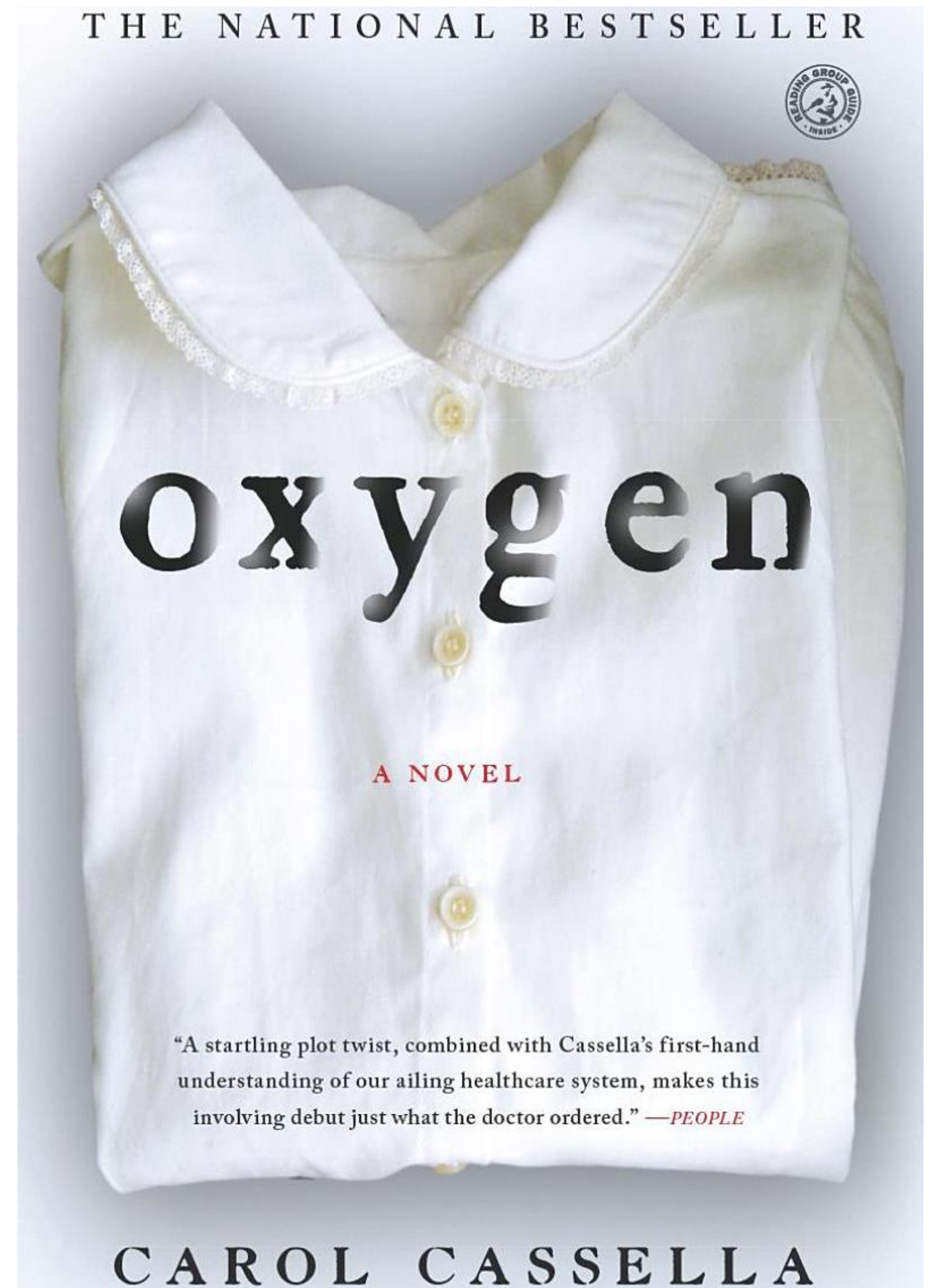


It starts with us.

CRNAs are uniquely positioned to play an immense role, from before the time of surgery throughout the entire perioperative period.



“We are in an unspoken physiologic communion, my patient and I. I stand like a **sentry at the gate of surgical trespass.**”



Objectives

01.

Ground Zero

Define causes and influencing mechanisms of surgical stressors

02.

Chasing Waterfalls

Review the inflammatory cascade and mitigation strategies

03.

Oxygen Against Us

Understand the unique role of oxygen in cellular damage and repair



01.

Ground Zero

Define causes and influencing mechanisms of surgical stressors



“The systemic stress response triggered by surgical trauma is characterised by **sterile inflammation** preceding metabolic and neuroendocrine dysregulation.”

Manou-Stathopoulou, et al. (2019)

The Surgical Stress Response

Physiological

Neuroendocrine
Inflammatory

Pathophysiological

Adrenocortical insufficiency
Oxidative stress



A blurred background image showing a medical setting. On the left, a blue stethoscope is visible. Below it, a portion of a silver smartphone is shown. The background is a mix of light and dark tones, with a white triangular shape pointing towards the center.

Major Determinants

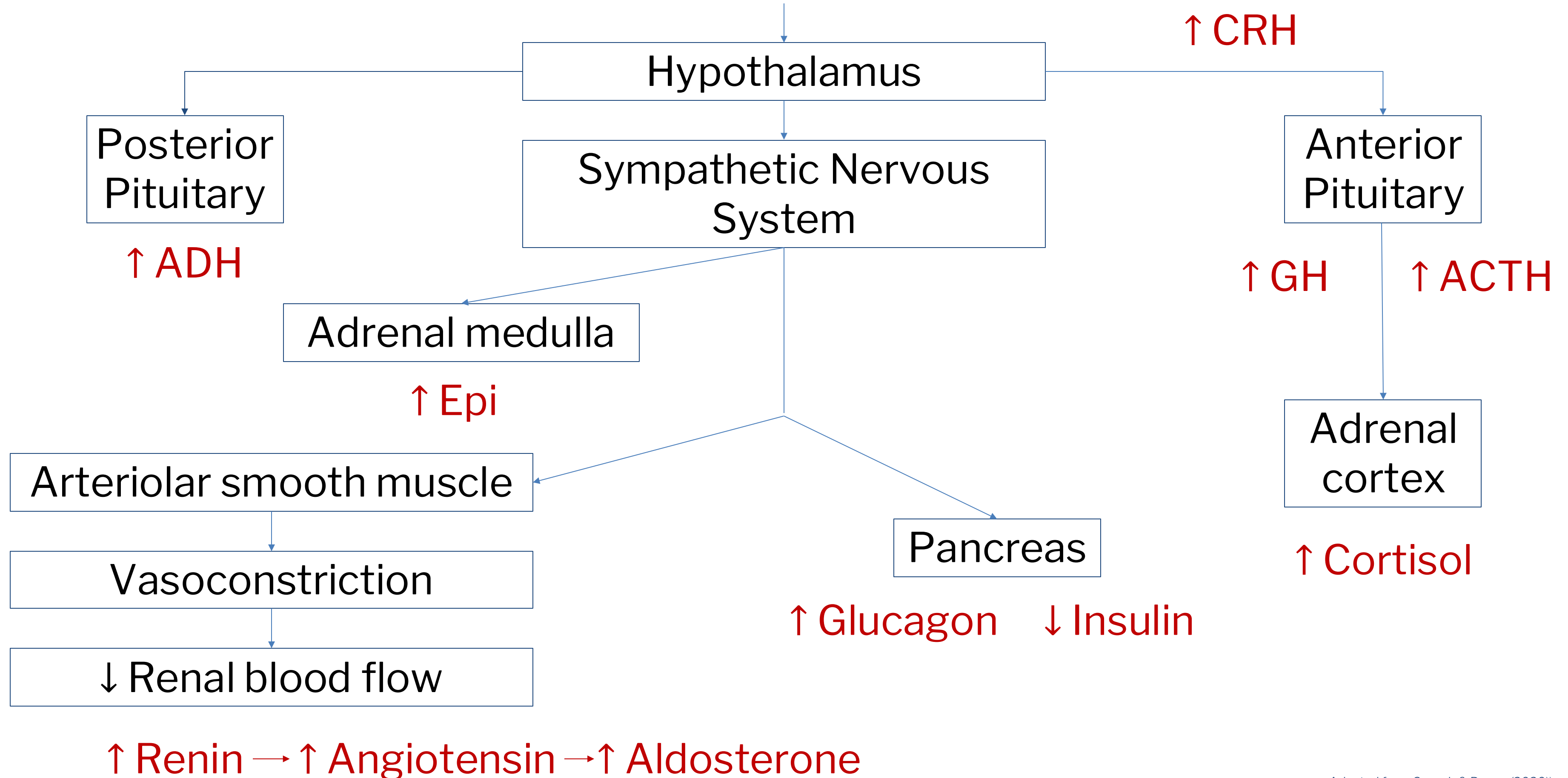
Magnitude, invasiveness,
duration of surgery

A blurred background image showing a medical setting. On the right, a hand wearing a blue nitrile glove is holding a black stethoscope. The background is a mix of light and dark tones, with a white triangular shape pointing towards the center.

Top Surgical Insults

1. Major open vascular/abdominal
2. Joint replacement
3. Cardiac surgery on CPB

Surgical Stress



HPA Axis

Hypothalamus

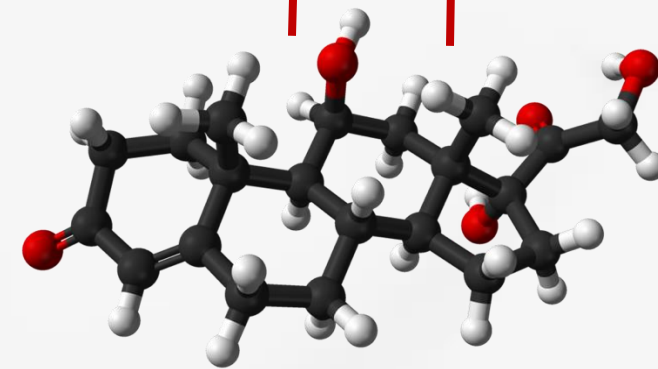
Pituitary

Inflammation (TNF- α , IL1, IL6)



Adrenal

ACTH



Cortisol

Tissue injury

Pain

Inflammation (TNF- α , IL1, IL6)

NPO status, anxiety, psych
history, frailty, poor exercise
tolerance

THE Aging

- Higher basal cortisol
- Blunted negative feedback

THE Frail

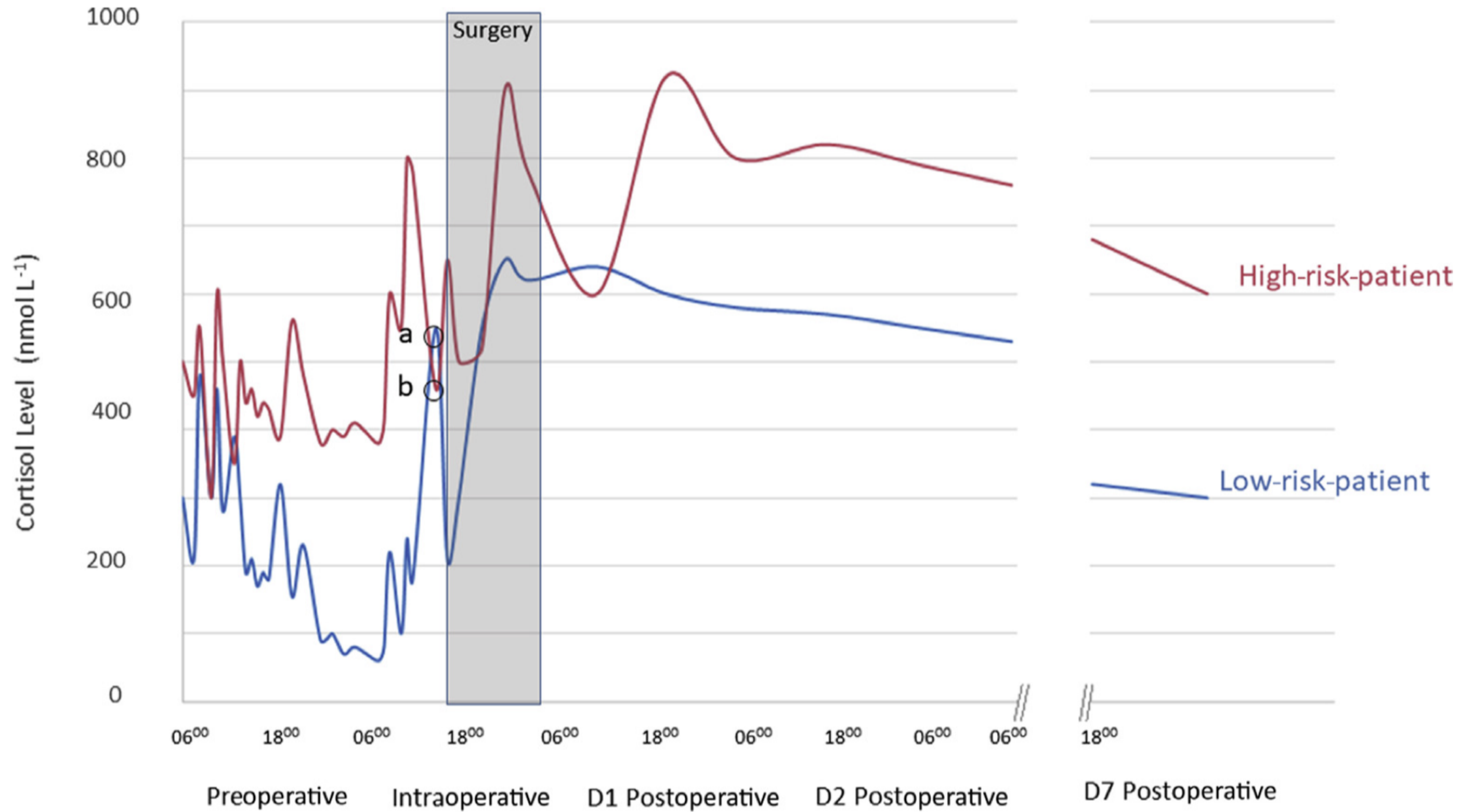
- Muscle protein synthesis suppression
- Neural degeneration and apoptosis

THE Cardiovascular Deconditioned

- Increased cardiac events in established heart failure
- Increased morbidity and mortality after noncardiac surgery

Who is at high
risk?







When problematic
cortisol becomes
worse

Adrenal sensitization

Reduced carrier proteins

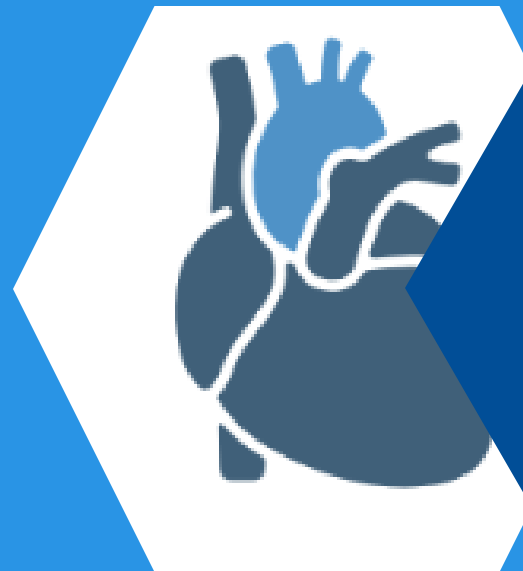
Reduced plasma clearance

Postoperative Implications

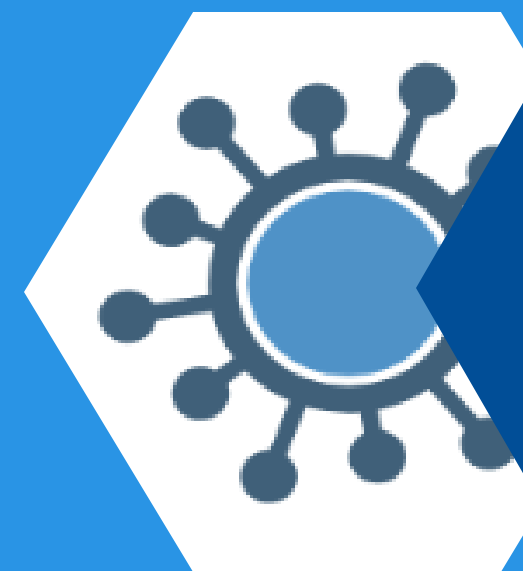
Perioperative stress response in chronic disease



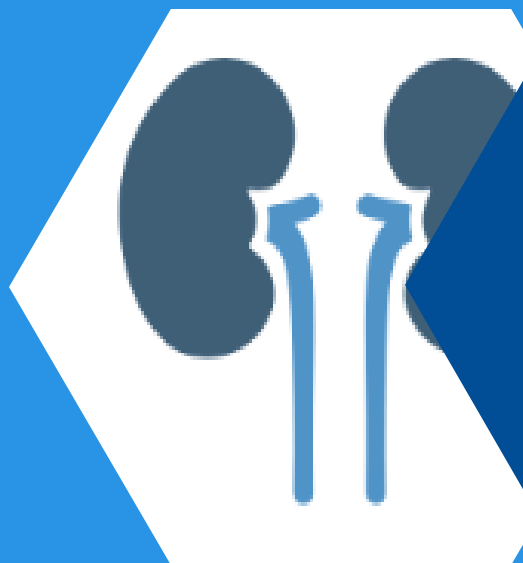
**Cognitive
dysfunction**



**Myocardial
Injury**



Infection



**Acute
Kidney
Injury**



**Muscle
Atrophy**



02.

Chasing Waterfalls

Review the inflammatory cascade and mitigation strategies

A photograph of an operating room with surgical equipment, including a large overhead light and a patient table, serving as a background for the text.

Inflammation is present in all chronic disease, and in surgery

Inflammatory Response

01.

Part of innate immunity

02.

No memory component

03.

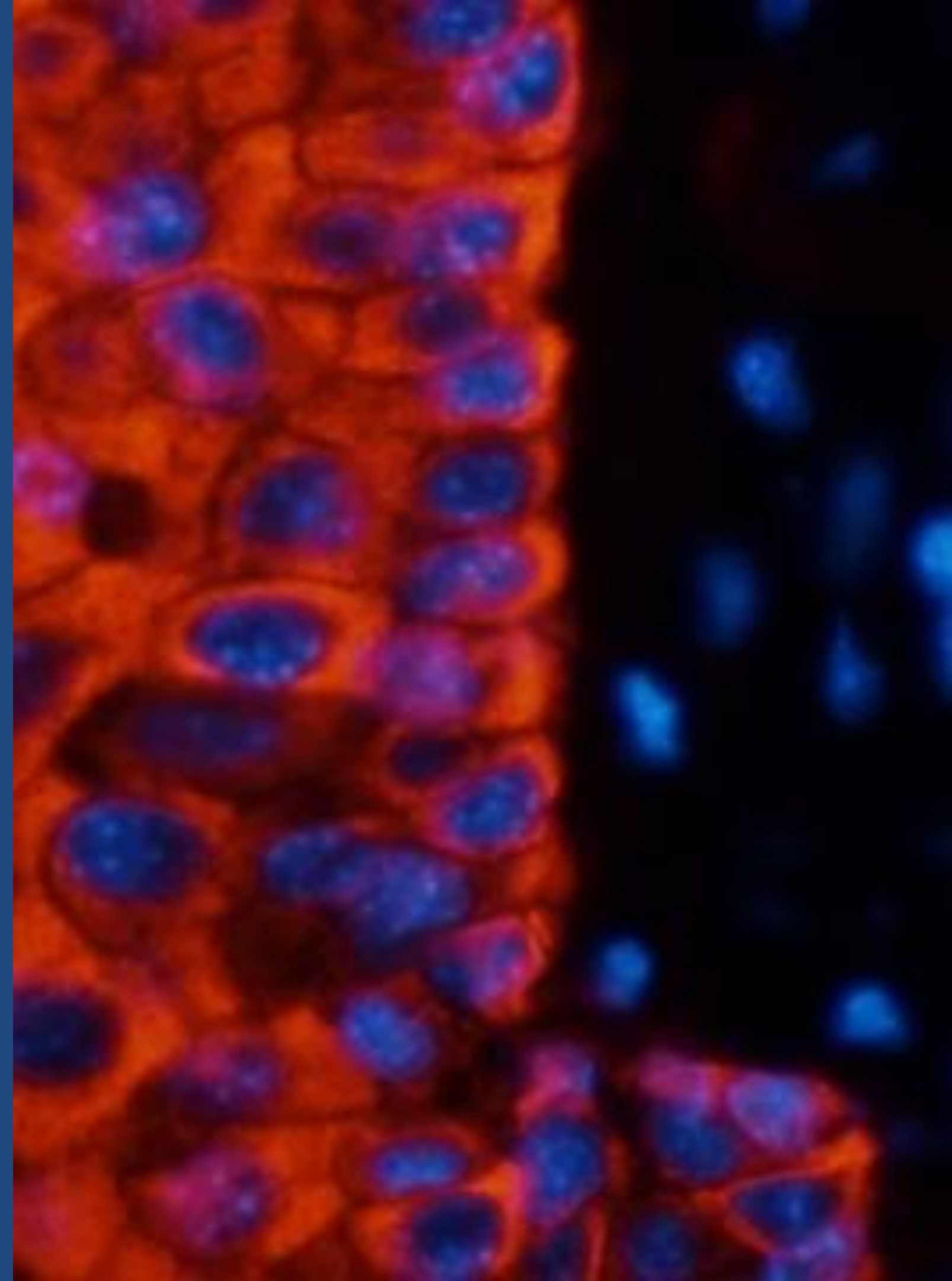
ACUTE phase: occurs immediately and continues until threat is gone

04.

CHRONIC: persists until healing and repair is complete

Vascular events and cellular mediators regulate the inflammatory response

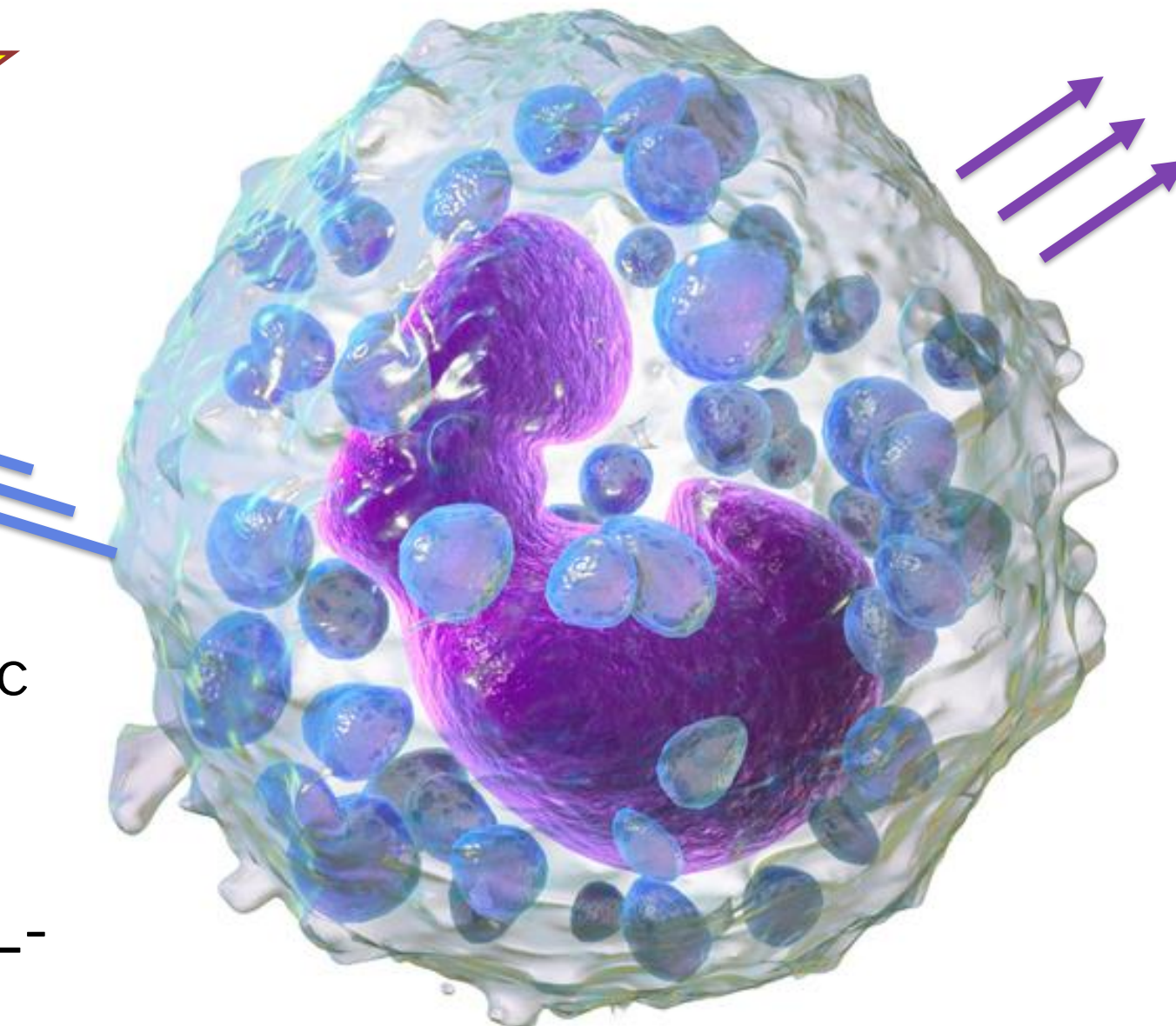
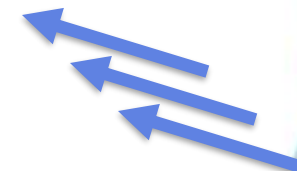
- ❖ Vasoconstriction precedes vasodilation
- ❖ Vasodilation accompanies cell wall permeability
- ❖ Mast cell degranulation and release of mediators is a central event



Mast Cell Degranulation

Performed Mediators

- **Histamine**
 - **Increases vascular permeability and vasodilation**
- Proteoglycans
 - Heparin
 - Chondroitin sulfate
- Tryptase
 - Key marker in anaphylactic reactions
- Serotonin
- Cytokines, Chemokines (IL-4, TNF, GM-CSF)
 - Immunomodulatory proteins



Central event in inflammation; can be initiated by IgE complexes, complement components (circulating proteins), mechanical trauma, endotoxins, and free radicals as some examples

Newly Synthesized

- Prostaglandins
 - Associated with pain, bronchoconstriction, inhibited platelet aggregation
 - Pyrogenic
- Leukotrienes
- Platelet-activating factor (PAF)
- Cytokines
- Chemokines
- Growth factors
- Free radicals
- Substance P
 - Important neuropeptide and neuromodulator in pain perception

Surgical stress mediation





“Prehabilitation” vs. ERAS

C. Gillis, O. Ljungqvist, F. Carli (2022)



Functional capacity



Nutritional status



Physical status



Psychosocial status

Psychological Interventions

Systematic reviews (Villa et al., 2020; Lanini et al., 2022) have supported the following:

- Cognitive-behavioral therapies
- Relaxation techniques
- Mindfulness
- Hypnosis
- Coping strategies
- Written emotional disclosure
- Narrative medicine



Additional considerations for the plan of care

- Patients with chronic disease may demonstrate **glucocorticoid resistance/insufficiency**
- Critical care and perioperative trials suggest **glucocorticoid administration** reduces inflammation

Selective hydrocortisone administration (“stress dosing”) is highly debated among anesthesia professionals.



Suppressed HPA Axis



**≥ 20 mg prednisone /
day or equivalent**



Corticosteroid coverage for surgery in patients taking exogenous corticosteroids

For minor procedures or surgery under local anesthesia (eg, inguinal hernia repair), take usual morning steroid dose. No extra supplementation is necessary.

For moderate surgical stress (eg, lower extremity revascularization, total joint replacement), take usual morning steroid dose. Give 50 mg hydrocortisone intravenously just before the procedure and 25 mg of hydrocortisone every eight hours for 24 hours. Resume usual dose thereafter.

For major surgical stress (eg, esophagogastrectomy, total proctocolectomy, open heart surgery), take usual morning steroid dose. Give 100 mg of intravenous hydrocortisone before induction of anesthesia and 50 mg every eight hours for 24 hours. Taper dose by half per day to maintenance level.

UpToDate®

Benzodiazepines

- Inhibit cortisol at the HPA axis
- Decrease pro-inflammatory cytokine levels

FRIEND



Propofol

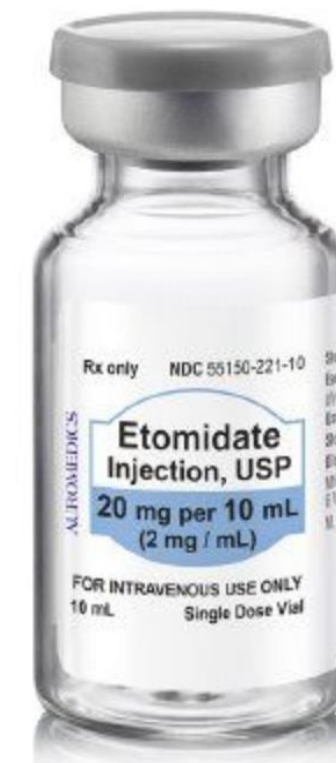
- A single induction dose suppresses circulating cortisol levels.
- Continuous infusion may completely block cortisol secretion.
- Also decreased pro-inflammatory cytokines

FRIEND



Etomidate

- Suppresses adrenocortical function for up to 8 hours after single dose.
- Increased mortality when used as an infusion in critical care



FOE

Volatiles

- Inhibit ACTH, cortisol, catecholamine, and GH more than IV agents
- Impair platelet aggregation more than propofol
- Many immunosuppressive and immunoactivating effects

FRIEND AND FOE



Opioids

- Reduce ACTH and GH secretion
- Possible immunomodulatory role
- Morphine demonstrates dose-dependent *immunosuppression*
- May influence tumor cell growth

FRIEND AND FOE



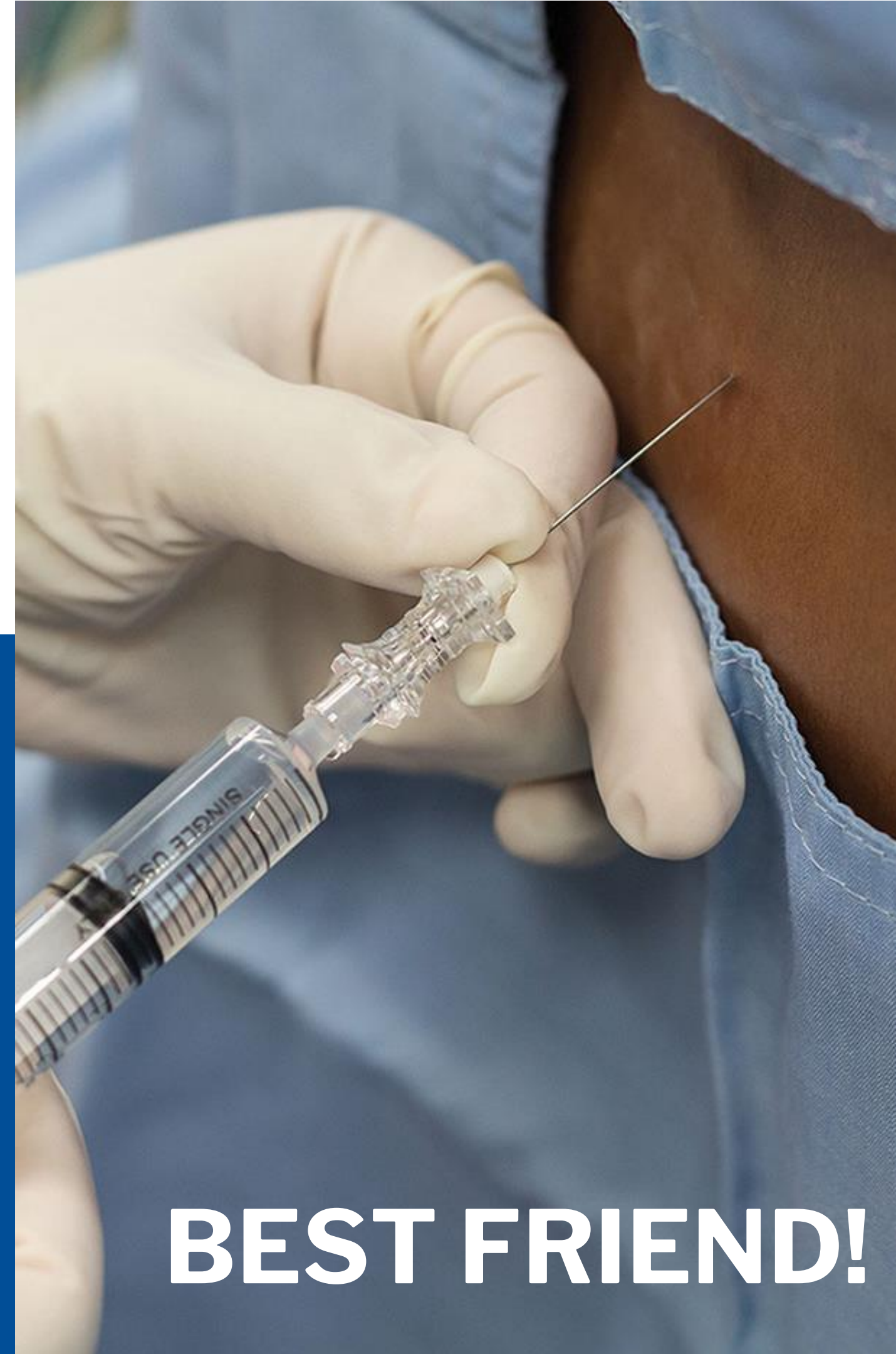
Neuraxial / Regional

Earlier return
of gut function

Reduced
pulmonary
dysfunction

Reduced
inflammatory
response

Beneficial
coagulative status



BEST FRIEND!

ELSEVIER

Brazilian Journal of Anesthesiology



[Braz J Anesthesiol.](#) 2021 Sep-Oct; 71(5): 538–544.

PMCID: PMC9373480

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PMID: [34537124](https://pubmed.ncbi.nlm.nih.gov/34537124/)

Efficacy of ultrasound-guided Transversus Abdominis Plane (TAP) block in inguinal hernia surgery and the immunomodulatory effects of proinflammatory cytokines: prospective, randomized, placebo-controlled study

[Ebru Canakci](#),^{a,*} [Murat Cihan](#),^b [Ali Altinbas](#),^a [Zubeyir Cebeci](#),^a [Ahmet Gultekin](#),^c and [Nilay Tas](#)^a

- Visual Analog Scale (VAS) scores decreased in TAP group at 0, 4, 24 hours
- TNF- α and IL-1 β levels at 4, 24 hours significantly lower than preoperative levels ($p < 0.001$ for all comparisons)

Effects of DEX (Wang, et al., 2019)

EPINEPHRINE	NOREPINEPHRINE	CORTISOL	INFLAMMATORY MARKERS
Significantly decreased in DEX group (MD: -21.06; 95% CI: -25.82 to -16.29; $p < .000001$)	Significantly decreased in the DEX group (MD: e177.37; 95% CI: e230.86 to e123.88; $p < .000001$)	Significantly lower in the DEX group (MD: e13.73; 95% CI: e17.22 to e10.24; $p < .000001$)	Reduced: • Interleukin (IL)-6 • Tumor necrosis factor -α • C-reactive protein

03.

Oxygen Against Us

Understand the unique role of O₂ in cellular damage and repair

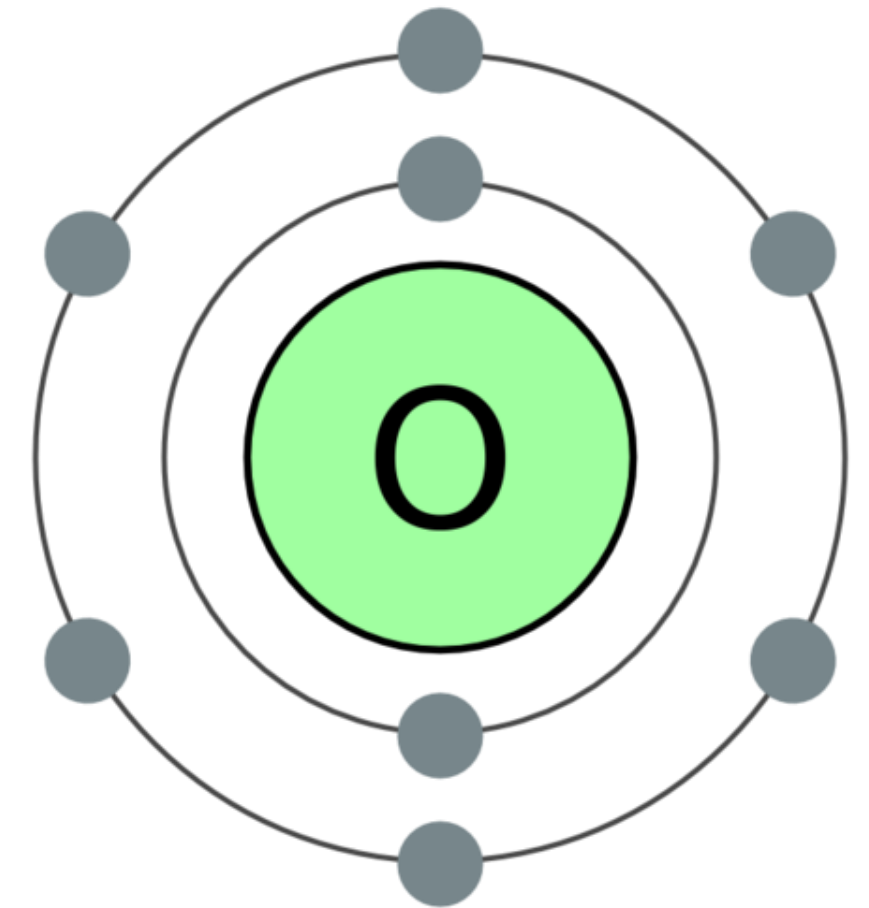
Free Radicals

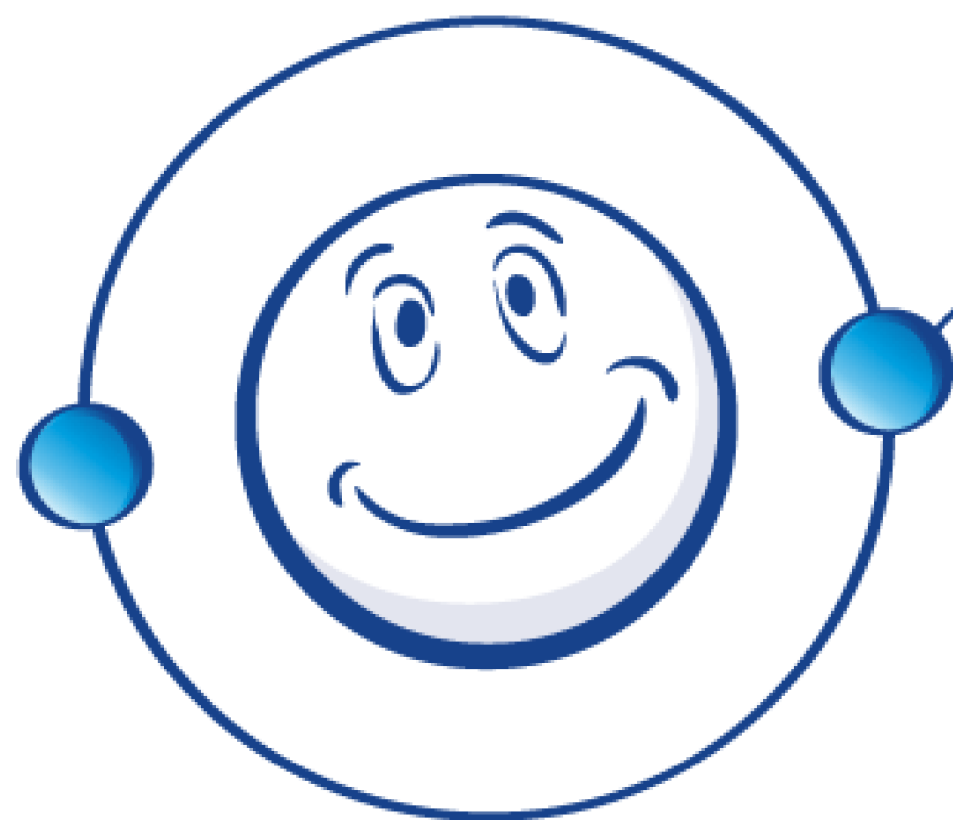
- Atom, molecule, or ion that has one or more unpaired valence electron
- Occur as intermediates during chemical reactions
- Normal process
- Excess accumulation can lead to series of chain reactions that destabilize molecules and cell membranes
- Implicated in human diseases

Reactive oxygen species (ROS)

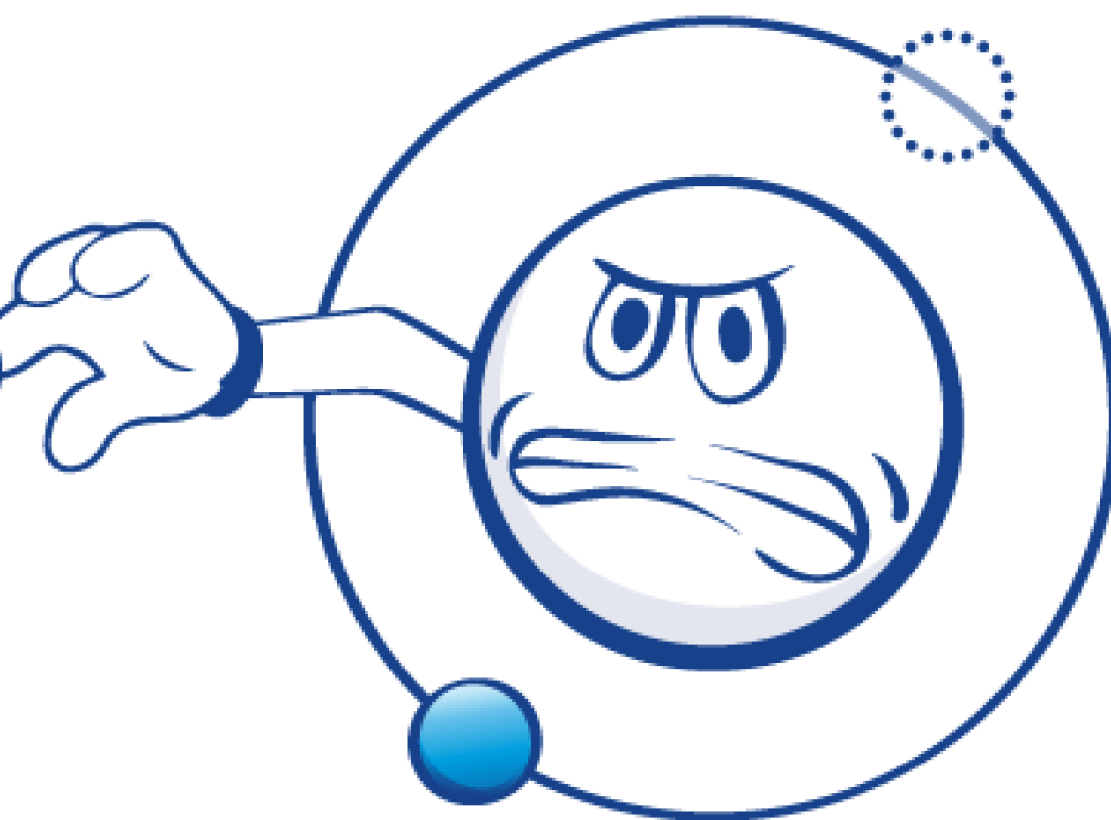
- Oxygen-derived free radicals
- Electron borrowing chain destabilizes nearby atoms
- Causes: smoking, stress, pollution, poor diet
- ROS-metabolizing enzymes and antioxidants stabilize free radicals

Vitamins C & E, transferrin, beta-carotene, CoQ10

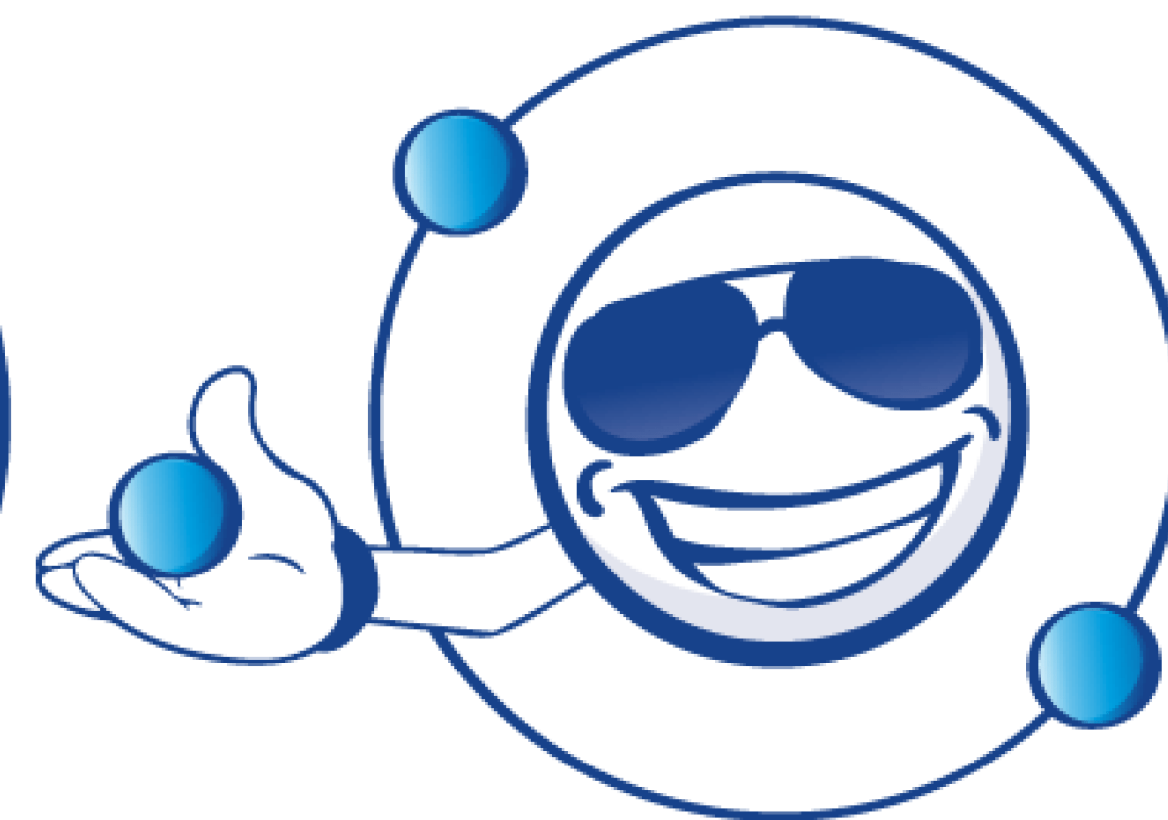




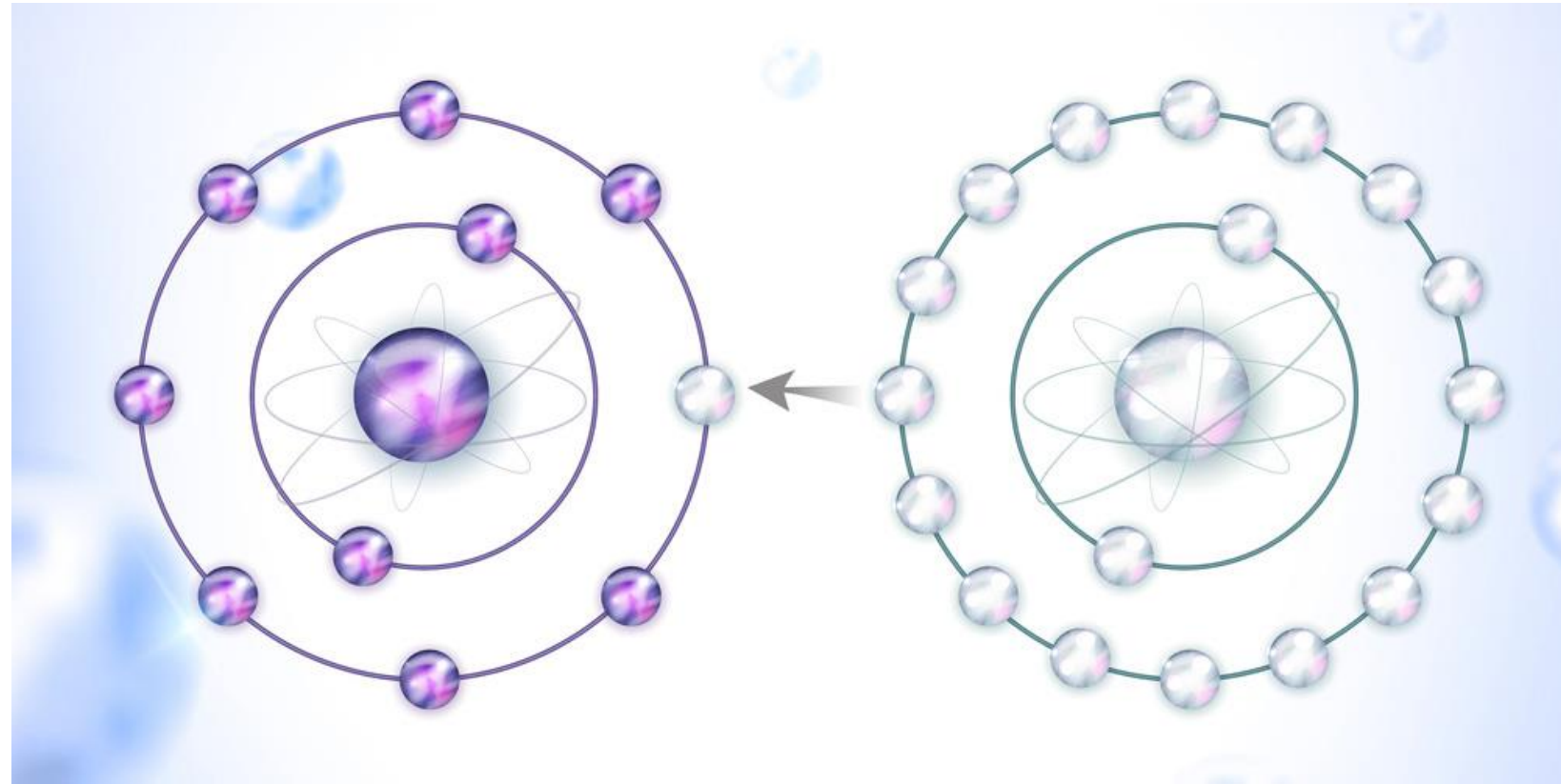
**HEALTHY
ATOMS**



**FREE
RADICALS**



ANTIOXIDANTS



Free radical

Antioxidant



Knock out free radicals.

POM
WONDERFUL
ANTIOXIDANT SUPERPOWER

Need more antioxidants in your corner?

POM Wonderful 100% Pomegranate Juice is here to help you fight the free radicals that cause oxidative stress with 700 mg of polyphenol antioxidants per 8oz serving. Drink it daily. Feel it forever.

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■ NARRATIVE REVIEW ARTICLE

Perioperative Oxidative Stress: The Unseen Enemy

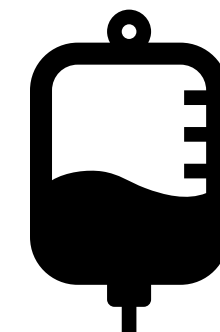
Jia L. Stevens, MBBS,*† Martin Feelisch, PhD,‡ and Daniel S. Martin, PhD*†

Reactive oxidative
species (ROS)

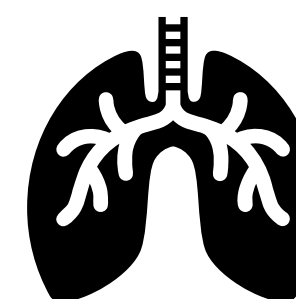
Interventions



Supplements



TIVA



FiO2 .30



In conclusion

Balanced anesthesia is all we could ever strive toward



Ability to determine individual
preoperative HPA axis functional status

Determinable outcomes related to
preoperative HPA phenotype

Highly individualized, targeted therapies
and patient care

Looking to the
future



Thank you!



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