Non-CME Webinar Series
designed with the trainee in mind
second Tuesdays of odd-numbered months

Brought to you by ASRA & THE ASSOCIATION OF PAIN PROGRAM DIRECTORS

Pain Procedures and Anticoagulation: **Common Pain Medications & Herbal Supplements**

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EMORY UNIVERSITY SCHOOL OF MEDICINE

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DISCLOSURES: None


Photographer: Ryan Patterson

OBJECTIVES

Understand the interventional pain impact of:

1) Common pain medications
   - Antidepressants (SSRI, SNRI, TCA)
   - Non-steroidal anti-inflammatory drugs (NSAID's)

2) Common herbal & dietary supplements

ANTIDEPRESSANTS & PAIN

- 60-80% of chronic pain patients in U.S. pain clinics have psychiatric illness
  - Major Depression & Anxiety in 30-50%
- Treatment improves pain, function, & QOL
- Both SSRI's & SNRI's increase bleeding risk via inhibiting platelet aggregation via **depleting serotonin inside platelets** (reuptake blockade)
- Nonserotonergic TCA's & Bupropion do **not** impact bleeding

Benzon HT et al. *Essentials of Pain Medicine*, 4th ed. 2018.
Narouze S et al. *Reg Anesth Pain Med* 2018; 43(3): 225-62.
Silvia Pelissero, Agnes-Cecile ~ "Dark Visions"

ANTIDEPRESSANT PROCEDURE RECS

- Routine discontinuation **not** recommended
- **Balanced decision**: procedure risk, serotonin reuptake of antidepressant, patient risk (severity of depression / suicide risk, concomitant antiplatelet/anticoagulants, ESLD and CKD)
- Coordinate with **Psychiatrist** if **high risk procedure:**
  - Uncontrolled depression: ⇧ **suicide** risk, ⇧ pain, worse procedural outcome
  - Gradual tapering for risk of **withdrawal syndrome** (venlafaxine & paroxetine = short $t_{1/2}$)
  - Consider **switch** to **non-serotonergic drug** (eg. bupropion, some TCA)
  - If stable depression: **5 $t_{1/2}$ Hold** (1-2 wks for most antidepressants except Fluoxetine = 5 wks)
  - **Restart** day after procedure

Procedure Risk	Patient Risk	Action
Low	Any	Continue
Intermediate	Any	Continue
High	Any	**Discuss with psychiatrist**

Narouze S et al. *Reg Anesth Pain Med* 2018; 43(3): 225-62.

Highest bleeding risk

Lowest bleeding risk

Antidepressant	Class	5HT Transporter Occupancy %	NorEpi Transporter Occupancy %	$t_{1/2}$ hrs	5-$t_{1/2}$ days	Active Metab	5-$t_{1/2}$ days
Paroxetine	SSRI	96	11	**21**	5 d		
Escitalopram	SSRI	94	5	27-32	5-6 d		
Citalopram	SSRI	93	0.4	35	7 d		
Fluoxetine	SSRI	89	7	24-72	5-15 d	Norfluoxetine	5-10 wks
Sertraline	SSRI	88	1	24	5 d	N-desmethyl-sertraline	2-3 wks
Imipramine	TCA	86	39	24	5 d	Desipramine	4-5 d
Venlafaxine	**SNRI**	85	12	**5**	1 d	O-desmethyl-venlafaxine	2 d
Doxepin	TCA	67	82	15	3 d		
Amitriptyline	TCA	66	49	13-36	3-7 d	Nortriptyline	1-3 wks
Duloxetine	**SNRI**	56	15	12	2-3 d		
Nortriptyline	TCA	19	80	30	7 d		

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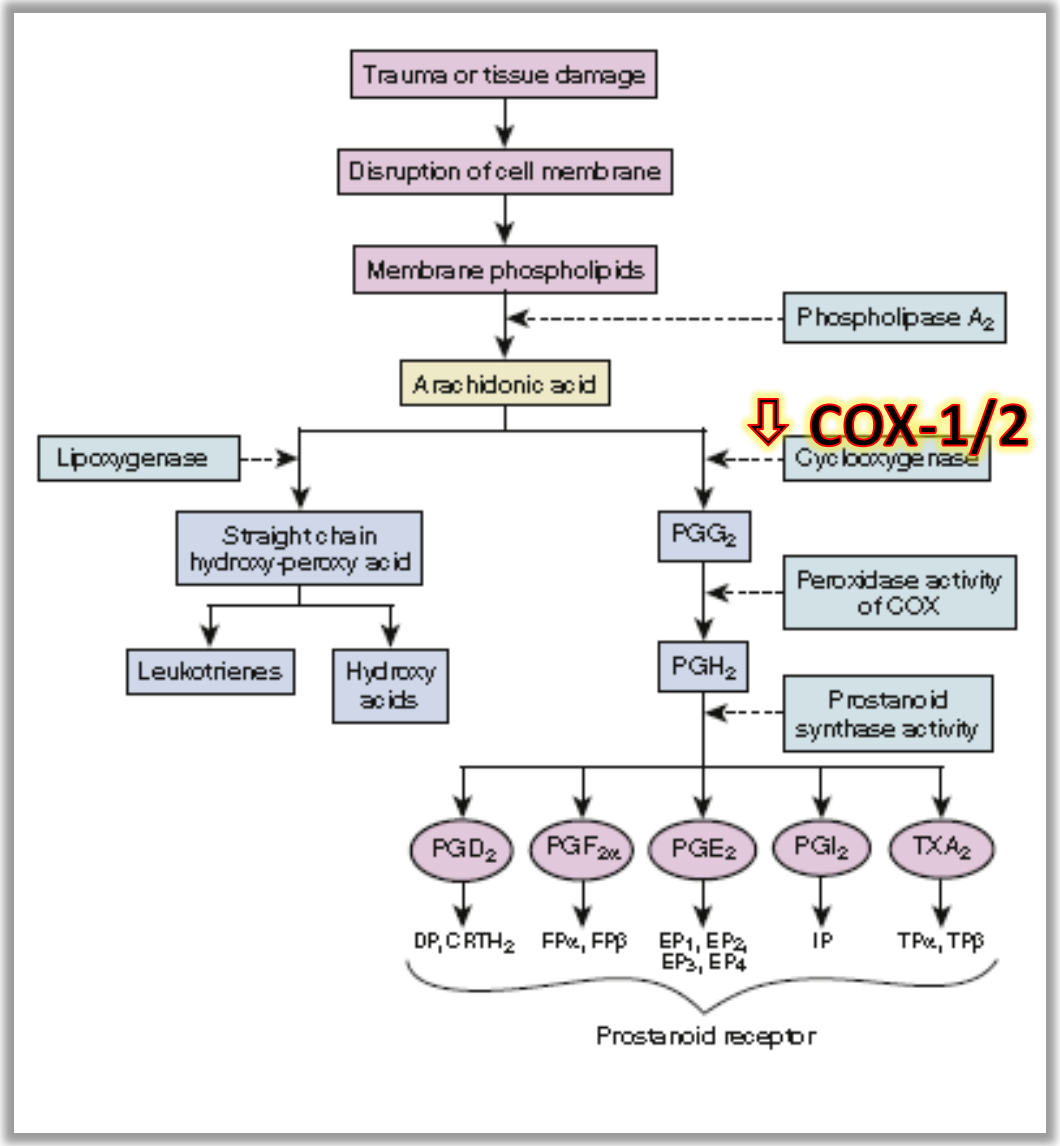
NSAID & PAIN

- Most widely prescribed drug class worldwide for acute & chronic pain
  - $6-7 billion annually across the world
  - 60% of U.S. OTC analgesic market
- **Reversibly & Competitively Inhibit COX-1 & COX-2** conversion of: arachidonic acid → prostaglandins
- ⇩ **Platelet COX-1 activity**: ⇩ platelet aggregation & ⇧ bleeding risk



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NSAID PROCEDURE RECS

- NSAID Platelet inhibition ≈ **plasma drug concentration**
- **5 $t_{1/2}$ Hold** → 97% drug elimination
- If held, restart 24 hours post-procedure

Procedure Risk	Patient Risk	Action
Low	Any	Continue
Intermediate	Low High	Consider hold 5 $t_{1/2}$ **Hold 5 $t_{1/2}$**
High	Any	**Hold 5 $t_{1/2}$**

TABLE 2. Half-lives of Commonly Administered Non-ASA NSAIDs

Agent	Half-life, h	Discontinuation Time 5 Half-lives, h	Recommended Discontinuation Time, d
Diclofenac[119]	1–2	5–10	1
Etodolac[120]	6–8	30–40	2
Ibuprofen[121]	2–4	10–20	1
Indomethacin[122]	5–10	25–50	2
Ketorolac[123]	5–6	25–30	1
Meloxicam[124]	15–20	75–100	4
Nabumetone[125]	22–30	110–150	6
Naproxen[126]	12–17	60–85	4
Oxaprozin[127]	40–60	200–240	10
Piroxicam[128]	45–50	225–250	10

Narouze S et al. *Reg Anesth Pain Med* 2018; 43(3): 225-62.

COX-2 SELECTIVE NSAIDS

- **Celecoxib** – 1st COX-2 inhibitor approved by FDA in 1998
  - Only available U.S. selective COX-2 inhib
- Minimal effect on platelets (COX-1)
- Can be CONTINUED for all procedures and patients on celecoxib
- Meloxicam (COX-2 preferential 18:1)
  - Follow regular NSAID recommendation, hold 5 $t_{1/2}$ for high & intermediate risk procedures

Table 40.2 IC_{50} Ratios for Inhibition of COX-1 and COX-2 in Human Whole Blood*

Drug	IC_{50} Ratio
Lumiracoxib	700
Etoricoxib	344
Rofecoxib	272
Valdecoxib	61
Celecoxib	30
Meloxicam	18
Naproxen	0.7
Ibuprofen	1.5
Indomethacin	0.02
Aspirin	0.007

IC_{50} concentration needed to inhibit 50% of COX-1 and COX-2.
*A higher ratio indicates greater COX-2 selectivity.

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COMPLEMENTARY RX & PAIN

- 33% of U.S. adults use complementary & integrative therapies
- Leading indication: **Chronic Pain**
- $30.2 billion

Chen L and Michalsen A. *BMJ* 2017; 357: 1284-1303.

The D's: DONG QUAI & DANSHEN

	Dong Quai	Danshen
Uses:	Menstrual cramping Menopausal symptoms	Cardiovascular disease (+ inotrope, - chronotrope, coronary vasodilator)
Bleeding Mechanism:	Inhibit platelet aggregation and ⇧ INR	Inhibit platelet aggregation Prolongs warfarin

Procedure Risk	Patient Risk	Action
Low	Low High	Continue Check INR with warfarin; stop if ⇧INR
Intermediate	Any	Check INR with warfarin; stop if ⇧INR
High	Any	Check INR with warfarin; stop if ⇧INR

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The G's: GARLIC, GINKGO & GINSENG

	Garlic	Ginkgo Biloba	Ginseng
Uses:	HTN, cholesterol, atherosclerosis, immunity	Memory, dementia, claudication, hearing	General wellbeing, sexual function, immunity
Bleeding Mechanism:	Inhibits platelet aggregation (**dose**-dependent)	Inhibits platelet aggregation	Inhibits platelet aggregation
Hold Recommendations:	Low risk = continue; Intermed & high risk = Hold x 7 days; Platelet function if **>1g/day**	Low risk = continue; Intermed & high risk = Consider platelet function assay	Continue

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The O's (Other): VIT E, FISH OIL & TURMERIC

	Vitamin E (Tocopherol)	Fish Oil (Omega-3)	Turmeric (Curcumin)
Uses:	Antioxidant, dementia, cancer	Atherosclerosis, hypertriglyceridemia	Anti-inflammatory for pain, antioxidant
Bleeding Mechanism:	Inhibits platelet aggregation (*dose-dependent*)	Inhibits platelet aggregation	Inhibits platelet aggregation; anticoagulant (thrombin vs Xa inhib)
Hold Recommendations:	Low risk = continue; Medium & high risk = Hold x 6 days if >400 IU dose	Low risk = continue; Medium & high risk = Hold x 6 days	**No ASRA recs** Medium & high risk = CAUTION

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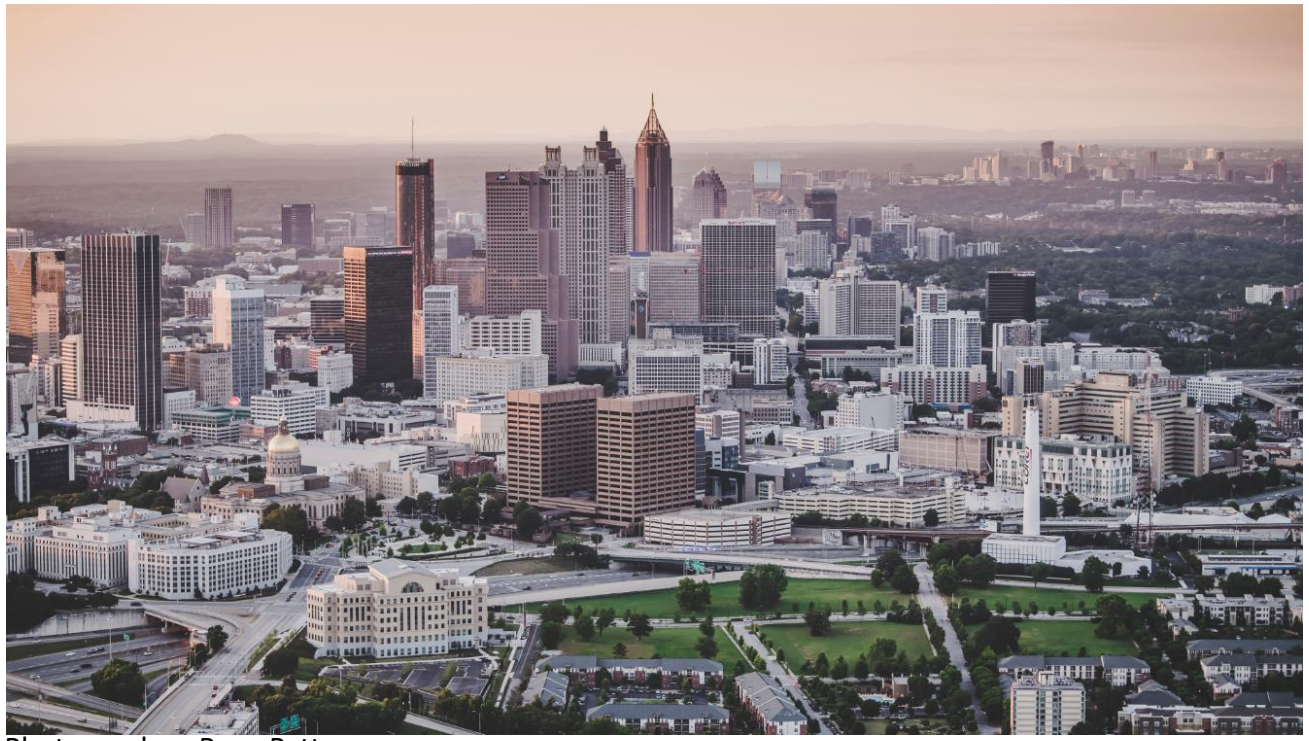
Keihanian F et al. *J Cell Physiol* 2018; 233: 4497-4511.

Thank You !



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