Let's Talk Drugs: A Pharmacist's Perspective on Orthopedic Surgery Patient Care

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Disclosures

- I have no relevant commercial relationships to disclose.

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Objectives

- Describe main principles of peri-operative pain management in orthopedic patients
- Understand common DVT prophylaxis regimens and pharmacology approved and used for various orthopedic surgery procedures
- Explain peri-operative antibiotic use in orthopedic surgical procedures
- Outline the approach for managing emergent care of contaminated wounds

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Peri-operative pain management

- Setting expectations
  - Start strategies **BEFORE** for planned surgeries
  - Patients being heard *vs.* balancing expectations for pain management

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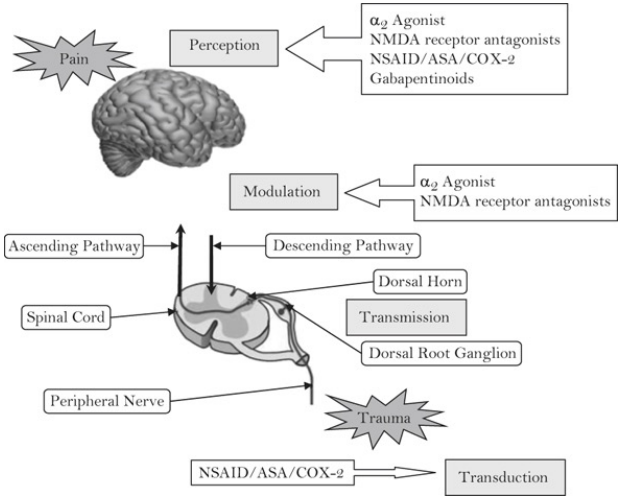
Liang JL, et al. MMWR Recomm Rep 2018;67(No. RR-2):1–44.

Peri-operative pain management

- **Non-pharmacologic methods**
  - Physical therapy
  - Occupational therapy
- **Pharmacologic methods**
  - Multimodal analgesia



Williams BS, et al. Multimodal analgesia (sites of analgesic activity). In: *The Essence of Analgesia and Analgesics.* 2010:57-65..

PRE & INTRA-operative pain management

- **Pre-operative:**
  - Oral multimodal analgesics (unless contraindicated):
    - acetaminophen 1000 mg x1 dose
    - celecoxib 400 mg x1 dose
    - pregabalin 150 mg x 1 dose

- **Intra-operative (epidural or PNB placement):**
  - Focus on use in *high risk patients* in collaboration with anesthesiology and acute pain service management post-op

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Mao J, et al. Anesth Analg. 2000;91(3):680–7.

POST-operative pain management

- **Acetaminophen:**
  - Scheduled acetaminophen is key: **1000mg oral every 6 hours**
  - Significant hepatic impairment, no more than 2000mg-3000mg per day
  - Don't use IV acetaminophen!
- **NSAIDs:**
  - ketorolac 15 mg, intravenous, EVERY 6 HOURS for 2 doses
  - naproxen 500 mg, oral, TWICE DAILY starting POD1 at 0900
  - omeprazole 20 mg, oral, BEFORE BREAKFAST starting POD1 at 0630 (GI prophylaxis for bleeding risk)

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Mao J, et al. Anesth Analg. 2000;91(3):680–7.

POST-operative pain management

- **Gabapentinoids**
  - Typically start gabapentin 300mg QHS
    - older adults, start at 100mg; titrate **every 3-4 days**
  - *To consider:* **Drug cost**
    - Recommend trialing gabapentin over pregabalin

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POST-operative pain management

Opioids:

-Prescribe the lowest effective dose for immediate-release (ie. 2.5mg-5mg oxycodone for age >65 yo & 5-10mg oxycodone for all others)

-Provide opioids for the shortest time period possible

*Goal to <u>not</u> discharge with **more than 5-7 day supply** with plan to wean

-Do not use extended-release opioids

-Involve anesthesiology/acute pain service to consider local or regional block anesthesia

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Mao J, et al. Anesth Analg. 2000;91(3):680–7.

POST-operative pain management

Chronic pain patients and key points:

- CONTINUE long acting opioids patients were taking pre-operatively
- Consider morphine milligram equivalent (MME) of long acting opioids in initial immediate opioid agent dose
- Dose ranges? What do you think? Safety concerns?

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DVT Prophylaxis Principles

- How do we classify VTE risk and need for pharmacologic DVT prophylaxis?
- HIGH risk: TKA, THA, hip fracture surgery
- **Agents of choice**: enoxaparin, DOACs

Falck-Ytter, Y, et al. CHEST 2012; 141(2)(Suppl)e278S-e325S.

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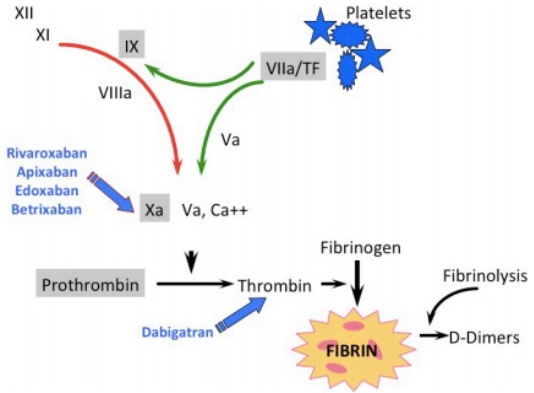
DVT Prophylaxis Principles

- Agents of choice:
  - Low-molecular-weight heparin (LMWH)
    - enoxaparin SC 40mg daily is the standard
  - Direct Oral Anticoagulants (DOACs)
    - **apixaban**
    - **rivaroxaban**
    - dabigatran
    - edoxaban



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Falck-Ytter, Y, et al. CHEST 2012; 141(2)(Suppl)e278S-e325S
AAOS. (2011) https://www.aaos.org/globalassets/quality-and-practiceresources/vte/vte_full_guideline_10.31.16.pdf

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DVT Prophylaxis Principles

- **rivaroxaban:** 10mg by mouth daily
- **apixaban**: 2.5mg by mouth twice daily
- Usually started POD1
- Duration of therapy
  - Optimal duration of prophylaxis unknown
  - **minimum of 10-14 days and can be extended for up to 35 days**

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Falck-Ytter, Y, et al. CHEST 2012; 141(2)(Suppl)e278S-e325S

RECORD 3 - rivaroxaban

- Randomized, double-blind trial
- Patients undergoing total knee arthroplasty
- **Intervention:**
  - oral rivaroxaban 10mg daily (n=1254)
  - subcutaneous enoxaparin 40 mg once daily (n=1277)
- **Primary efficacy outcome:** composite of any deep-vein thrombosis, nonfatal pulmonary embolism, or death from any cause within 13 to 17 days after surgery
- **Primary safety outcome:** Incidence of major bleeding

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Lassen, M, et al. N Engl J Med. 2008 Jun 26;358(26):2776-86.

RECORD 3 - rivaroxaban

	Rivaroxaban (N=824)	Enoxaparin (N=878)	P-value
Primary efficacy outcome	79/824 (9.6%)	166/878 (18.9%)	<0.001
Death	0/824	2/878 (0.23%)	0.23
PE	0/824	4/878 (0.46%)	0.06
DVT	78/824	160/878 (18.2%)	<0.001
	Rivaroxaban (N=1220)	**Enoxaparin (N=1239)**	**P-value**
Major bleeding	7/1220 (0.6%)	6/1239 (0.5%)	0.77

- "Rivaroxaban was superior to enoxaparin for thromboprophylaxis after total knee arthroplasty, with similar rates of bleeding."

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Lassen, M, et al. N Engl J Med. 2008 Jun 26;358(26):2776-86.

ADVANCE 2- apixaban

- Multicenter, randomized, double-blind phase 3 study
- Patients undergoing elective unilateral or bilateral TKA
- **Intervention:**
  - oral apixaban 2.5 mg twice daily (n=1528)
  - subcutaneous enoxaparin 40 mg once daily (n=1529)
- **Primary efficacy outcome:** composite of asymptomatic and symptomatic DVT, non-fatal PE, and all-cause death during treatment

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Lassen, M, et al. Lancet. 2010. Mar 6;375:807-15.

ADVANCE 2- apixaban

	Apixaban (N=976)	Enoxaparin (N=997)	P-value
Primary outcome			
All VTE and all cause death	147/976 (15.06%)	243/997 (24.37%)	<0.0001

- Major or clinically relevant non-major bleeding occurred in:
  - 53 (4%) of 1501 patients receiving apixaban
  - 72 (5%) of 1508 treated with enoxaparin (p=0·09).

- "Apixaban 2.5 mg twice daily is a convenient and more effective alternative to enoxaparin 40 mg SC daily, without increased bleeding"

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Lassen, M, et al. Lancet. 2010. Mar 6;375:807-15.

ADVANCE 3- apixaban

- Double-blind, double-dummy study
- Patients undergoing THA
- Major exclusion criteria: active bleeding, contraindication to anticoagulant prophylaxis, or need for ongoing anticoagulant or antiplatelet treatment
- **Intervention:**
  - oral apixaban 2.5 mg twice daily
  - subcutaneous enoxaparin 40 mg once daily
  - Prophylaxis for 35 days after surgery, followed by bilateral venographic studies
- **Primary efficacy outcome:** composite of asymptomatic or symptomatic DVT, nonfatal PE, or death from any cause during treatment period

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Lassen, M, et al. N Engl J Med. 2010 ;363(26):2487-98.

ADVANCE 3- apixaban

	Apixaban (N=1949)	Enoxaparin (N=1917)	P-value
Asymptomatic or symptomatic DVT, nonfatal PE, or death from any cause	27/1949 (1.4%)	74/1917 (3.9%)	*<0.001 (both noninferiority & superiority)*

	Apixaban (N=2673)	Enoxaparin (N=2659)	P-value
Major bleeding	22/2673 (0.82%)	18/2659 (0.68%)	*0.54*
Clinically relevant non-major bleeding	109/2673 (4.1%)	120/2659 (4.5%)	*0.43*

"Apixaban at a dose of 2.5 mg twice daily was superior to enoxaparin at a dose of 40 mg per day, preventing one episode of major venous thromboembolism for each 147 patients treated, without adding to the risk of bleeding".

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Lassen, M, et al. N Engl J Med. 2010 ;363(26):2487-98.

DVT Prophylaxis Tips

- DOAC advantages over LMWH
  - Route of administration
- Check for insurance coverage prior to hospital discharge!
- Role of aspirin
  - Consider for patients where anticoagulant may be contraindicated or not preferred

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Peri-operative antibiotic use

- Clean *vs.* clean-contaminated *vs.* contaminated procedures
  - All require PRE-operative antibiotic prophylaxis
- Common agents:
  - Cefazolin
  - Allergies?
    - Vancomycin

Berríos-Torres SI, et al. *JAMA Surg.* 2017;152(8):784–791.
Kamel C, et al. [Internet]. Canadian Agency for Drugs and Technologies in Health; 2011 Jun. Appendix 1, Classification of surgical wounds

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Peri-operative antibiotic use

- Post-operative prophylaxis?
  - Contaminated procedures
  - Concern for infection
- Duration of therapy
  - No more than 24 hours post-operative*

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Emergent care: contaminated wounds

- Tetanus vaccination

  -Anaerobic conditions carry risk of germination of *C. tetani* spores

- Tetanus toxoid-containing vaccine indicated (Tdap preferred):

  -Less than 3 tetanus toxoid containing vaccines in the past

  OR

  -More than 5 years has passed since last tetanus toxoid containing vaccine

Antimicrobial Therapy, Inc. (2020). Sanford Guide To Antimicrobial Therapy (4.2.13) [Mobile application software
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Emergent care: contaminated wounds

Type	Symptoms/Presentation	Treatment
Uncomplicated	-Mild/moderate infection -Afebrile -ED/outpatient management	-Debridement (if necessary) -TMP/SMX DS 1-2 tabs PO BID **OR** -Clindamycin 300-450mg PO TID *-If Gram Neg Bacilli suspected* : **ADD** amoxicillin clavulanate 875/125mg PO BID
Complicated	-Febrile -ED→hospital admission	-Debridement (if necessary) -<u>Empiric IV antibiotic treatment:</u> -Piperacillin-Tazobactam **OR** carbapenem **PLUS** -Vancomycin (goal trough 15-20 mg/L)

Antimicrobial Therapy, Inc. (2020). Sanford Guide To Antimicrobial Therapy (4.2.13) [Mobile application software].

Emergent care: contaminated wounds

- Wound infections by water (fresh and sea)
  - ***Aeromonas* spp.:** TMP/SMX, amoxicillin clavulanate
  - **non-cholera *Vibrio* spp.**: ceftazidime and doxycycline
  - **(more uncommon) *Pseudomonas* or other Gram-negative rods**: fluoroquinolones (levofloxacin, moxifloxacin)
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Antimicrobial Therapy, Inc. (2020). Sanford Guide To Antimicrobial Therapy (4.2.13) [Mobile application software].

Take Home Points

- Focus on multimodal analgesia to address pain control
- DOACs have advantages over LMWH for DVT prophylaxis with similar efficacy and less bleeding risk overall
- When indicated, cefazolin is the first line peri-operative antibiotic prophylaxis option
- Don’t forget tetanus vaccination review for patients presenting with contaminated wounds

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Questions?

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