OBJECTIVES

- MISCELLANEOUS RANTINGS OF AN AGING ORTHOPAEDIC SURGEON
- PAIN and PAIN MANAGEMENT
- DVT PROPHYLAXIS
- OSTEOPOROSIS
- INJECTABLES
- DMARDS
- NO DISCLOSURES

Schedule I
Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence. Some examples of Schedule I drugs are heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methyleneoxyamphetamine (ecstasy), methamphetamine, and peyote.

Schedule II
Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, less abuse potential than Schedule I drugs, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are: Combination products with less than 15 milligrams of hydrocodone per dosage unit (Vicodin, Lortab). methamphetamine, methyleneephedrine (Oxidil), mepiperone (Demerol), oxymorphone (OxyContin), fenanyl, Desomorphine, methadone, and Ritalin.

Schedule III
Schedule III drugs, substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV. Some examples of Schedule III drugs are: Products containing less than 90 milligrams of codeine per dosage unit (Tylenol with codeine), ketamine, anabolic steroids, testosterone.

Schedule IV
Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence. Some examples of Schedule IV drugs are: Xanax, Serax, Soma, Darvocet, Vicodin, Tylenol, Ambien, Darvocet.

Schedule V
Schedule V drugs, substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes. Some examples of Schedule V drugs are cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin.

Opioid Epidemic

- Prescribing too quickly, too frequently, too long.
- Unrealistic expectations
- Opioids are viewed as “medication” and “safe” because prescribed by physician.
  - Patients feel a false sense of security and may increase dose and/or frequency without consulting the prescriber
- Leftover medications from prior prescriptions are a potential source for diversion.
  - Stolen, given away, purchased.
  - Addicts report that their access is through friends and family rather than physicians.*

Compton, W.M. Drug and ETOH Dependence. 2006;81:103-107

Russell Portenoy, M.D. (LATE 80’S)

- Instrumental in the drive to expand use of opioids
- Pain physician
- Past president of American Pain Society
- Past director of American Pain Foundation
- Urged use
- Claimed only 1% of population at risk for addiction
- Easy to discontinue
- Overdoses were extremely rare
- Misleading information about safety and efficacy
- Minimal scientific evidence to back claims


Second Thoughts

THE WALL STREET JOURNAL.

- Portenoy gave statement to The Wall Street Journal in December of 2012—second thoughts about encouraging use of opioid medications.
  - “Did I teach about pain management, specifically about opioid therapy, in a way that reflects misinformation? Well, against the standards of 2012, I guess I did.”
  - “We didn’t know then what we know now.”
  - “I gave innumerable lectures in the late 1980s and ’90s about addiction that weren’t true…”
  - “Clearly, if I had an inkling of what I know now then, I wouldn’t have spoken in the way that I spoke. It was clearly the wrong thing to do.”

Under Investigation

- Possible financial relationship between pharmaceutical companies and doctors who advocated opioid use.
- Dr. Portenoy included in this investigation.


Opioid Induced Hyperalgesia

- Paradoxical response
- Neuroplastic change in pain perception
- Sensitivity to painful stimuli increases with use of opioids
- Continuous opioid receptor occupation produces hyperalgesia during less painful states
- Increased sensitivity during cold and thermal testing
- Leads to inability to cope with sudden acute pain
- Can be confused with tolerance, but tolerance is overcome by increasing dosage.


Soooo... I CURRENTLY TELL MY PATIENTS WHO ARE ON 60MG OF OXYCONTIN EVERY 3 MINUTES WITH A FENTYNL PATCH ON THEIR ASS AND FOREHEAD ..... THAT THEIR “CARING “ DOCTOR IS MAKING THEM A BALL LESS ZOMBIE WITH NO PAIN TOLERANCE

OPIOIDS HAVE NO PLACE IN CHRONIC PAIN MANAGEMENT UNLESS LIFE EXPECTANCY IS LIMITED.......PERIOD

INFORMED CONSENT FOR THE TREATMENT OF OPIOID ANALGESICS

A. Opioid Definition: "A medication or illegal drug that is either derived from the opium poppy, or that mimics the effect of an opiate (a synthetic opiate). Opiate drugs are narcotic sedatives that depress activity of the central nervous system, reduce pain and induce sleep." Prescription opioids are pain-relieving medications used to treat moderate to severe pain. These medications can have side effects as well as serious negative physiological and psychological effects. The risks of complications and side effects increase when used with other medications. A complete review of all recent medications administered, ingested and/or prescribed will be performed at each office visit. Failure to provide all requested medication in their original prescription containers can result in discontinuance of narcotic medication.

B. Opiates can cause psychological, cognitive and physiological changes when used long term. Below is terminology that is used to describe these changes:

- Thromboembolism
- Pharmacologic
- Prophylaxis

Qualities of an ideal prophylactic agent:
- Effective
- Minimal adverse effects
- Does not require monitoring
- Oral administration
- Cost effective

The rate of fatal pulmonary emboli has been unchanged over the last 10 years.
AAOS Clinical Practice Guidelines on VTE Prophylaxis (2011):

• In the absence of reliable evidence about how long to employ these prophylactic strategies, it is the opinion of this work group that patients and physicians discuss the duration of prophylaxis.

  (Grade of Recommendation: Consensus)

PAIN
BLEEDING
HEMATOMA
INFECTION
RE-OPERATION

DVT
PROPHYLAXIS

Presently Approved Pharmacologic Agents

• Warfarin
• Low molecular weight heparin - LOVENOX
• Fondaparinux – ARIXTRA
• Aspirin
• Rivaroxaban - XARELTO
• Dabigatran (Europe only)
• Apixaban (Europe only)

SCIP

• Surgical Care Improvement Project
• New measures regarding appropriate VTE prophylaxis went into effect January 1, 2014
• These changes represent a greater alignment regarding VTE prophylaxis recommendations between the American College of Chest Physicians (ACCP) and the AAOS
Most significant change to SCIP:
- **Aspirin** is now approved for VTE prophylaxis in the setting of total joint arthroplasty
  - American College of Chest Physicians most recently developed evidence-based guidelines now recommend aspirin after total joint arthroplasty versus no prophylaxis at all
  - Based on the results of the Pulmonary Embolism Prevention (PEP) Trial (2000)

Low-Molecular-Weight Heparin
**ENOXAPARIN - LOVENOX**

**Pros:**
- Rapid antithrombotic activity
- Half-life of 4.5 hours
- Does not require monitoring
- CAN BE REVERSED WITH PROTAMINE SULFATE

**Cons:**
- Increased cost
- Increased risk of bleeding
- Increased risk of postoperative drainage
- Risk for heparin-induced thrombocytopenia
- Subcutaneous injection

Low-Molecular-Weight Heparin

**Primary mechanism of action:**
- Inhibition of Factor Xa
Fondaparinux - ARIXTRA

**Pros:**
- Significantly more effective than enoxaparin in limiting asymptomatic clot formation in TKA patients

**Cons:**
- Subcutaneous administration
- Limited use in North America due to concerns about bleeding
- 17-21 HR HALF LIFE
- NO ANTIDOTE

Rivaroxaban - XALERLTO

**Pros:**
- Oral agent
- Requires no monitoring
- 5-9 HOUR HALF LIFE

**Cons:**
- Associated with a higher rate of reoperation than LMWH after TKA
- NO ANTIDOTE

Rivaroxaban - XALERLTO

**Mechanism of action:**
- Direct Factor Xa inhibitor
Aspirin

- Mechanism of action:
  - Potent inhibitor of prostaglandin synthesis and platelet aggregation via inactivation of cyclooxygenase
  - CURRENTLY MY AGENT OF CHOICE
  - 325 MG BID

To summarize...

- LARGEST FACTOR DECREASING THE RATES OF THROMBOEMBOLISM OVER THE PAST 10 YEARS IS **EARLY MOBILIZATION**
- 35 % OF ALL THA’S PERFORMED AT AGH ARE DISCHARGED TO HOME **SAME DAY SURGERY**
Medications

2 medications discussed:
1. Corticosteroids
2. Local Anesthetics

Injectable Glucocorticoids

Short Acting
- Cortisone (Cortone)
- Hydrocortisone (Cortef)

Intermediate Acting
- Methylprednisolone (Medrol)
- Prednisone (Deltasone)
- Prednisolone (Prelone)
- Triamcinolone (Kenalog)

Long Acting
- Betamethasone (Celestone)
- Dexamethasone (Decadron)

Glucocorticoid Comparison

<table>
<thead>
<tr>
<th>Name</th>
<th>Glucocorticoid Potency</th>
<th>Duration of action (t\textsubscript{1/2} in hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Cortisone acetate</td>
<td>0.8</td>
<td>8</td>
</tr>
<tr>
<td>Prednisone</td>
<td>3.5-5</td>
<td>16-36</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
<td>16-36</td>
</tr>
<tr>
<td>Triamcinolone (Kenalog)</td>
<td>5</td>
<td>12-36</td>
</tr>
<tr>
<td>Methylprednisolone (Medrol)</td>
<td>5-7.5</td>
<td>12-36</td>
</tr>
<tr>
<td>Dexamethasone (Decadron)</td>
<td>25-80</td>
<td>36-54</td>
</tr>
<tr>
<td>Betamethasone (Celestone)</td>
<td>25-30</td>
<td>36-54</td>
</tr>
</tbody>
</table>
Problems with Dexa

Chrysis, D. et al., Sweden 2005

- Dexamethasone induces apoptosis in proliferative chondrocytes through activation of caspases and suppression of the Akt-phosphatidylinositol 3'-kinase signaling pathway.

- Dexa (25 microm) increased apoptosis (cell death ELISA) by 39% and 45% after 48 and 72 h, respectively (P < 0.01 and P < 0.05, respectively)

Preservatives

Davis et al. Tulane Univ. 2010

- In Vitro Cytotoxic Effects of Benzalkonium Chloride in Corticosteroid Injection Suspension

- Betamethasone corticosteroids per se did NOT cause cell death, whereas benzalkonium chloride (Preservative) caused death of articular chondrocytes.

Local Anesthetics

Local Anesthetics Commonly Used in Orthopaedic Offices and OR's

- Lidocaine (Xylocaine)

- Bupivicaine (Sensorcaine, Marcaine)

- Ropivicaine (Naropin)
**Duration of Action – MAX. DOS**

<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>Duration</th>
<th>Max. Dos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine (Xylocaine)</td>
<td>Medium (30-60 min)</td>
<td>4.5 ml/kg or 300 mg</td>
</tr>
<tr>
<td>Lidocaine with epinephrine</td>
<td>Long (120-360 min)</td>
<td>3% or 5% solution</td>
</tr>
<tr>
<td>Bupivacaine (Marcaine)</td>
<td>Long (120-240 min)</td>
<td>3% or 5% solution</td>
</tr>
<tr>
<td>Bupivacaine with epinephrine</td>
<td>Long (180-420 min)</td>
<td>3% or 5% solution</td>
</tr>
<tr>
<td>Ropivacaine (Naropin)</td>
<td>Long (120-360 min)</td>
<td>3% or 5% solution</td>
</tr>
</tbody>
</table>

- **1CC/KG OF .5% MARCANE WITH EPI UPTO 80 CC (400 MG)**

### Problems with Local

**Chu et al. UPMC 2010**

- 48 rats joints injected and then sacrificed at multiple time frames
- Quantitative histological analysis of the 0.5% bupivacaine-treated knees at six months revealed an up to 50% reduction in chondrocyte density compared with that of the saline-solution-treated knees (p = 0.01).

**Grishko, et al. 2010**

- Exposure of primary human chondrocytes to a 2% concentration of lidocaine caused massive necrosis of chondrocytes after twenty-four hours
- 1% lidocaine and 0.5% bupivacaine caused a detectable, but not significant, decrease in viability after twenty-four hours
- While 0.5% lidocaine, 0.25% bupivacaine, and both concentrations of ropivacaine (0.5% and 0.2%) did not affect chondrocyte viability
Medication Recommendations

Therefore:

- **Betamethasone (Celestone)**
  - Less cartilage toxicity, less concentration of crystal deposits, longer half life with greater potency.

- **Ropivacaine (Naropin)**
  - Long lasting and significantly less cartilage toxicity

Time Frame

New Zealand Medical Journal 2008

- Looked at incidence of infection in TKA after receiving preoperative intraarticular steroid injections
- 38 infected knees and 352 knees without infection were reviewed
- No increase in incidence of post op infection
- Average length of time before surgery from last injection was 16 months.

**I WAIT 3 MONTHS**

OSTEOPOROSIS

Today's Random Medical News
Incidence of Osteoporotic Fractures in Women

Osteoporotic Fractures: Comparison with Other Diseases

All fractures are Associated With Morbidity
Vertebral Fractures

- Most common fracture type
- Often silent
- Insidious, progressive nature
- Associated with significant morbidity
- Predict future spine and hip fractures
- Associated with 2-fold increase in risk of death

WHO Criteria for Diagnosis of Bone Status

A “T” SCORE OF ZERO IS NORMAL!

<table>
<thead>
<tr>
<th>T score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T ≥ -1</td>
<td>Normal</td>
</tr>
<tr>
<td>T between -1 and -2.5</td>
<td>Osteopenia (low bone mass)</td>
</tr>
<tr>
<td>T ≤ -2.5</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>T ≤ -2.5 + fx</td>
<td>Severe or est. osteoporosis</td>
</tr>
</tbody>
</table>

*Measured in “T scores.” T score indicates the number of standard deviations below or above the average peak bone mass in young adults.

10-Year Fracture Risk: Age and BMD

For a given BMD, risk increases with age.

WHO Absolute Fracture Risk Model

- FRAX
  - Estimates absolute fracture risk using epidemiology of osteoporosis, risk factors and therapeutic data.
  - By basing treatment decisions on fracture probability, therapy can be targeted to those who would receive the greatest benefit.
  - Calculation tool is online and calculates the 10 year risk for hip fractures and any osteoporosis related fracture.
  - Using a series of clinical questions, BMD data, weight and height the tool calculates these risks for individual patients.
  - Treatment is recommended for a 10 year hip fracture risk over 3% and a 10 year osteoporotic fracture risk over 20%.


**How Often Test with DEXA Scan?**

<table>
<thead>
<tr>
<th>Result of Bone Test</th>
<th>Interval between Baseline Testing and the Development of Osteoporosis in 10% of Study Participants, According to the Result of Baseline Testing.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal BMD</td>
<td>17.4 (11.5-26.3) Unadjusted, 16.8 (11.5-24.6) Adjusted</td>
</tr>
<tr>
<td>Mild osteopenia</td>
<td>16.5 (13.6-20.2) Unadjusted, 17.3 (13.9-21.5) Adjusted</td>
</tr>
<tr>
<td>Moderate osteopenia</td>
<td>4.6 (4.1-5.1) Unadjusted, 4.7 (4.2-5.2) Adjusted</td>
</tr>
<tr>
<td>Advanced osteopenia</td>
<td>1.0 (0.8-1.1) Unadjusted, 1.1 (0.8-1.3) Adjusted</td>
</tr>
</tbody>
</table>

T score > -1.5
T score = -2.0

Pharmacologic Treatment Targets

**Osteoclast**

**Osteoblast**

Inhibition of resorption

Stimulation of formation

Pharmacologic Treatment Targets

**DIDRONEL**

**SKELID**

**AREDIA**

**FOSAMAX**

**BONIVA**

**CALCITONIN**

**PROLIA**

**ESTROGEN**

**EVISTA**

**EST**

**FORTEO**

**PDNA**

**PTH**

Pharmacologic Treatment of PMO: Overview

---

Classification – BPNs

Classified in generations (chronological):

<table>
<thead>
<tr>
<th>Generation</th>
<th>compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td><strong>DIDRONEL</strong></td>
</tr>
<tr>
<td></td>
<td><strong>SKELID</strong></td>
</tr>
<tr>
<td>2nd</td>
<td><strong>AREDIA</strong></td>
</tr>
<tr>
<td></td>
<td><strong>FOSAMAX</strong></td>
</tr>
<tr>
<td></td>
<td><strong>BONIVA</strong></td>
</tr>
<tr>
<td>3rd</td>
<td><strong>ACETOMEL</strong></td>
</tr>
<tr>
<td></td>
<td><strong>RECLAST IV INFUSION</strong></td>
</tr>
</tbody>
</table>

ANNUALS OF INT. MED. 2008
It’s Not All Bone Density

- Similar changes in BMD may not translate into consistent efficacy for reduction in fracture risk when comparing agents eg. Fluoride
- Patients with higher bone turnover may be at higher risk of fracture eg. glucocorticoids even with a normal bone mineral density
- Bone density may not capture all aspects of fracture reduction eg. Sensory or drug effects

Figure 1

Atypical Fractures of the Femoral Diaphysis in Postmenopausal Women Taking Alendronate.
Lenart, Brett; Lorich, Dean; Lane, Joseph

Atypical Femoral Fracture

Conventional AP radiograph of the pelvis (A) shows bilateral focal cortical thickening from periosteal new bone formation (arrows). Corresponding bone scintigraphy (B) demonstrates focal increased radionuclide uptake in the proximal lateral femoral cortices (arrows). MRI images of the femurs (C) demonstrate subtle decreased signal on T1-weighted and increased signal on T2-weighted images only of the right femur on this section. Similar findings on AP DXA hip images (D) show focal bilateral cortical thickening consistent with early, evolving femoral insufficiency fractures.

Bisphosphonate Use and the Risk of Subtrochanteric or Femoral Shaft Fractures in Older Women

Population-based, nested case-control study in a cohort of women aged 68 years or older from Ontario, Canada treated with oral bisphosphonate between April 1, 2002, and March 31, 2008. Primary analysis - association between hospitalization for a subtrochanteric or femoral shaft fracture and duration of bisphosphonate exposure
Secondary analysis - association of bisphosphonate use and ATYPICAL femoral fractures

Bisphosphonate Therapy - Risks
- Initial studies taken to the FDA to gain approval for these drugs identified a lower than expected risk of GI side effects
- No unexpected side effects were seen in these studies
- However, about 15 years ago, cases of osteonecrosis of the jaw which dentists had not seen for at least a century, began to appear
- Subsequently, the possibility of an increased risk of atypical femur fractures in patients treated with these drugs was proposed.

Bisphosphonate Therapy Benefits
- Decreased risk of breast cancer
- Decreased risk of colorectal cancer
- Decreased risk of stroke
- Decreased risk of gastric cancer
- Decreased overall mortality

Nelson Watts – Endocrine Society National Meeting - 2012
Bisphosphonates for Osteoporosis — Where Do We Go from Here?

- The available data do not identify patients likely to benefit from treatment beyond 3-5 years.
- ... decisions to continue treatment must be based on individual assessment of risks and benefits and on patient preference.

NEJM 366:2048, 2012

How Long to Treat With Bisphosphonates?

- Patients who did not need treatment in the first place
  - Discontinue Treatment
- Lower risk patients, if DXA is stable/increasing
  - Consider a drug holiday after 3-5 years of treatment
- Higher risk patients (fractures, corticosteroid Rx, very low BMD)
  - Consider a drug holiday after 10 years of therapy
    - May use teriparatide, Forteo, or raloxifene, Evista, bone stimulators (but not another potent antiresorptive agent – ie. Denosumab, Prolia) during the holiday from bisphosphonates

Watts and Dial JCEM, 2010 95:1555.
Use FRAX to estimate risk

Watts and Diab JCEM, 2010 95:1555.

**Proposed Guidelines for Use of Bisphosphonates**

- Patients with bone density T-scores of -2.5 or lower at femoral neck after 3 to 5 years of treatment at highest risk for vertebral fractures and appear to benefit most from continued therapy (for up to 10 years).
- Patients with an existing vertebral fracture and T-scores up to −2.0 may also benefit from continued therapy.
- **Patients with femoral neck T-scores above −2.0 have low risk of vertebral fractures and are unlikely to benefit from continued treatment after 3–5 years.**

Black et al. 2012, NEJM 366:2051

**FORTEO - TERIPARATIDE**

- rDNA HUMAN PARATHYROID HORMONE
- PARATHYROID HORMONE - CAUSES BONE REABSORPTION
- SMALL FREQUENT INJECTIONS ACTIVATE OSETOBLASTS ------ NET EFFECT IS BONE FORMATION
- $$$$$$$$$$$
- NO PATH FX

Black et al. 2012, NEJM 366:2051
**PROLIA - DENOSUMAB**

- Antiresorptive agent anti RANK ligand ab
- IV twice a year
- Evidence for prevention of vertebral, non-vertebral and hip fractures
- Risk of significant hypocalcemia – particularly in renal failure
- May be safer in renal failure (key word is may)
- Not any safer than bisphosphonates with regards to ONJ and atypical femur fractures.

**Summary**

- Bisphosphonates remain the most potent antiresorpive agents available
- Recent analysis of the risks and benefits of bisphosphonate therapy have started to clarify how long they can be used
- Adequate vitamin D and calcium supplementation should be instituted
- **FORTEO AND EVISTA WILL MOST LIKELY AVOID COMPLICATIONS OF ONJ AND SUBTROCHANTERIC FX**
Will I choose a woman or a car
It don’t matter…
The result will always be the same...........
Antirheumatic Drugs

• Synthetic disease-modifying antirheumatic drugs (DMARDs)
  ◦ Methotrexate
  ◦ Hydroxychloroquine
  ◦ Leflunomide
• Corticosteroids
• Biologics
  ◦ Tumor necrosis factor inhibitors

Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

• DMARDs have played a substantial role in improving the life of patients with rheumatoid arthritis (RA)
• These drugs may have played a role in decreasing the need for arthroplasty in RA patients

Antirheumatic Drugs

• RA patients are at higher risk for prosthetic joint infection than osteoarthritis (OA) patients
• Comparative rates of infection between RA and OA patients within 5 years of arthroplasty:
  ◦ OA – 1.4%
  ◦ RA – 4.2%

Perioperative Pharmacologic Management of Arthroplasty Patients with Inflammatory Arthritis

- The perioperative management of medications used for the treatment of inflammatory arthritis is critical
  - These medications increase risk for infection
  - Also increase risk for compromised wound healing

Withholding these drugs can result in disease flare, which adversely impacts rehabilitation

Methotrexate

- Methotrexate inhibits enzymes involved in purine metabolism
  - Adenosine accumulates
  - Intercellular adhesion molecule expression by T-cells is suppressed

Methotrexate

- A randomized study comparing patients that either continued or discontinued methotrexate therapy against a control group of rheumatoid patients found that those that discontinued methotrexate were at highest risk for infection as well as disease flare
Methotrexate

- Patients on methotrexate should continue on this therapy through the perioperative period.
- **MOST SURGEONS AND RHEUMATOLOGISTS HOLD FOR 2WKS PRE AND POST**

Corticosteroids

- The most widely prescribed anti-inflammatory and immunosuppressant agents.
- There is a dose-dependent relationship between corticosteroids and infection.
  - **Risk of infection rises with doses of over 5 mg/day**
  - Risk of infection also increases with duration of therapy.
Corticosteroids

- Chronic steroid use results in suppression of the adrenal axis
  - Surgery represents a significant stress
  - Atrophic adrenal response results in hypotension and even shock

Corticosteroids

- For minor procedures (arthroscopy), continue to provide patients with their daily steroid regimen
- For more extensive procedures (arthroplasty), provide a single intra-operative supplemental hydrocortisone dose of 100 mg
- For extreme procedures (bilateral arthroplasty), provide intra-operative stress dose
  - Administer 4 additional doses at 8 hour intervals
  - Taper to baseline within 48 hours

Leflunomide - ARAVA

- Effective DMARD
- Inhibits synthesis of RNA, DNA
  - Increases risk of perioperative infection
  - Conflicting findings in the literature
  - Usually held 2wks pre-op very long half life
  - And post op
**Leflunomide - ARAVA**

- In an observational study of rheumatoid or psoriatic arthritis patients undergoing elective orthopaedic surgery, patients treated with continuous leflunomide were compared to patients treated with methotrexate
  - Infection rate among leflunomide cohort: 40.6%
  - Infection rate among methotrexate cohort: 13.6%

**Leflunomide - ARAVA**

- A separate study demonstrated conflicting findings
  - No difference in rates of infection between patients continued on leflunomide vs. patients in which drug was withheld
Leflunomide - ARAVA

- A recent review in JAAOS recommends withholding leflunomide until there is evidence of satisfactory wound healing and until normal bowel and kidney function have been reestablished post-op


HYDROXYCHLOROQUINE
PLAQUENIL

- No known studies of perioperative use of plaquenil
- Anti malarial
- Lyme's disease
- Inhibition of lysosomal proteases

Biologic Agents
TNF –A Antagonist

- Tnf- a is an inflammatory cytokine that plays a crucial role in mediating tissue destruction
- Tnf-a antagonist came to market 1990's
- MAJOR COMPLICATION IS INFECTION
- ANTI-TNF AGENTS WERE ORIGINALLY DEVELOPED TO TREAT SEPSIS BUT THEY INCREASED MORTALITY
Biologic Agents

- Anti-TNF agents represent an increased risk for infection
- An increased risk for septic arthritis has been demonstrated in rheumatoid patients on anti-TNF therapy
  - This risk is compounded by the presence of a prosthetic joint

Biologic Agents

TNF – A ANTAGONISTS

- ETANERCEPT – EMBREL
- ADALIMUMAB – HUMIRA
- INFLIXIMAB - REMICADE

Biologic Agents

GRANULOCYTE MACROPHAGE COLONY-STIMULATING FACTOR
Current expert opinion recommends discontinuing biologic therapeutics before elective orthopaedic surgery.

- Timing of cessation is determined by individual agent dosing interval.
- See Table I.

Biologic therapeutics may be restarted once sutures have been removed and wound demonstrates clear evidence of healing.
Blood Loss Secondary to Arthroplasty

- Surgical blood loss is of interest to arthroplasty surgeons due to the perioperative complications it can cause
  - Anemia
  - Angina
  - Myocardial infarction
  - Heart failure
  - Allogeneic transfusion - Increased infection rate
  - Delayed rehabilitation

Tranexamic Acid

- Recent interest has surrounded tranexamic acid (TXA) due to the compelling capacity it has demonstrated to reduce perioperative blood loss

TRANEXAMIC ACID

- Tranexamic acid is a synthetic derivative of the amino acid lysine
- It inhibits fibrinolysis by blocking the lysine binding sites on plasminogen and facilitates the coagulation process
TXA led to a significant reduction in the proportion of patients requiring blood transfusion (RR 2.56, p<0.001). TXA also reduced total blood loss by an average of 591 ml (p<0.001).

Patients in this study were divided into 2 groups:
- Group I: placebo
- Group II: received intra-articular tranexamic acid during surgery

Primary outcome measure was post-op blood transfusion
- Secondary outcomes included drain blood loss, Hgb concentration drop, quality of life, length of stay, and cost analysis.
TRANEXAMIC ACID

- These investigators demonstrated a significant reduction in post-op blood loss and need for blood transfusion with the application of topical tranexamic acid
- They also demonstrated a significant cost saving and a trend toward decreased length of stay

TRANEXAMIC ACID

- Clearly TXA has a role to play in arthroplasty
- The potential for reduced perioperative morbidity has been demonstrated in multiple studies

Dexamethasone

- A high-potency and long-acting glucocorticoid
- Exhibits multiple qualities of interest to the arthroplasty surgeon:
  - Prophylactic against post-op nausea/vomiting
  - Analgesic
  - Anti-inflammatory
Dexamethasone

- Post-operative nausea and vomiting is a common adverse event after anesthesia.
- Arthoplasty procedures result in significant post-operative pain which can be a challenge to control.
- Post-op nausea/vomiting and inadequate pain control contribute to the following:
  - Discomfort
  - Emotional distress
  - Lower patient satisfaction
  - Delayed rehabilitation
  - Longer hospitalization

The inclusion of dexamethasone in perioperative drug regimens has been an area of interest in arthroplasty research.

A recent prospective randomized controlled trial evaluated the effect of dexamethasone inclusion in a perioperative multimodal drug regimen:

- Backes JR et al. Dexamethasone reduces length of hospitalization and improves postoperative pain and nausea after total joint arthroplasty: a prospective, randomized controlled trial.

This study included 120 patients (47 THA and 73 TKA) divided into 3 groups:

- Group 1: control
- Group 2: 10 mg IV dexamethasone administered intra-op
- Group 3: 10 mg IV dexamethasone administered intra-op and 10 mg IV dexamethasone administered 24 hours post-op
I CURRENTLY USE 10MG IV INTRAOP SECOND DOSE 24 HRS

Comparison of Adductor Canal, EXPAREL and Femoral Nerve Blocks in Primary TKA

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Matt Delarosa M.D.
Methods

- 65 adults
  - 23 FNB
  - 35 ACB
  - 7 Exparel Only

- Single shot blocks
  - Administered by an anesthesiologist
    - Ropivacaine 0.2%
    - Decadron 1 mg
    - Clonidine 25 mcg
    - Epinephrine 1:200k
  - 30 min preoperatively
  - In combination with spinal anesthesia

- Periarticular Exparel injection intraoperatively
  - Two 20cc syringes
  - 25 g needle
  - After all bony cuts
  - Tourniquet only during cementing

- Pts were measured POD 1, 2, and 3
  - Visual analog pain scale
  - Gait distance
  - AROM
  - PROM
  - Length of hospital stay

ACB had a statistically significant decreased pain score (2.5) compared with femoral nerve block (5.3) and Exparel only (5.5)

- ACB vs. FNB p-value = 0.0001
- ACB vs. Exp only p-value = 0.0008
- FNB vs. Exp only p-value = 0.77
Tramadol Mechanism of Action

- Modulates μ-opiate receptors in the CNS
- Inhibits ascending pain pathways
- Alters perception and response to pain
- Inhibits reuptake of serotonin and norepinephrine
- These neurotransmitters are involved in the descending inhibitory pain pathway responsible for pain relief
Tramadol

- A recent study evaluated the effect of a multimodal analgesic regimen on postoperative pain, function, adverse effects, and patient satisfaction
- This regimen was compared to patient-controlled analgesia (PCA)

Multimodal Rationale

- A multimodal drug regimen utilizes multiple agents
- Each agent works through varying mechanisms
- Multiple agents modulate nociceptors and different regions of common pain pathways
- Decreases opioid consumption and incidence of opioid-induced adverse effects

- The multimodal regimen consisted of the following a periarticular injection of bupivacaine and ketorolac prior to wound closure and the following post-op oral medications:
  - Oxycodone
  - Tramadol
  - Ketorolac
  - PRN narcotics
• The study was a prospective randomized controlled trial
  ◦ 36 participants
  ◦ All patients undergoing TKA

Multimodal and Control Protocols Compared

Total Narcotic Consumption Compared

• Multimodal regimen patients require significantly less total narcotics over course of hospitalization
Total Narcotic Consumption Compared

- Multimodal regimen patients require significantly less total narcotics over course of hospitalization.

Narcotic-Related Adverse Effects Compared

- P < 0.007.
- P < 0.01.
- P < 0.1.

Efficacy of Pain Control Compared

- Pain control is improved in multimodal group.