**OBJECTIVES**

- Discuss medication reconciliation
- Review principles for stopping or continuing medications before and after surgery

**GENERAL PRINCIPLES**

For example, abrupt withdrawal of ...... may cause ......

| Selective Serotonin Reuptake Inhibitors | Dizziness, lightheadedness, insomnia, fatigue, anxiety, agitation, nausea, headache, sensory disturbances |
| Beta-blockers | Rebound hypertension, angina, arrhythmias, MI, worsening heart failure |
| Statins | Rapid loss of its vascular protective effects & possible prothrombotic activity ➔ vascular event (e.g. stroke) |
| Corticosteroids | Arthralgias, dizziness, hypotension, nausea, severe tiredness or weakness |
| Opioids | Restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, mydriasis, irritability, anxiety, insomnia, back/joint pain, abdominal cramps, N/V/D, increased BP/RR/HR |

**POTENTIAL FOR COMPLICATIONS - PATIENTS ON CHRONIC DRUGS**

- Prospective survey, inpatients, general surgery unit (N = 1,025)
- Aims
  - Identify drug usage profile
  - Identify patients at greatest risk of polypharmacy and importance of those drugs to surgical outcome
  - Identify frequency and duration of drug withdrawal; relate drug withdrawal to outcome
# RESULTS

- 49% taking meds unrelated to surgical admission
- Mean number of meds: 2.4 ± 2.8
- Number of meds increased with age
- Vascular surgery patients: 4.0 ± 2.7 meds
- 48% on two or more cardiovascular drugs
- Diuretics, beta blockers, ACEI
- 45% taking CNS drugs
- Antidepressants, sedatives
- 34% taking GI drugs (laxatives, H₂ blockers, antiemetics)
- 235 (23%) patients had 373 complications

Taking a medication increased relative risk of a post-op complication by 2.7 (95% CI 1.76 – 4.04)

Risk of complication was increased if:
- Taking CV or CNS drug
- Surgery > 1 hour
- > 24 hours without oral meds

# RESULTS (CONTINUED)

Complications may be due to:
1) Destabilization of disease process
2) Drug withdrawal

<table>
<thead>
<tr>
<th>Drug Withdrawn</th>
<th>Symptoms</th>
<th>Consequences</th>
<th>Resolved after drug restarted?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinemet</td>
<td>Movements were difficult</td>
<td>Mobilization delayed; chest complications</td>
<td>Yes</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Tearful, anxious, depressed</td>
<td>Mobilization delayed</td>
<td>Yes</td>
</tr>
<tr>
<td>Sotalol, lisinopril</td>
<td>Pulmonary edema, hypertensive</td>
<td>PRN nifedipine to control hypertension</td>
<td>Yes</td>
</tr>
<tr>
<td>Captopril, pindolol, bumetanide</td>
<td>Hypertensive; labile BP</td>
<td>IV metoprolol, PRN nifedipine</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Asthma and COPD medications are typically continued up to and including the day of surgery.
- Inhaled bronchodilators, ipratroprium, corticosteroids
- Theophylline

Continuing chronic pulmonary medications reduces postoperative pulmonary complications

# CARDIOVASCULAR MEDICATIONS

- General recommendations are to continue up to and including the day of surgery
  - Nitrates, digoxin, clonidine, beta-blockers, calcium channel blockers, hydralazine, antiarrhythmic, statins

- EXCEPTIONS may be:
  - Diuretics
  - Angiotensin-converting enzyme (ACE) inhibitors
  - Angiotensin II receptor blockers (ARBs)

- Concerns
  - Presumed hypovolemic state (fasting, bowel prep) is augmented
  - Risk of hypokalemia / arrhythmias

- Acute use: reduced extracellular fluid volume and cardiac output
- Chronic use: blood volume returns to near normal; predominant (antihypertensive) effect is decreased SVR
- Hold day of surgery; some may continue hydrochlorothiazide on day of surgery if it’s taken for hypertension

# PULMONARY MEDICATIONS

- Asthma and COPD medications are typically continued up to and including the day of surgery

# DIURETICS
Renin-angiotensin system is involved in cardiovascular and fluid hemostasis

- **ACE Inhibitors** block the production of angiotensin II
  - Lisinopril, benazepril, enalapril, quinapril
- **ARBs** block the effects of angiotensin II
  - Losartan, irbesartan, olmesartan, valsartan

ACE I & ARBs interfere with arterial BP regulation

- Direct sympathetic blockade
- Inhibit effects of angiotensin II
- Increased bioavailability of vasodilators
  (bradykinin, nitric oxide, prostacyclins)
- Reduced secretion of aldosterone → less sodium & water retention by kidneys

**ACEI/ARB & ANESTHESIA**

- Retrospective study
- 267 hypertensive adults undergoing surgery
- Hypothesis: Frequency of postinduction hypotension correlates with duration of absence from ACE inhibitor/ARB therapy

**RESULTS**

- Incidence of moderate hypotension 0-30 min after induction significantly greater in patients who took ACEI/ARB <10 hrs before anesthesia
- No difference between groups in severe hypotension or use of vasopressors

**ACE INHIBITOR THERAPY & OUTCOME**

- Retrospective, observational study
- 3,052 patients on ACE inhibitors prior to CABG surgery matched to control patients
- Purpose: to evaluate the effects of preoperative ACE inhibitor treatment on early clinical outcome after CABG
  - Primary endpoint: Death within 30 days of surgery
  - Secondary endpoints: Post-op renal function, atrial fibrillation, myocardial infarction, stroke, inotrope use

**RESULTS**

In patients undergoing CABG, preoperative administration of ACE inhibitors is associated with an increased risk of:
- Death
- Post-op inotropic support
- Post-op renal dysfunction
- Post-op atrial fibrillation

**Conclusion: ACEI/ARB**

- Usual recommendation is to hold ACEI/ARB on the day of surgery
  - Same for aliskiren (Tekturna, a direct renin inhibitor)
- In some cases (uncontrolled hypertension, heart failure), ACEI/ARB may be continued with great care to avoid hypovolemia, hypotension and concurrent use of multiple drugs (e.g. amiodarone)
  - Treatment of ACEI/ARB hypotension
    - Intravascular volume repletion
    - Ephedrine, phenylephrine
    - Vasopressin
    - ACEI/ARB blocks angiotensin II, which is a potent vasococonstrictor and physiologic stimulus for vasopressin release
    - Vasopressin potentiates response to endogenous catecholamines

- Postgrad Med J 2011;87:472
**BETA-BLOCKERS:**

**HISTORY**

  - Surgical patients with CAD or multiple cardiac risk factors randomized to atenolol or no atenolol
  - Atenolol patients had lower mortality at 2 years

  - Patients with positive dobutamine stress echo undergoing vascular surgery randomized to bisoprolol or placebo
  - Bisoprolol patients had lower mortality or nonfatal MI at 30 days

  - Retrospective cohort study (> 600,000 pts)
  - Beta-blockers reduced mortality in high cardiac risk patients but may cause harm in low risk patients

- AHA guideline update 2009 (Circulation 2009;120:e169)
  - Continue beta-blocker in those already taking them
  - Vascular surgery recommendation changed from Class I to Class II

- CMS Core Measures SCIP CARD 2 – Beta Blocker Therapy
  - Patients on beta-blocker therapy prior to arrival receive a beta-blocker during the perioperative period (day prior to surgery through POD 2)
  - If withheld, indicate reason (HR < 50, BP < 100, on vasopressor)

- AHA guideline 2006 (Class I recommendations)
  - Continue beta-blockers in patients already receiving them
  - Beta blockers for vascular surgery patients with positive pre-op stress test

- POISE trial 2008 (Lancet 2008;371:1839)
  - > 8,000 patients with or at risk of atherosclerotic disease undergoing noncardiac surgery randomized to metoprolol or no metoprolol
  - 100 mg/day ER if HR was > 50 bpm and BP > 100 mmHg
  - Metoprolol patients had fewer CV death, nonfatal MI or nonfatal cardiac arrest at 30 days
  - Metoprolol patients had more hypotension, bradycardia, stroke and total mortality

**STATINS**

- Strategies to reduce the risk of perioperative MI in high risk patients generally involve:
  - Aspirin to minimize prothrombotic conditions that can develop following surgery
  - Beta blocker to reduce myocardial oxygen demand / inhibit plaque rupture
  - Statin: Reduce coronary inflammation and inflammatory stress response to surgery
  - Platelet stabilization
  - Decreased thrombogenesis
  - Acute withdrawal of statins following surgery
  - Increased markers of inflammation and oxidative stress
  - Increased cardiac events
  - Animal models suggest discontinuation of statins in patients who have been taking them chronically can produce a rebound prothrombotic state

- Recommendation: continue statin up to and including day of surgery

**GASTROINTESTINAL MEDICATIONS**

- Patients with history of PUD / GERD generally receive prophylactic H2 blockers (famotidine, ranitidine) throughout the perioperative period
  - If gastric stasis is present, metoclopramide may be indicated
PSYCHOTROPIC DRUGS

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI, SNRI</td>
<td>Citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, trazadone, venlafaxine</td>
<td>Safe in perioperative period</td>
</tr>
<tr>
<td>TCA</td>
<td>Amitriptyline, nortriptyline,</td>
<td>Potential concern for arrhythmias, enhanced effects of sympathomimetics, yet no reports in literature</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Alprazolam, clonazepam, diazepam, lorazepam</td>
<td>Safe in perioperative period</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Aripiprazole, olanzapine, quetiapine, risperidone, haloperidol</td>
<td>Metabolic adverse effects (weight gain, dyslipidemia, diabetes) may increase cardiovascular risk in schizophrenics</td>
</tr>
</tbody>
</table>

**Antidepressant Discontinuation**

- Drug withdrawal reactions are frequent
  - Appear within 1 – 3 days
  - Relieved within 24 hours by restarting antidepressant
  - If untreated, symptoms can last 1 – 3 weeks
    - Anxiety, insomnia, irritability, labile mood
    - Nausea/vomiting
    - Dizziness, headache, paresthesia, tremor
    - Fatigue, myalgia, chills, diaphoresis
- Recurrence of depression or mania, with delirium and confusion
- Symptoms can be confused with acute postoperative complications (e.g. stroke)

**Antipsychotic Discontinuation**

- 101 adults with schizophrenia undergoing minor surgery under GA
- Randomized to continue antipsychotics or discontinue 72 hrs before surgery
  - Antipsychotics resumed 24 hours after surgery in both groups
- Primary outcome: postoperative complications (POD 0 – 4)
- Results
  - Significantly lower incidence of postoperative confusion in patients who continued antipsychotics (14% vs 31%, P = 0.048)
  - Confusion was more severe in patients who discontinued antipsychotics
  - No difference in intraoperative hypotension or dysrhythmias
- Conclusion: continue antipsychotic meds perioperatively in patients with chronic schizophrenia

**MAO Inhibitors**

- Monoamine oxidase (MAO) is an enzyme that breaks down monoamine (serotonin, norepinephrine, dopamine) neurotransmitters in the central and peripheral nervous system
- Agents
  - Phenylzine
  - Tranylcypromine
  - Selegiline
- MAO inhibition is irreversible
  - Recovery of function requires formation of new enzyme (2 – 3 weeks)
- Concern
  - Hypertensive crisis with increased dietary tyramine or when sympathomimetics are used to treat intra-op hypotension
  - Selegiline transdermal patch 6 mg/24 hrs bypasses gut avoiding dietary restrictions

**Serotonin Syndrome**

- Unexplained deaths in patients who received MAOI and meperidine
- Altered serotonin function implicated in pathophysiology of many psychiatric / neurologic diseases
- Serotonin neurotransmission can be increased by:
  - Increase synthesis
  - Increase release \( \rightarrow \) MAO I inhibitor
  - Inhibit reuptake \( \rightarrow \) meperidine
  - Inhibit metabolism
  - Directly postsynaptic stimulation

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**18 year old college freshman presents to ED with high fever (103.5° F), agitation and “strange jerking movements”**

- History of depression, on phenylzine
- Hydration (suspect viral syndrome); acetaminophen given
- Meperidine given for shivering and agitation
- Agitation worsened, confusion, thrashing around in bed
- Restrained, haloperidol given, agitation resolved
- Agitation quickly returned, temp rose to 107° F
- Patient suffered respiratory and cardiac arrest and could not be revived
- Level of supervision / work hours \( \rightarrow \) current work hour rules for resident physicians

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Check and Share Journal of Medicine 2008;76(Suppl 4); Cur Opin Psychiatry, 2010;22:574; Cur Opin Anesthesiology, 2005;18:333

Critical Care Clinics 1997;13(4):763

Critical Care Clinics 1997;13(4):763
CONCLUSION: MAOIs

• Withdrawal of MAOIs two weeks before surgery is no longer recommended because it puts the patient at risk for exacerbation of the underlying major depressive disorder

• Continue MAOI and use a safe regimen
  - Avoid meperidine and other serotonergic drugs
  - Use direct-acting sympathomimetics (phenylephrine) to treat hypotension

• Withdrawal of MAOI two weeks before surgery requires close collaboration between psychiatrist, anesthesiologist and surgeon

NSAIDS

• Reversibly inhibit platelet cyclooxygenase (COX)
  - Block formation of thromboxane A
  - Impairs thromboxane-dependent platelet aggregation
  
  EXCEPTION: celecoxib

• Effect on platelet function varies with duration of action of NSAID (e.g. short vs long half-life)
  - In 11 healthy adult patients receiving 7 days course of ibuprofen, platelet function normalized in 24 hours (Ann Intern Med 2005;142:506)
  - Short half-life: ibuprofen, diclofenac
  - Long half-life: meloxicam, nabumetone

• Although NSAIDs are often discontinued one week prior to surgery, NSAIDs with a short half-life can be continued until 2 – 3 days before surgery in patients with OA or RA

• EXCEPTIONS: celecoxib and acetaminophen

CHRONIC OPIOID USE & LENGTH OF STAY

• Retrospective review of 535 patients undergoing appendectomy, cholecystectomy or primary inguinal hernia repair

• 26 patients received at least 44 days of opioids prior to surgery

• After controlling for age, gender, race, comorbidities and type of surgery,
  - Length of stay increased from 3.5 to 5.2 days (49%) in chronic opioid group vs. non-opioid group
  - Costs increased from $12,290 to $ 21,313 (73%) in chronic opioid group vs. non-opioid group

• Longer hospital stays and costs thought to be related to poor post-op pain control

American Society of Regional Anesthesia, Feb 2006, A-16

RECOMMENDATION

Sublingual Buprenorphine
(Suboxone, Subutex)

Buprenorphine has a higher affinity for the opioid receptor and blocks pure opioid agonists (heroin, morphine, fentanyl, hydromorphone) from exerting their full effect.

Because buprenorphine is a partial agonist, it provide some analgesia and prevents withdrawal.

http://www.naabt.org/education/buprenorphine_treatment.cfm

## IN GENERAL….

- Meds to continue on day of surgery
  - Antihypertensive meds, beta blockers, cardiac meds, statins
  - Antidepressants, anti-anxiety, psych meds
  - Anti-seizure meds
  - Asthma
  - Birth control meds
  - Heartburn, reflux meds
  - Opioids, methadone
  - Eye drops
  - Corticosteroids (oral, inhaled)
  - Thyroid, myasthenia gravis, Parkinsons disease

- Meds to **discontinue** on day of surgery
  - ACEI, ARB, diuretics (furosemide, hydrochlorothiazide), oral hypoglycamic agents

- Meds that might require discontinuation up to 7 days before surgery
  - Herbal and other (non-vitamin) supplements
  - Antiplatelet agents, anticoagulants, NSAIDs
  - Sublingual buprenorphine (Suboxone, Subutex)