Perioperative Medication Use

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Case
A 72-year-old female with multiple medical problems is admitted with a hip fracture. Surgery is scheduled in 48 hours. How should her home medications be managed?

- Aspirin
- Carbidopa/Levodopa
- Celecoxib
- Clonidine
- Estradiol
- Ginkgo
- Lisinopril
- NPH insulin
- Prednisone 20 mg 7-day burst two weeks ago
- Sulfasalazine

Objectives
- Guiding principles
- Rationale behind continuing or discontinuing:
  - Antiplatelet drugs
  - Cardiovascular drugs
  - CNS-active drugs
  - Diabetic drugs
  - Hormones
  - Non-steroidal anti-inflammatory drugs (NSAIDs)
  - Corticosteroids
  - Disease-modifying antirheumatic drugs (DMARDs)
  - Biological response modifiers (BRMs)
  - Herbal medicines
Guiding Principles

- Avoid progression or decompensation of disease
- Avoid withdrawal
- Avoid interactions with anesthesia
- Avoid perioperative complications

Drugs to Continue

- Very long half-life or biologic effect
- Significant withdrawal symptoms
- No significant interactions with anesthesia
- No significant risk of perioperative complications

Antiplatelet Drugs to Continue

- **Aspirin**
  - Irreversibly inhibits platelet aggregation
  - Continue if history of CAD, POBA, or PCI\(^1\)
  - Stop 7 days before surgery, if indicated\(^2\)

- **Clopidogrel**
  - Irreversibly inhibits platelet aggregation
  - Continue *with* aspirin if surgery within 30 days of bare-metal or 365 days of drug-eluting stent\(^1\)
  - Stop 7 days before surgery, if indicated\(^2\)

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\(^2\) Micromedex.
### CV Drugs to Continue

**Beta-blockers**
- Continue if already taking
- Start if increased cardiac risk with RCRI ≥ 2
- Titrate to HR < 65

**Statins**
- Continue if already taking
- Start if increased cardiac risk with RCRI ≥ 2
- Withdrawal associated with a 4.6-fold increase in post-operative troponin release and a 7.5-fold increase in post-operative MI and cardiovascular death

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### CV Drugs to Continue

**Amiodarone**
- Elimination $t_{1/2}$ up to 142 days

**Calcium-channel blockers**
- Caution if LVEF < 40%

**Clonidine**
- Risk of severe rebound hypertension with reports of encephalopathy, stroke, and death, especially if concomitant beta-blocker therapy
- Convert to patch and tape off oral dose 48-72 hours in advance if anticipate extended NPO status

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### CV Drugs to Continue

**Digoxin**
- Elimination $t_{1/2}$ up to 48 hours

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CNS Drugs to Continue

- Antiepileptics, antipsychotics, benzodiazepines, bupropion, gabapentin, lithium, mirtazapine, SSRIs, SNRIs, TCAs, valproic acid.
  - Risk of withdrawal and disease decompensation
- Carbidopa/Levodopa
  - Rapid worsening of Parkinson’s symptoms
- Monoamine oxidase inhibitors (MAOI)
  - Use MAOI-safe anesthesia without dextromethorphan, epinephrine, meperidine, or norepinephrine

Diabetic Drugs to Continue

- Insulin
  - Continue glargine without dose adjustment
  - Continue usual basal rate with insulin pump
  - No short-acting insulin or insulin mixes within 4 hours of surgery
  - Give half the intermediate insulin (e.g. NPH) dose the day of surgery with D5 drip perioperatively
  - No preoperative insulin if D5 drip will not be used
- Incretins (exenatide, sitagliptin)
  - Do not cause hypoglycemia in the absence of insulin
- Thiazolidinediones
  - Extremely long duration of action

Hormones to Continue

- Antithyroid medications (methimazole, PTU)
- Levothyroxine
  - Elimination t1/2 up to 7 days
Continuing Corticosteroids

- Prednisone 5 mg/day for 5 days within 30 days of surgery can result in adrenal insufficiency\(^1\)
- Corticosteroid therapy does not result in mineralocorticoid deficiency\(^1\)
- Normal cortisol release from surgery 50-150 mg\(^1\)
- Recent systematic review suggests stress-dose steroids may not be routinely indicated\(^2\)
- Continue outpatient corticosteroid dose plus add a stress dose


Stress-Dose Corticosteroids

- Minor surgery (local anesthesia, duration less than one hour):
  - Hydrocortisone 25 mg IV or methylprednisolone 5 mg IV during surgery
- Moderate surgery (lower extremity vascular, joint replacement, open cholecystectomy):
  - Hydrocortisone 50-75 mg IV or methylprednisolone 10-15 mg IV during surgery, tapering to baseline dose over 1-2 days
- Major surgery (cardiothoracic, Whipple):
  - Methylprednisolone 10 mg IV every 8 hours, tapering to baseline dose over 2-3 days


Other Drugs to Continue

- Selective COX-2 inhibitors
  - No effect on platelet aggregation
  - Hold 2-3 days before surgery if concern for impaired renal function
- HIV therapy
- Hydroxychloroquine
- Inhaled beta-agonists, corticosteroids, ipratropium, tiotropium
- Myasthenia gravis therapy
- Theophylline
Drugs to Stop

- Risk of significant interactions with anesthesia
- Risk of significant perioperative complications

CV Drugs to Stop

- ACEI and ARB
  - Risk of hypotension requiring vasopressors during induction of anesthesia 50% higher in a systematic review\(^1\)
  - Risk of post-operative acute renal failure after cardiothoracic surgery 28% higher in one recent study\(^2\) but 52% lower in another\(^3\)
  - Stop 1 day before surgery

- Diuretics
  - Risk of dehydration and electrolyte imbalance due to NPO status.

Diabetic Drugs to Stop

- Metformin
  - FDA Black Box Warning to discontinue before any intravascular radiocontrast study or surgical procedure\(^1\)
  - Lactic acidosis is rare but carries a mortality of 50%\(^1\)
  - Stop 24 hours before surgery, restart 48-72 hours after\(^2\)
  - Confirm normal renal function before restarting\(^2\)

- Sulfonylureas (glimepiride, glipizide, glyburide)
  - Risk of hypoglycemia
  - Stop the night before surgery

Hormones to Stop

- Oral contraceptives, hormone replacement therapy, raloxifene
  - In analysis of HERS trial, DVT risk was 4.9 times higher for 90 days after surgery in patients taking estrogen/progesterone hormone replacement therapy, although unclear if routine DVT prophylaxis was used
  - Non-surgical DVT risk remained 2.5 times higher for 30 days after cessation of HRT
  - Consider stopping 4 weeks before surgery when prolonged immobilization is expected
  - Consider longer and more intensive DVT prophylaxis


NSAIDs to Stop

- Non-selective COX inhibitors
  - Reversibly inhibit platelets only while drug is present in circulation
  - Stop 1-3 days before surgery

1 Micromedex.

DMARDs to Stop

- Methotrexate
  - Increased risk of wound infections and dehiscence
  - Decreased risk of post-operative disease flare
  - Stop 2 weeks before surgery if medical comorbidities, advanced age, or on prednisone over 10 mg/day

- Leflunomide
  - Renally cleared with elimination t1/2 of 2 weeks
  - Risk of myelosuppression
  - Stop 2 weeks before surgery, restart 3 days after

- Azathioprine, sulfasalazine
  - Renally cleared with risk of myelosuppression
  - Stop 1 day before surgery, resume 3 days after

1 Curr Opin Rheumatol. 2006;18:151-156.
BRMs to Stop

- Anti-TNF-\_ (adalimumab, etanercept, infliximab)
- IL1 antagonists (anakinra)
- Anti-CD20 (rituximab)
  - Increased risk of wound infections and dehiscence
  - Decreased risk of post-operative disease flare
  - Stop 1 week before surgery, resume 1-2 weeks after

Herbal Medicines to Stop

- Used by up to a third of U.S. population
- Can have significant implications for anesthesia:
  - Cardiovascular instability (ginseng, ma huang)
  - Hypoglycemia (ginseng)
  - Immunosuppression (echinacea use for > 8 weeks)
  - Increased risk of bleeding (garlic, ginkgo, ginseng)
  - Prolongation of anesthesia (kava, St. John's wort, valerian)
- STOP 1-2 weeks before surgery

Case Revisited

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Summary

Balance risks vs. benefits of drugs in each patient

Continue
- Antiplatelet therapy
- Beta-blockers
- Statins
- Calcium channel blockers
- Clonidine
- Amiodarone
- All CNS drugs
- Insulin, with adjustments
- TZDs and metformin
- Thyroid drugs
- Corticosteroids, with stress dose
- COX-2 inhibitors
- HIV drugs
- Hydroxychloroquine

Stop
- ACEI and ARBs
- Diuretics
- Metformin
- Sulfonylureas
- OCPs, HRT, SERMs
- NSAIDs
- DMARDs
- BRMs
- Herbal medicines

References