INTRODUCTION — At least 50 percent of patients undergoing surgery take medications on a regular basis [1]. Clinicians often must decide if chronic medications should be continued in the perioperative period. Unfortunately, there are few outcome data about the majority of medications taken in the perioperative period.

This lack of medical evidence is reflected by the large variation in perioperative management recommendations among anesthesiologists [2]. The recommendations in this review are to a large degree expert opinion, based on information from other reviews [3,4] and textbooks, along with clinical experience and theoretic considerations.

This topic will focus on medications known to have perioperative effects, those known to interact with anesthetic agents, and those in common use will be discussed. An overview of preoperative patient assessment and details about perioperative management for specific medications are presented separately. (See "Overview of the principles of medical consultation and perioperative medicine" and "Perioperative management of hypertension" and "Management of anticoagulation before and after elective surgery" and "The surgical patient taking glucocorticoids".)

PRINCIPLES OF MEDICATION MANAGEMENT — The following principles inform the management of chronic medications in the perioperative period:

- A complete medication history should be obtained, and all clinicians involved in patient management (eg, surgeon, anesthesiologist, medical consultants) should review the medication history. Medication use reported by the patient should be verified (medication reconciliation) to address accuracy of drugs and doses [5]. This should include all over-the-counter and herbal/complementary medications, as well as prescription drugs. In addition, substance use information (including alcohol, nicotine, and illicit drugs) should be elicited.

- Medications associated with known medical morbidity if withdrawn abruptly should be continued in the perioperative period, or tapered if feasible. Intravenous, transdermal, or transmucosal medicines should be substituted when absorption will be impaired because of loss of gastrointestinal function or restrictions on oral intake. Medications thought to increase the risk of anesthetic or surgical complications and not essential for the short-term should be held through the perioperative period [3].

- Medications not meeting either of the above principles can be discontinued or continued based on clinician judgment.

- The many medications administered perioperatively during a relatively short period increase the potential for drug-drug interactions.
The metabolism and elimination of medications and their metabolites may be altered during the perioperative period. In particular, gastrointestinal absorption of oral medications may be impaired due to changes in splanchnic blood flow and edema [6].

CARDIOVASCULAR MEDICATIONS — (table 1)

Beta blockers

- **Benefit/risk** — Beta blockers have a number of potential beneficial effects when taken perioperatively. Beta blockers reduce ischemia by decreasing myocardial oxygen demand due to increased catecholamine release in the perioperative period, and may help prevent or control arrhythmias. Patients who take beta-blockers chronically for management of angina are at risk of ischemia with withdrawal of beta blockade. Acute withdrawal of a beta blocker pre- or postoperatively can lead to substantial morbidity and even mortality [7]. Withdrawal issues are of less concern when beta blockers are used for hypertension or migraine prophylaxis.

Whether to initiate beta blockers as prophylaxis for ischemia in the perioperative period in patients at increased risk for coronary disease, is complex and discussed separately. (See "Management of cardiac risk for noncardiac surgery", section on 'Role of beta blockers'.)

Potential adverse effects of perioperative beta blockade include bradycardia and hypotension. Nonselective beta blockers can interact with epinephrine, used for infiltration anesthesia or management of intraoperative anaphylaxis [8]. (See "Management of cardiac risk for noncardiac surgery" and "Major side effects of beta blockers", section on 'Beta blocker withdrawal'.)

- **Continue/discontinue** — In light of the potential benefits of perioperative beta blockade, minimal adverse effects, and consequences of acute withdrawal, we recommend that beta blockers be continued in the perioperative period and continued throughout the hospital stay.

- **Formulations/alternatives** — Intravenous forms of beta blockade, such as metoprolol, propranolol, and labetalol should be given if the patient cannot take oral medications [9,10]. We have a slight preference for beta 1 cardioselective beta blockers (eg, metoprolol) since they are less likely to cause adverse pulmonary and peripheral vascular effects; however, patients who are taking a nonselective beta blocker (eg, propranolol) chronically do not need to switch to a beta 1 selective agent perioperatively.

Alpha 2 agonists

- **Benefit/risk** — Administration of centrally acting sympatholytic drugs such as clonidine may possibly improve perioperative outcomes [11-13]. Abrupt withdrawal of clonidine can precipitate rebound hypertension [14-16], which usually occurs after abrupt cessation of fairly large oral doses (eg, greater than 0.8 mg/day), but has also been noted with transdermal clonidine [17]. Withdrawal symptoms have also been reported with methyldopa and guanfacine withdrawal but are less likely because of their slower onset of action [18]. (See "Withdrawal syndromes with antihypertensive therapy'.)

Other potential benefits of continuing alpha 2 agonists perioperatively include [19,20]:

- Decrease in the stress response to endotracheal intubation and surgery.
- Sedative/anxiolytic, analgesic, and antishivering properties [19,20].
• **Continue/discontinue** — Given the potential benefits of continuing alpha 2 agonists perioperatively and the possible negative consequences of withdrawal, we recommend that these drugs be continued in the perioperative period.

• **Formulations/alternatives** — Transdermal clonidine is available for patients who likely will not be able to resume oral medications by 12 hours after surgery. The decision to substitute this form of therapy must be made before surgery; an equivalent dose of the transdermal preparation should be started three days prior to surgery while the oral clonidine is tapered. The persistent effect of transdermal clonidine for 24 to 48 hours after patch removal should be considered when transitioning back to the oral form.

Other centrally acting sympatholytic agents (eg methyllopa or guanabenz) are rarely used today. Withdrawal from abrupt discontinuation has been reported but is less common because of their slower onset of action [21,22]. For patients unable to take oral medications perioperatively, we recommend withholding methyllopa and guanabenz and using other parenteral hypertensive agents if hypertension becomes a problem [14]. An intravenous form of methyllopa is available in the rare cases in which abrupt stoppage appears to be leading to a withdrawal syndrome.

### Calcium channel blockers

• **Benefit/risk** — Data are limited regarding the risks and benefits of calcium channel blockers in the perioperative setting. Small trials have shown a more stable intraoperative hemodynamic profile in patients treated with continuous diltiazem, compared to placebo, during coronary bypass surgery [23], but these studies are not large enough to demonstrate improved outcomes. A meta-analysis found that use of calcium channel blockers was associated with reduced ischemia and atrial arrhythmia in patients undergoing noncardiac surgery [24].

There are no serious interactions between calcium channel blockers and anesthetic agents [25]. A withdrawal syndrome is not typical of calcium channel blockers, although abrupt discontinuation of these drugs has been reported to cause severe vasospasm in patients undergoing coronary revascularization [26].

Concerns have been raised about a possible association between calcium channel blockers and an increased risk of bleeding [27]. A randomized trial in valvular surgery patients found that, compared with placebo, patients receiving nimodipine had increased bleeding [28,29]. Reports conflict on whether there is a greater incidence of anemia in patients receiving calcium channel blockers after hip surgery [30,31]. Two large trials in cardiac surgery patients did not find any association between bleeding risk and use of calcium channel blockers [32].

• **Continue/discontinue** — Despite little data regarding calcium channel blockers during the perioperative period, these agents appear safe and have theoretic benefit [33]; data regarding bleeding risk are contradictory. Thus, we recommend that calcium channel blockers be continued in patients who are already taking them preoperatively [33].

• **Formulations/alternatives** — Intravenous diltiazem is available for patients who are unable to tolerate oral agents, although we recommend using intravenous beta blockers rather than calcium channel blockers in the perioperative period as these are more proven to prevent myocardial ischemia. (See 'Beta blockers' above and "Management of cardiac risk for noncardiac surgery".)
Most calcium channel blockers are formulated as extended release and should not be crushed for administration in enteral tubes. Short acting calcium channel blockers are available (diltiazem, verapamil) and can be substituted with appropriate dosing interval adjustments. Amlodipine has a long washout period, and short acting substitutes may not be necessary.

ACE inhibitors and angiotensin II receptor blockers

- **Benefit/risk** — The management of patients taking angiotensin converting enzyme (ACE) inhibitors preoperatively is controversial [34]. ACE inhibitors and angiotensin II receptor blockers can theoretically blunt the compensatory activation of the renin-angiotensin system during surgery and result in prolonged hypotension. At least two clinical trials have investigated this issue:

In one study, 51 patients undergoing peripheral arterial surgery were randomly assigned to ACE inhibitor continuation or withdrawal [35]. Patients continuing ACE inhibitors through the morning of surgery had significantly more episodes of hypotension requiring treatment with pressor agents compared with patients who stopped therapy at least 12 hours (captopril) or 24 hours (enalapril) before surgery. No difference was noted in the incidence of hypertensive episodes.

A second study randomly assigned 40 patients with good left ventricular function who were undergoing coronary artery bypass graft surgery to continue or omit ACE inhibitors before surgery [36]. Patients who omitted their ACE inhibitors required less vasopressors during surgery but required more vasodilators to control hypertension in the early postoperative period.

Angiotensin II receptor blockers (ARBs) have similar physiologic effects as ACE inhibitors on hypertension and renal perfusion. It is not surprising then that a study in vascular surgery patients found a statistically significant increase in the number of hypotensive episodes in patients treated with ARBs prior to surgery compared with those treated with beta blockers or calcium channel blockers [37].

A retrospective review of 267 hypertensive patients undergoing surgery in a general hospital found that taking either an ACE inhibitor or ARB within 10 hours of surgery, compared to holding medication for at least 10 hours, increased the odds of moderate postinduction hypotension (OR 1.74) [38]. However, there was no increase in severe hypotension or need for vasopressors.

Nonrandomized studies suggest a possible myocardial protective effect of ACE inhibitors in patients undergoing coronary artery bypass graft surgery [39]. However, reports conflict on the effect of ACE inhibitors on the risk of acute kidney injury in these patients [40,41].

- **Continue/discontinue** — These findings suggest that continuing ACE inhibitors up to the time of surgery increases perioperative hypotension, but possibly reduces the incidence of postoperative hypertension. While the data do not lead to clear recommendations, we recommend continuing ACE inhibitors or ARBs in patients who are taking them for the management of hypertension. Substitution of shorter acting drugs (eg captopril for patients who can take ACE inhibitors) may allow more flexibility for patients with postoperative labile blood pressure. On the other hand, it is reasonable to withhold these drugs one dose interval before surgery in patients who are taking them for heart failure, particularly if the baseline blood pressure is low, to avoid significant hypotension during anesthesia induction [4]. It is also reasonable to withhold these drugs for surgeries where substantial fluid shifts or bleeding
are anticipated.

Based upon limited data, we recommend resuming ACE inhibitors or ARBs postoperatively as long as the patient is not hypotensive and has normal renal function.

- **Formulations/alternatives** — Enalapril (Enalaprilat) is available for short-term intermittent intravenous administration, although used infrequently.

**Diuretics**

- **Benefit/risk** — The two major physiologic effects of loop and thiazide-type diuretics of concern are hypokalemia and hypovolemia. Hypokalemia can theoretically increase the risk of perioperative arrhythmia, although observational studies of patients with structural heart disease have failed to find such a relationship [42,43]. Additionally, hypokalemia might potentiate the effects of muscle relaxants used during anesthesia, as well as provoke paralytic ileus.

Systemic vasodilatation induced by anesthetic agents may cause hypotension in patients who are intravascularly depleted from diuretics.

- **Continue/discontinue** — There is no consensus whether diuretics should be discontinued prior to elective surgery [2]. Since diuretics may increase the risk of hypotension if continued on the morning of surgery, and a quick diuresis can be initiated by intravenous administration should the need be discovered during surgery, we recommend they be held on the morning of surgery, and resumed when the patient is taking oral fluids.

For patients who require diuretics perioperatively, clinicians should pay close attention to volume and potassium replacement.

- **Formulations/alternatives** — Intravenous preparations of loop diuretics are available, if necessary, and are commonly used.

**Non-statin hypolipidemic agents**

- **Benefit/risk** — Niacin and fibric acid derivatives (gemfibrozil, fenofibrate), cause myopathy and rhabdomyolysis. The risk is higher when these agents are used in combination with statins, and surgery may also increase the risk of myopathy [44-48]. (See "Muscle injury associated with lipid lowering drugs".)

Lipid lowering agents that are bile sequestrants (cholestyramine and colestipol) interfere with bowel absorption of multiple medications that may be required perioperatively.

The benefits or risks of ezetimibe in the perioperative period are unknown.

- **Continue/discontinue** — We recommend temporary discontinuation of niacin, fibric acid derivatives, bile sequestrants, and ezetimibe perioperatively. Discontinuation is likely to be safe since these agents are given for the goal of long-term reduction in vascular morbidity [45].

The optimal interval to discontinue these agents before surgery is unknown; we recommend they be stopped the day before surgery to allow for drug elimination.
Statins

**Benefit/risk** — Evidence has become convincing that HMG CoA reductase inhibitors (statins) may prevent vascular events through mechanisms other than cholesterol lowering (eg, plaque stabilization, reduction in inflammation, decreased thrombogenesis) and may be of benefit in the perioperative period. (See "Mechanisms of benefit of lipid lowering drugs in patients with coronary heart disease" and "Management of cardiac risk for noncardiac surgery".)

In the DECREASE III trial, 497 patients who were not taking statin therapy and were scheduled to undergo elective noncardiac vascular surgery were randomly assigned to take either 80 mg of extended release fluvastatin daily or placebo at least 30 days before the procedure, and continue therapy for at least 30 days after surgery [49]. The statin-treated patients had significantly lower rates of myocardial ischemia and decreased occurrence of the composite end point (cardiovascular death or myocardial infarction) compared to the control group (HR 0.55; 95% CI 0.34-0.88). In the DECREASE IV study, 1066 patients at intermediate risk for cardiac events were randomly assigned to fluvastatin 80 mg versus placebo before nonvascular surgery. Myocardial infarction and death within 30 days of surgery were decreased from 4.9 to 3.2 percent, although the reduction did not meet statistical significance (HR 0.65; CI 0.35–1.20) [50]. The relative reduction in events shown in DECREASE III (vascular surgery) compared to DECREASE IV (non vascular surgery) was similar.

- **Continue/discontinue** — Based on the current evidence, we recommend continuing statin therapy in patients undergoing surgery, particularly in patients at high risk for cardiovascular events. Furthermore, we recommend that clinicians should start statins for patients undergoing vascular surgery, both for the benefit shown in a randomized trial and because most will have an indication for long term statin use.

- **Formulations/alternatives** — An intravenous statin preparation is not available. Patients treated with extended release fluvastatin had fewer perioperative cardiac events compared to those receiving shorter acting statin medications [51]. The risk of myopathy appears to be lowest with pravastatin and perhaps fluvastatin.

Statins can accumulate when there is hypoperfusion of liver (simvastatin, lovastatin) or kidney (pravastatin), increasing the risk of myopathy. Doses should be appropriately adjusted.

**GASTROINTESTINAL AGENTS**

- **Benefit/risk** — There are several potential advantages of continuing H2 blockers or proton pump inhibitors perioperatively. The stress of surgery and other conditions (eg, intensive care unit stay and mechanical ventilation) can increase the risk of stress-related mucosal damage, which may be minimized by administration of these drugs. (See "Stress ulcer prophylaxis in the intensive care unit"). In addition, gastric aspiration during anesthesia, though rare, can lead to severe pulmonary injury. Both H2 blockers and proton pump inhibitors decrease gastric volume and raise gastric fluid pH, thereby reducing the risk of chemical pneumonitis from aspiration [52,53]. (See "Aspiration pneumonia in adults", section on 'Chemical pneumonitis'.)

Neither H2 blockers nor proton pump inhibitors have been shown to interact with common anesthetic agents, although cimetidine can alter the metabolism of several drugs.

- **Continue/discontinue** — Based upon the potential benefits and lack of contraindications, we recommend that patients who are taking either H2 blockers or proton pump inhibitors remain...
on these medications in the perioperative period.

- **Formulations/alternatives** — Patients who are unable to take oral medications for a prolonged period should be switched to an intravenous form of H2 blocker or proton pump inhibitor (table 2). Intravenous H2 blockers are less costly.

**PULMONARY AGENTS** — (table 2)

**Inhaled beta agonists and anticholinergics**

- **Benefit/risks** — Inhaled medications used to control obstructive pulmonary disease such as beta agonists (albuterol, metaproterenol, salmeterol, formoterol) and anticholinergics (ipratropium, tiotropium) have been found to reduce the incidence of postoperative pulmonary complications in patients with asthma and chronic obstructive pulmonary disease and should be continued perioperatively. (See "Strategies to reduce postoperative pulmonary complications".)

- **Formulations/alternatives** — Inhaled beta agonists and anticholinergics are normally administered on the morning of surgery. The drugs can be administered through a nebulizer or in the circuit of the ventilator when use of metered-dose inhalers is not possible.

**Theophylline**

- **Benefit/risk** — There are no data whether continuation of theophylline in the perioperative period decreases pulmonary complications. Theophylline has the potential to cause serious arrhythmias and neurotoxicity at a level just beyond the therapeutic range and theophylline metabolism is affected by many common perioperative medications.

- **Continue/discontinue** — We recommend theophylline medications be discontinued the evening before surgery.

- **Formulations/alternatives** — Other medications for treatment of obstructive lung disease can be initiated or adjusted, including inhaled beta agonists, glucocorticoids, and anticholinergic medications. (See "Strategies to reduce postoperative pulmonary complications".)

**Glucocorticoids**

- **Benefit/risk** — Patients with pulmonary disease who are maintained on glucocorticoids (corticosteroids) are at risk of adrenal insufficiency if steroids are abruptly withdrawn, particularly in the face of increased stress related to surgery. Additionally, glucocorticoids in such patients may be necessary to maintain optimal lung functions.

- **Continue/discontinue** — Both inhaled and systemic glucocorticoids should be continued during the perioperative period. Issues related to preoperative stress dosing are discussed below. (See 'Endocrine agents' below.)

**Leukotriene inhibitors**

- **Benefit/risk** — The leukotriene inhibitors zileuton (Zyflo), zafirlukast (Accolate), and montelukast (Singulair) help maintain asthma control but are not used for acute therapy. (See "Agents affecting the 5-lipoxygenase pathway in the treatment of asthma".)

The elimination half-life of these agents is relatively short, but their effect on asthma
symptoms and pulmonary function continues for up to three weeks after cessation of treatment [54].

There is no evidence of a withdrawal syndrome with abrupt stoppage of these agents. We are aware of no evidence of harmful interactions of these drugs with anesthetics.

- **Continue/discontinue** — We recommend that leukotriene inhibitors be given on the morning of surgery and resumed when the patient is tolerating oral medications.

- **Formulations/alternatives** — No parenteral substitution is available nor necessary given the long duration of action for leukotriene inhibitors.

**ENDOCRINE AGENTS** — (table 3)

**Glucocorticoids**

- **Benefit/risk** — The management of patients taking glucocorticoids preoperatively is discussed in detail separately. (See "The surgical patient taking glucocorticoids".)

In general, the duration of use and dosing of glucocorticoids should identify appropriate management:

- Patients who have taken glucocorticoids for less than three weeks, or who have taken chronic alternate day therapy, are unlikely to have a suppressed hypothalamic-pituitary-adrenal (HPA) axis and should continue usual doses of glucocorticoids perioperatively.
- Patients taking prednisone at a dose greater than 20 mg/day for three weeks or more, and patients with a Cushingoid appearance should be assumed to have HPA axis suppression and may need an increased dose of corticosteroids perioperatively.
- Patients who have been taking glucocorticoids in a dose equivalent to prednisone 5 to 20 mg daily for more than three weeks may have HPA axis suppression, and either should undergo testing or receive empiric glucocorticoid coverage.

(See "The surgical patient taking glucocorticoids", section on 'Evaluation of HPA axis suppression'.)

**Diabetic medications** — The management of diabetes mellitus, including management of oral agents and insulin in the perioperative period, is discussed in detail separately. (See "Perioperative management of diabetes mellitus".)

**Oral contraceptives**

- **Benefit/risk** — Oral contraceptives are the most frequent cause of thrombosis in young women because of their widespread use. The risk of thrombosis increases within four months of initiation and decreases to previous levels within three months of stopping treatment. Surgery itself is a risk factor for thrombosis, and compounds the risk associated with oral contraceptives.

Oral contraceptives with greater estrogen content (≥35 mcg) have a higher risk of thromboembolism compared to those with lower estrogen content (≤30 mcg). Nevertheless, even the lower estrogen content pills are associated with an increased risk of thrombosis [55,56]. Estrogen/progestin patches also increase thrombosis risk. Risk also varies with type of progestin. (See "Risks and side effects associated with estrogen-progestin contraceptives", section on 'Venous thromboembolic disease'.)
• **Continue/discontinue** — The decision to continue or stop oral contraceptives before surgery must balance the risk of unwanted pregnancy against the risk of thromboembolism. It is reasonable to continue oral contraceptives in patients who are undergoing low risk surgery (table 4). Definitions of low, moderate, and high risk procedures are discussed elsewhere. (See "Prevention of venous thromboembolic disease in surgical patients").

In general, oral contraceptives should be discontinued four to six weeks prior to surgery in patients with increased risk. Other forms of contraception must be used to prevent unwanted pregnancy during this time. Oral contraceptives might be continued in moderate to high risk women who could have difficulty complying with other forms of contraception, recognizing that this may increase their risk of thromboembolism and that thromboembolic prophylaxis should be planned accordingly.

We recommend a serum pregnancy test prior to surgery in all women of childbearing age, particularly important in those who have stopped oral contraceptives preoperatively.

**Postmenopausal hormone therapy**

• **Benefit/risk** — The estrogen content of preparations used for postmenopausal hormone therapy (HT) is much lower than in oral contraceptive pills. However, use of HT, with either estrogen alone or estrogen plus a progestin, still appears to increase the risk of venous thromboembolism [57,58]. Although a case-control study did not find an increased risk of thromboembolism in women undergoing arthroplasty who received HT (OR 0.66, 95% CI 0.35-1.18), the results may have been confounded by women at lower risk for thromboembolism being more likely to be prescribed HT [59].

The risks associated with temporary discontinuation of hormone therapy are minimal, other than discomfort from hot flashes and other menopausal symptoms.

• **Continue/discontinue** — Women undergoing procedures associated with moderate to high risk for venous thromboembolism (VTE) should stop hormone therapy at least four to six weeks prior to surgery and resume treatment postoperatively once the period of elevated risk for VTE has resolved. Hormone therapy can be continued for surgical procedures associated with a low risk of venous thrombosis (table 4). (See "Prevention of venous thromboembolic disease in surgical patients").

**Selective estrogen receptor modulators**

• **Benefit/risk** — The indications for use of selective estrogen receptor modulators (SERMs) such as tamoxifen and raloxifene include breast cancer treatment, breast cancer chemoprevention, and, at least for raloxifene, the prevention and treatment of osteoporosis. (See "Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention" and "Selective estrogen receptor modulators for osteoporosis"). Both tamoxifen and raloxifene increase the risk of venous thromboembolism [60,61].

Brief discontinuation of SERMs used for prevention of breast cancer or osteoporosis is unlikely to result in harm. For patients with breast cancer who are being treated with SERMs, the risk of disease progression with preoperative cessation of treatment is a concern.

• **Continue/discontinue** — For patients receiving SERM for prevention of cancer or osteoporosis, we suggest discontinuing medication for four weeks for those surgical
procedures associated with a moderate or high risk of venous thromboembolism and restarting once the period of elevated risk has resolved; drugs can be continued for low risk surgeries (table 4). The decision to discontinue is more difficult when SERMS are used for cancer treatment, and consultation with an oncologist is recommended.

**Drugs used for thyroid disease** — The management of medications to control hypothyroid and hyperthyroid states is discussed in detail separately. (See "Nonthyroid surgery in the patient with thyroid disease".)

In brief, patients receiving chronic thyroxine (T4) therapy who undergo surgery and are unable to eat for several days do not need to be given T4 parenterally. T4 should be given intravenously or intramuscularly if oral intake cannot be resumed in five to seven days. The parenteral dose should be reduced to approximately 80 percent of the patient’s usual oral dose, to reflect the fraction of oral T4 that is absorbed.

**Drugs used for osteoporosis/osteopenia** — Bisphosphonate use, especially in malignancy, has been associated with osteonecrosis in patients undergoing dental surgery. The absolute risk is low, but osteonecrosis is difficult to manage. The duration of effect of bisphosphonates on bone remodeling is long, and the discontinuation of these agents for weeks or even months before surgery may not decrease the risk of osteonecrosis. Dentists should inform patients of this risk and consider strategies to lower the risk [62].

**MEDICATIONS AFFECTING HEMOSTASIS** — Many patients undergoing surgery are taking medications that are intended to impair coagulation (eg, warfarin, aspirin) or other antiplatelet agents (eg, clopidogrel), or take medications for another indication that have an unintended effect on hemostasis, such as nonsteroidal antiinflammatory drugs (NSAIDs) (table 5).

**Aspirin**

- **Benefit/risk** — Aspirin irreversibly inhibits platelet cyclooxygenase, which may increase intraoperative blood loss and hemorrhagic complications [63-68]. However, the same effect can help to prevent perioperative vascular complications, in particular cardiac complications.

  Observational studies suggest that withdrawal of aspirin preoperatively is associated with increased in-hospital mortality in patients undergoing coronary artery bypass graft surgery (CABG) or surgery for peripheral artery disease [69-71]. (See "Medical therapy to prevent perioperative complications after coronary artery bypass graft surgery", section on 'Aspirin'.)

  In addition, stopping aspirin therapy for five days or more in patients with underlying cardiovascular disease may increase the risk of an acute coronary syndrome or stroke [72-74]. (See "Benefits and risks of aspirin in secondary and primary prevention of cardiovascular disease" and "Antiplatelet therapy for secondary prevention of stroke", section on 'Aspirin'.)

  In patients undergoing cataract surgery, the risk of ocular hemorrhage in patients taking aspirin is low and similar to that in patients not taking aspirin [75]. (See "Cataract in adults", section on 'Aspirin and other antiplatelet agents'.)

  Aspirin also may prevent venous thromboembolism [76]. However, other agents are more effective [77]. (See "Prevention of venous thromboembolic disease in surgical patients", section on 'Aspirin'.)

- **Continue/discontinue** — The optimal perioperative management of patients who are taking aspirin is uncertain, and significant practice variation exists [2]. The decision to continue or withhold aspirin should reflect a balance of the consequences of perioperative hemorrhage
versus the risk of perioperative vascular complications.

Patients believed to be at high risk for perioperative vascular complications in whom perioperative hemorrhage would result in minimal morbidity should continue aspirin. This includes patients on maintenance aspirin therapy who have coronary stents or who are undergoing CABG or peripheral arterial surgery [69-71]. A 2007 update of a 2004 ACC/AHA task force recommended that aspirin should not be withheld before either elective or nonelective CABG after ST elevation MI [78].

Aspirin should be withheld prior to surgical procedures in which perioperative hemorrhage could be catastrophic (eg, central nervous system surgery) or impact surgical outcome.

Aspirin can be safely continued in most patients undergoing cataract surgery. (See "Cataract in adults", section on 'Aspirin and other antiplatelet agents'.)

If the decision is made to stop aspirin, seven to ten days should elapse before surgery is undertaken [79]. Use of the bleeding time to assess the effect of aspirin or NSAIDs on bleeding risk is not recommended as it is a poor predictor of perioperative hemorrhage [79,80]. (See "Preoperative assessment of hemostasis").

2008 ACCP guidelines on antithrombotic therapy recommend resuming aspirin approximately 24 hours (or the next morning) after surgery when there is adequate hemostasis [79].

- **Formulations/alternatives** — Aspirin is not available in parenteral forms, but is available as a rectal suppository for patients who are felt to need ongoing therapy but cannot take oral medication.

**Other antiplatelet agents**

- **Benefit/risk** — Dipyridamole has both vasodilator and antiplatelet activity. With the publication of the ESPS-2 trial [81], its use has become more common in patients with past stroke or transient ischemic attack (TIA). (See "Antiplatelet therapy for secondary prevention of stroke" and "Secondary prevention for specific causes of ischemic stroke and transient ischemic attack"). The half-life of the modified-release preparation is approximately 10 hours.

The thienopyridines, clopidogrel, prasugrel, and ticlopidine are platelet inhibitors used in patients who have had previous cerebrovascular events, recent acute coronary syndromes, or recent percutaneous coronary interventions with stenting [82]. The risk of coronary artery stent thrombosis after the premature cessation of clopidogrel is relatively low but stent thrombosis may be catastrophic. Elective surgery should be postponed whenever possible until the minimum period of therapy with the thienopyridines is completed. Issues related to reinstitution of clopidogrel are discussed separately. (See "Coronary artery stent thrombosis: Prevention and management", section on 'Early noncardiac surgery or gastrointestinal endoscopy'.)

- **Continue/discontinue** — There are no data on the safety of dipyridamole if continued in the perioperative period. Like aspirin, factors to consider in deciding whether to continue or hold dipyridamole reflect a balance between the risk of bleeding and risk of ischemic events. If discontinued, the drug should be stopped at least two days before surgery. Aggrenox (combination aspirin and dipyridamole) should be discontinued seven to ten days before surgery.
Many patients take both aspirin and thienopyridine therapy to prevent coronary stent thrombosis. Premature cessation of thienopyridine therapy is associated with an increased risk for stent thrombosis. Except for emergent settings, we recommend that surgery be delayed and therapy with thienopyridine and aspirin be continued for at least the minimum recommended duration for each stent type (one month for bare metal stents and ideally up to 12 months for drug eluting stents).

If surgery must be performed before these minimum time periods, it is best to consult with the treating cardiologist and surgeon. If the risk of major bleeding appears greater than the risk of stent thrombosis, thienopyridine therapy should be discontinued for as brief a period as possible. Clopidogrel should be discontinued at least five, and prasugrel at least seven, days before surgery [79]. Some experts recommend stopping 10 days before surgery. They should be resumed as early as possible in the postoperative period. In this setting, we suggest that surgery be performed in centers with 24 hour interventional cardiology coverage. Aspirin should be continued during this period if at all possible.

**Nonsteroidal antiinflammatory drugs**

- **Benefit/risk** — The antiplatelet effects of nonsteroidal antiinflammatory drugs (NSAIDs) are due to reversible inhibition of COX-1, an isoform of cyclooxygenase, leading to decreased production of thromboxane A2 (TxA2). TxA2 is released by platelets in response to a number of agonists, leading to platelet aggregation. (See "Nonselective NSAIDs: Overview of adverse effects", section on 'Antiplatelet effects'.) These antiplatelet effects increase the bleeding risk perioperatively but, like aspirin, may reduce the risk of perioperative vascular events [83].

  The selective COX-2 inhibitors, such as celecoxib, have minimal effects on platelet function, although the potential for renal toxicity remains. At least some selective COX-2 inhibitors appear to have deleterious cardiovascular effects. (See "Overview of selective COX-2 inhibitors" and "COX-2 selective inhibitors: Adverse cardiovascular effects".)

  Non acetylated nonsteroidals, such as salsalate, do not have an antiplatelet effect.

- **Continue/discontinue** — On balance, we recommend discontinuing NSAIDs, including selective COX-2 inhibitors, prior to surgery. For patients whose pain is dramatically responsive to COX-2 inhibitors, consideration may be given to continuing these agents since they have minimal effects on platelet function.

  The duration of cyclooxygenase inhibition varies by agent and correlates poorly with the elimination half-life. In healthy individuals receiving ibuprofen for one week, platelet function appears to return to normal within 24 hours after the last dose [84]. For most NSAIDs, platelet function normalizes within three days of discontinuation, suggesting that NSAIDs should be discontinued at least three days before surgery; ibuprofen can be stopped 24 hours prior to surgery.

  Nonacetylated NSAIDs can be continued in the perioperative period, and may be considered as alternatives to other NSAIDs for pain control.

**Warfarin** — The perioperative management of patients taking warfarin is discussed separately. (See "Management of anticoagulation before and after elective surgery".)

**MEDICATIONS AFFECTING RENAL FUNCTION** — Several medications used during the perioperative period may lead to acute kidney injury, including nonsteroidal antiinflammatory drugs,
ACE inhibitors, angiotensin II receptor blockers, diuretics, antibiotics (eg, aminoglycosides, penicillins), and intravenous contrast agents [85]. The benefits and risks vary based on each drug. (See 'ACE inhibitors and angiotensin II receptor blockers' above and 'Diuretics' above and 'Nonsteroidal antiinflammatory drugs' above and "Aminoglycosides", section on 'Nephrotoxicity' and "Overview of the beta-lactam antibiotics", section on 'Renal reactions' and "Prevention of contrast-induced nephropathy".)

Optimizing volume status and medications to prevent acute tubular necrosis are discussed elsewhere. (See "Possible prevention and therapy of postischemic acute tubular necrosis", section on 'Prevention'.)

PSYCHOTROPIC AGENTS — The perioperative management of patients taking psychotropic agents varies with the class of drugs used (table 6A-B). Evidence-based guidelines for these drugs are lacking; data are primarily derived from case reports and open trials [86].

Tricyclic antidepressants

- **Benefit/risk** — Tricyclic antidepressants inhibit the uptake of norepinephrine and serotonin at the synaptic cleft. These agents may increase the risk for arrhythmias in combination with some volatile anesthetics or sympathomimetic agents. Abrupt withdrawal of tricyclic antidepressants can lead to insomnia, nausea, headache, increased salivation, and sweating [87]. (See "Tricyclic and tetracyclic drugs for treating depressed adults".)

- **Continue/discontinue** — There is little primary literature on perioperative management of tricyclic agents. Recommendations in textbooks and reviews vary; most recommend continuing these agents in the perioperative period [2].

  We recommend continuation of tricyclic agents throughout the perioperative period, in particular for patients on high doses. For patients on low doses or in whom the risk of perioperative arrhythmia is increased, the agents should be discontinued seven days before surgery.

- **Formulations/alternatives** — No parenteral substitution is available.

Serotonin reuptake inhibitors

- **Benefit/risk** — SSRIs may increase the need for transfusion with surgery, perhaps because of their effects on platelet aggregation. (See "Selective serotonin reuptake inhibitors (SSRIs) for treating depressed adults", section on 'Bleeding'.)

  Stopping SSRIs could lead to exacerbation of mood and other disorders. The wash out period for SSRIs may be as long as three weeks, and reinitiation may not lead to clinical benefit for several weeks.

- **Continue/discontinue** — The decision to withhold SSRIs perioperatively should balance the consequences of bleeding with the severity of the underlying psychologic disorder. Patients undergoing surgical procedures in which postoperative bleeding could lead to significant morbidity (such as central nervous system procedures) should have SSRIs discontinued several weeks prior to surgery. Patients with severe mood disorders should generally be maintained on SSRIs through surgery.

  Consultation with a psychiatrist is recommended to consider alternative therapies during the perioperative period for the rare patient with a severe mood disorder who is undergoing a
procedure in which bleeding could lead to significant morbidity.

**Monoamine oxidase inhibitors**

- **Benefit/risk** — Monoamine oxidase (MAO) inhibitors require special attention preoperatively. These drugs are prescribed far less commonly than other antidepressants, but are used in patients with refractory mood disorders in whom withdrawal and recurrent depression may be problematic. MAO inhibitors are also used for treatment of conditions other than depression (table 7).

Use of MAO inhibitors results in accumulation of biogenic amines in central and autonomic system neurons. Concomitant administration of sympathomimetic agents, like ephedrine during anesthesia, can result in massive release of stored norepinephrine and severe hypertension. Administration of dextromethorphan and meperidine with MAO inhibitors can cause the serotonin syndrome (agitation, headache, fever, seizures, with possibility of coma and death) [88]. (See "Serotonin syndrome".)

A designated MAO-safe anesthetic technique is used in patients requiring emergency procedures [89]. This involves avoidance of meperidine and use of only direct acting sympathomimetic agents such as isoprenaline and phenylephrine.

- **Continue/discontinue** — The decision to continue or withhold MAO inhibitors before surgery requires close collaboration with the anesthesiologist and psychiatrist.

MAO inhibitors generally should be continued when two criteria are met: 1) the anesthesiologist is comfortable with use of MAO safe procedures; and 2) the psychiatrist believes temporary withdrawal of the agent will exacerbate or precipitate a mood disorder.

In the absence of either criteria, we recommend discontinuing MAO inhibitors before surgery. Many MAO inhibitors are irreversible antagonists, and recovery of MAO function requires two weeks after discontinuation of the drug. Thus, patients should discontinue MAO inhibitors two weeks before elective surgery.

If MAO inhibitors are continued perioperatively, the patient must be prescribed a diet that excludes foods containing high amounts of tyramine while an inpatient. Intra- and perioperative drug interactions must be closely monitored.

**Mood stabilizing agents**

- **Benefit/risk** — Lithium has a number of physiologic effects that may be important perioperatively. Lithium decreases release of neurotransmitters and may prolong the effect of muscle relaxants. Chronic lithium use has a multitude of effects on the thyroid. (See "Lithium and the thyroid".)

Nephrogenic diabetes insipidus has been described in up to 20 percent of patients taking lithium. Patients who have impaired renal concentrating ability maintain euvoolemia and a normal serum sodium through polydipsia. Access to free water may be impaired during the perioperative period and lead to volume depletion and hyponatremia. (See "Renal toxicity of lithium".)

Valproic acid is another mood stabilizer increasingly used in patients with bipolar disorder. There are no reports demonstrating problems in patients continuing valproic acid
perioperatively.

- **Continue/discontinue** — We recommend continuation of lithium perioperatively with increased attention to fluid and electrolyte monitoring and a low threshold to check thyroid function tests before surgery.

We recommend that valproic acid be continued.

Serum levels of lithium and valproate should be monitored regularly.

- **Formulations/alternatives** — Lithium must be held in patients who cannot take oral medications since no parenteral substitution is available. Valproate sodium is available as a parenteral form.

Antipsychotics

- **Benefit/risk** — Antipsychotics are effective in controlling psychoses that may become problematic perioperatively in patients with underlying psychiatric illness. However, findings from a large observational study indicate that use of antipsychotics, both typical and atypical, is associated with an increased risk for sudden death [90]. Both typical and atypical antipsychotics may prolong the QT interval and cause arrhythmia, particularly when coadministered with volatile anesthetic agents or drugs such as erythromycin, quinolones, amiodarone, and sotalol. (See "First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects" and "Second-generation antipsychotic medications: Pharmacology, administration, and comparative side effects" and "Acquired long QT syndrome").

In a randomized trial of 495 patients at risk for delirium undergoing joint replacement surgery, olanzapine versus placebo was administered to prevent delirium [91]. The incidence of delirium decreased from 40 to 1 percent, although those who experienced delirium in the olanzapine group had more severe and longer-lasting delirium. Resource use during hospitalization (sitters, consultations) did not decrease. More patients in the olanzapine arm were discharged to home versus rehabilitation facilities. Further studies are needed prior to widespread use of perioperative antipsychotics for delirium prevention.

- **Continue/discontinue** — Antipsychotics should be used cautiously in patients at risk for exacerbation of psychoses. These agents should be withheld in patients whose baseline or follow-up ECG demonstrates prolongation of the QT interval. Shorter acting and low dose antipsychotics should be considered and complete discontinuation may be preferable after consultation with a psychiatrist.

For all patients receiving antipsychotic medication, caution should be used in selection of antibiotics and other medications to avoid drug interactions.

- **Formulations/alternatives** — Several parenteral antipsychotics are available, including haloperidol, aripiprazole, chlorpromazine, olanzapine, and ziprasidone. If a prolonged period of bowel rest is anticipated in a patient with a difficult to control psychosis, the long acting parenteral form of haloperidol (haldol decanoate) or risperidone can be started well before surgery, in consultation with a psychopharmacologist.

Antianxiety agents
• **Benefit/risk** — Abrupt withdrawal of chronic benzodiazepines can lead to an excitatory state with hypertension, agitation, delirium, and seizures. Many of these agents have active metabolites, and withdrawal can occur several days to weeks after discontinuation.

Benzodiazepines are commonly used short-term to relieve preoperative anxiety and are generally safe, with proper monitoring, in the perioperative period.

There are no data regarding the safety of buspirone in the perioperative period.

• **Continue/discontinue** — We recommend that benzodiazepines or buspirone used chronically for antianxiety or sedative effects be continued perioperatively.

• **Formulations/alternatives** — Parenteral forms of benzodiazepines are available, including diazepam and lorazepam. Buspirone is only available in oral formulation; parenteral benzodiazepines can be substituted if the patient cannot take oral medications and anxiety is a significant problem. Intravenous administration can cause blood pressure lability.

**Psychostimulants** — Psychostimulant medications, used in the treatment of attention deficit hyperactivity disorder, may increase risk for hypertension and arrhythmias, lower the seizure threshold, and interact with medications that could be needed in the perioperative period (eg, vasopressors). There is a risk of sudden blood pressure increase when halogenated anesthetics are used in conjunction with methylphenidate, and, per drug labeling, the stimulant should be withheld on the day of surgery.

A case series report of eight patients found no adverse effects when amphetamines were continued on the day of surgery [92]. However, none of the patients required vasopressor support.

• **Benefit/risk** — Psychostimulants are not associated with adverse effects when discontinued in the non-abusing patient. Patients generally do not need to be concerned about alertness on the day of surgery.

• **Continue/discontinue** — Data are limited but risks are low of temporarily discontinuing psychostimulant medications. We recommend they be withheld on the day of surgery and resumed when the patient is stable.

**CHRONIC OPIOID THERAPY**

• **Benefit/risk** — Abrupt discontinuation of chronic opioid use may result in withdrawal symptoms including abdominal cramps, nausea, vomiting, diarrhea, insomnia, anxiety, irritability, temperature instability, diaphoresis, and salivation.

• **Continue/discontinue** — Patients taking long term opioids for the management of chronic pain need to continue these agents around the time of surgery (table 8). Special consideration needs to be given to patients who are chronically maintained on methadone or buprenorphine for opioid addiction. (See "Treatment of opioid use and dependence", section on 'Hospitalization'.)

• **Formulations/alternatives** — For patients unable to take oral medications, rectal, transmucosal, transdermal, and parenteral forms are available. (See "Overview of the treatment of chronic pain"). In general, parenteral doses equivalent to oral doses should be used (table 9), although higher doses may temporarily be required because of pain related to
the surgical procedure.

NEUROLOGIC AGENTS — The majority of drugs taken by patients with neurologic disease around the time of surgery are discussed in detail separately. (See "Perioperative care of the surgical patient with neurologic disease".) A brief summary of recommendations is found in a table (table 10).

Antiepileptic drugs

- **Benefit/risk** — There are little data to guide the clinician regarding the perioperative management of antiepileptic drug therapy. Major motor seizures that occur during a surgical procedure can increase morbidity and mortality.

- **Continue/discontinue** — Anticonvulsant medications generally need to be continued perioperatively in most patients with known seizure disorders. Drug maintenance is not as vital for patients with pure absence seizures, which pose little threat perioperatively. (See "Perioperative care of the surgical patient with neurologic disease".)

For patients who will be unable to tolerate oral medications only temporarily (one or two days), and in whom generalized seizures are infrequent, it is reasonable to withhold the antiepileptic agent and resume it when oral administration is feasible, since the half-life of most of these agents is long.

- **Formulations/alternatives** — Options are available for patients who require antiepileptic drugs perioperatively and cannot take oral medications. Phenytoin, valproate, levetiracetam, and phenobarbital are available parenterally. (See "Pharmacology of antiepileptic drugs".) There are no parenteral forms of carbamazepine, ethosuximide, gabapentin, topiramate, or lamotrigine.

Phenytoin has a narrow therapeutic range, and serum drug levels should be checked preoperatively. When parenteral administration is considered, dosing should be individualized; a pharmacokinetic consultation is helpful, when available.

Suspensions of carbamazepine and valproic acid can be administered via nasogastric tube, and valproic acid syrup can be given rectally.

Topiramate can cause anion gap acidosis and dose reduction should be considered in the postoperative period.

Antiparkinson agents

- **Benefit/risk** — Patients with Parkinson disease present several challenges related to medications in the perioperative period. The effect of anti-Parkinson drugs on dopamine increases the potential for perioperative hemodynamic and arrhythmogenic complications. However, abrupt withdrawal of anti-Parkinson drugs may lead to flares of Parkinson symptoms and the neuroleptic malignant syndrome [93-95]. (See "Neuroleptic malignant syndrome".)

- **Continue/discontinue** — It is recommended that dopaminergic drugs be tapered to the lowest possible dose at least two weeks prior to surgery and restarted at this dose as soon as possible following surgery. This reduces the risk of the neuroleptic malignant syndrome with medication withdrawal, while still controlling symptoms.

**Carbidopa-levodopa** has a short duration of action (three to four hours) and can be given the
night before surgery. Dopamine agonists have a longer half-life and should be discontinued the evening before surgery to avoid hypotension in the perioperative period. (See "Perioperative care of the surgical patient with neurologic disease").

- **Formulations/alternatives** — Parenteral anticholinergic drugs can be used in patients who are unable to take oral medication, but should be used in as low a dose as possible as they may precipitate an acute confusional state, especially in the elderly.

### RHEUMATOLOGIC AGENTS

#### Rheumatoid arthritis drugs

- **Benefit/risk** — Agents used in managing rheumatoid arthritis can be divided into three main categories: NSAIDs, glucocorticoids, and disease modifying antirheumatic drugs (DMARDs). The first two are discussed above. (See 'Nonsteroidal antiinflammatory drugs' above and 'Glucocorticoids' above.)

DMARDs include traditional agents such as methotrexate, hydroxychloroquine, sulfasalazine, azathioprine, and leflunomide, as well as biologic response modifiers that inhibit tumor necrosis factor and interleukin-I (etanercept, infliximab, adalimumab, anakinra, and rituximab).

A randomized trial in orthopedic patients found the rate of infection was not increased in patients who continued weekly methotrexate, compared with discontinuing methotrexate two weeks before surgery [96]. Data regarding other DMARDs in the perioperative period are not available [97,98]. Many DMARDs are renally excreted, and impaired kidney function can lead to accumulation of DMARDs or their metabolites with consequent bone marrow suppression.

- **Continue/discontinue** — We recommend that methotrexate be continued in the perioperative period in patients with normal renal function and should be held for two weeks preoperatively in patients with renal impairment. Sulfasalazine and azathioprine should be held for a week prior to surgery and resumed after surgery. The long half life of leflunomide argues for discontinuation, if at all, two months before surgery; given the lack of known increased risk associated with this drug, it is reasonable to continue the drug up to surgery. Hydroxychloroquine has few potential side effects and can be continued without interruption, if the patient can take oral medications. The biologic response modifiers should be stopped one to several weeks prior to surgery and resumed once the wound is fully closed.

### Gout therapy

- **Benefit/risk** — Surgery is known to precipitate acute gouty arthropathy [99]. The optimal management strategy for patients who are maintained on chronic hypouricemic therapy or colchicine in the perioperative period is unknown.

- **Continue/discontinue** — We recommend that colchicine and the hypouricemic agents allopurinol and probenecid be held on the morning of surgery and resumed when the patient is able to tolerate oral medications (table 9).

- **Formulations/alternatives** — There is no parenteral substitution for allopurinol or probenecid. Parenteral colchicine is no longer available in the United States; it can cause myelotoxicity, as well as significant skin necrosis if infiltration occurs [100].

Should an acute gouty flare occur in a postoperative patient unable to tolerate oral
medications, parenteral ketorolac [101], intraarticular steroids, or systemic steroids can be used. (See "Treatment of acute gout").

MEDICATIONS FOR BENIGN PROSTATIC HYPERTROPHY

- **Benefit/risk** — Some patients treated with alpha-1-antagonists (eg, terazosin, doxazosin, tamsulosin, alfuzosin) have developed intraoperative floppy iris syndrome (IFIS), a condition involving intractable intraoperative iris prolapse with cataract surgery [102-104].

- **Continue/discontinue** — Patients should be asked about use of alpha-1-antagonists during the preoperative evaluation. It is not known if discontinuing alpha-1-antagonists reduces the risk of IFIS; clinical impression is that the drug effect is long-lasting (weeks, months, or years), and most eye surgeons do not insist that these agents be discontinued. Various operative regimens can reduce the occurrence of IFIS. It is important to make sure the surgeon is aware if the patient was receiving such a medication. (See "Cataract in adults").

HERBAL MEDICATIONS — Herbal medications, used frequently, may have effects that could be deleterious in the perioperative period, including clotting abnormalities and interactions with anesthetics [105]. Clinicians should specifically inquire about herbal medication use in presurgical patients, as patients often do not readily disclose use.

A review that examined eight commonly used herbal remedies found the following [106]:

- Ephedra (ma huang) may increase the risk of heart attack and stroke and should be discontinued at least 24 hours prior to surgery.

- Garlic may increase bleeding risk and should be discontinued at least seven days prior to surgery.

- Ginkgo may increase bleeding risk and should be discontinued at least 36 hours prior to surgery.

- Ginseng lowers blood sugar and may increase bleeding risk and should be discontinued at least seven days prior to surgery.

- Kava may increase the sedative effect of anesthetics and should be discontinued at least 24 hours prior to surgery. An association between kava use and fatal hepatotoxicity has been reported. (See "Hepatotoxicity due to herbal medications and dietary supplements").

- St. John's wort may diminish the effects of several drugs by induction of cytochrome p450 enzymes and should be discontinued at least five days prior to surgery.

- Valerian may increase the sedative effect of anesthetics and is associated with benzodiazepine-like withdrawal. There are no data on preoperative discontinuation. Ideally it is tapered weeks before surgery; if not, withdrawal is treated with benzodiazepines.

- Echinacea is associated with allergic reactions and immune stimulation. There are no data on preoperative discontinuation.

- Risk/Benefit - There is no evidence that herbal medications improve surgical outcomes, and there are theoretic reasons that these agents may increase perioperative morbidity.

- **Continue/discontinue** - For simplicity and because the purity and nature of some herbal medications is unclear, we recommend stopping herbal agents at least one week before surgery.

ANTIRETROVIRAL AGENTS — The perioperative management of patients taking antiretroviral
agents is discussed separately. (see "Surgical issues in HIV infection").

**RECOMMENDATIONS** — General recommendations for the management of several medications are found in the following tables:

- Cardiovascular agents ([table 1](#))
- Gastrointestinal and pulmonary agents ([table 2](#))
- Endocrine agents ([table 3](#))
- Agents affecting hemostasis ([table 5](#))
- Psychotropic agents ([table 6A-B](#))
- Opioids ([table 9](#))
- Neurologic agents ([table 10](#))
- Rheumatologic agents ([table 11](#))

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<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blockers</td>
<td>Abrupt withdrawal can result in hypertension, tachycardia and myocardial ischemia. Perioperative initiation can prevent postoperative myocardial ischemic events in patients with significantly increased cardiac risk, but may increase risk for stroke; perioperative initiation of beta blockers is not recommended for other patient populations.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Substitute IV propranolol, metoprolol or labetalol during NPO state.</td>
</tr>
<tr>
<td>Alpha 2 agonists</td>
<td>Withdrawal can cause extreme hypertension and myocardial ischemia</td>
<td>Continue therapy up to and including day of surgery</td>
<td>Continue therapy up to and including day of surgery. Substitute transdermal clonidine or rarely IV methyl dopa.</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Conflicting evidence on whether there is an increased risk of bleeding</td>
<td>Continue therapy up to and including day of surgery</td>
<td>Continue therapy up to and including day of surgery. No IV substitution necessary unless poor hemodynamics (hypertension or arrhythmia).</td>
</tr>
<tr>
<td>Ace inhibitors and angiotensin receptor blockers</td>
<td>Continuation can result in hypotension.</td>
<td>Continue therapy up to and including day of surgery if using for hypertension. Discontinue on day of surgery if using for HF and baseline blood pressure is low.</td>
<td>Continue therapy up to and including day of surgery if using for hypertension. Discontinue on day of surgery if using for HF and baseline blood pressure is low. Use parenteral enalaprilat as needed in postoperative period.</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Continuation can result in hypovolemia and hypotension.</td>
<td>Continue therapy up to day of surgery but discontinue morning dose.</td>
<td>Continue therapy up to day of surgery but discontinue morning dose. Use parenteral forms as needed in postoperative period.</td>
</tr>
<tr>
<td>Statins</td>
<td>Continuation may elevate risk of myopathy, but provides cardiovascular</td>
<td>Continue statins.</td>
<td>Continue statins up to and including day of surgery.</td>
</tr>
<tr>
<td>Non-statin lipid-lowering agents</td>
<td>Niacin and fibric acid derivatives may cause rhabdomyolysis. Bile acid sequestrants interfere with absorption of other medications.</td>
<td>Discontinue day before surgery.</td>
<td>Discontinue day before surgery. Resume with oral intake.</td>
</tr>
<tr>
<td>Name or class of drug</td>
<td>Clinical considerations</td>
<td>Recommended strategy for surgery with brief NPO state</td>
<td>Recommended strategy for surgery with prolonged NPO state</td>
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<tr>
<td>H2 blockers</td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Substitute IV forms available for prolonged postoperative NPO state.</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Substitute IV H2 blockers for prolonged postoperative NPO state.</td>
</tr>
<tr>
<td>Inhaled bronchodilators (beta agonists and anticholinergics)</td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Use nebulized forms if patient unable to comply with inhalation maneuver.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>No known adverse effects but very narrow range between therapeutic and toxic level.</td>
<td>Continue up to day before surgery. Discontinue the evening before surgery</td>
<td>Continue up to day before surgery. Discontinue the evening before surgery. Resume with PO intake. Use nebulized or inhaled beta agonist or anticholinergics</td>
</tr>
<tr>
<td>Leukotriene inhibitors</td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery and resume when patient able to take oral medications.</td>
</tr>
<tr>
<td>Name or class of drug</td>
<td>Clinical considerations</td>
<td>Recommended strategy for surgery with brief NPO state</td>
<td>Recommended strategy for surgery with prolonged NPO state</td>
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<tr>
<td>Oral contraceptives</td>
<td>Continuation may increase risk of venous thromboembolism. Stopping can result in unwanted pregnancies.</td>
<td>Continue up to and including the day of surgery for procedures with low to moderate risk of venous thromboembolism. Stop 4-6 weeks before surgery for procedures with high risk for thromboembolism. Instruct on alternate forms of contraception and obtain serum pregnancy test immediately before surgery.</td>
<td>Continue up to and including the day of surgery for procedures with low to moderate risk of venous thromboembolism. Stop 4-6 weeks before surgery for procedures with high risk for thromboembolism. Instruct on alternate forms of contraception and obtain serum pregnancy test immediately before surgery.</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>Continuation may increase risk of venous thromboembolism.</td>
<td>Continue up to and including the day of surgery for procedures with low to moderate risk of venous thromboembolism. Stop 4-6 weeks before surgery for procedures with high risk for thromboembolism.</td>
<td>Continue up to and including the day of surgery for procedures with low to moderate risk of venous thromboembolism. Stop 4-6 weeks before surgery for procedures with high risk for thromboembolism. Resume when tolerating oral medications.</td>
</tr>
<tr>
<td>Selective estrogen receptor modulators</td>
<td>Continuation may increase risk of venous thromboembolism.</td>
<td>Continue for surgeries with low risk of venous thromboembolism, and discontinue for surgeries with moderate to high risk for venous thromboembolism. When stopped should be stopped at least 4-6 weeks prior to surgery. When SERMs are used for breast cancer treatment consult oncologist.</td>
<td>Continue up to and including the day of surgery for procedures with low risk of venous thromboembolism. Stop 4-6 weeks before surgery for procedures with moderate to high risk for thromboembolism. Resume when tolerating oral medications When SERMs are used for breast cancer treatment consult oncologist.</td>
</tr>
<tr>
<td>Oral hypoglycemics and insulin</td>
<td>See &quot;Management of diabetes mellitus in the acute care setting&quot; topic</td>
<td></td>
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<tr>
<td>Glucocorticoids</td>
<td>See &quot;The surgical patient taking glucocorticoids&quot; topic</td>
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</table>
### Categories of risk for venous thromboembolism in surgical patients

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Description</th>
<th>DVT Risk</th>
<th>PE Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk:</strong></td>
<td>Minor surgery in patients &lt;40 years of age with no additional risk factors present*</td>
<td>Risk of calf DVT: 2 percent</td>
<td>Risk of fatal PE: &lt;0.01 percent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of proximal DVT: 0.4 percent</td>
<td>Risk of clinical PE: 0.2 percent</td>
</tr>
<tr>
<td><strong>Moderate risk:</strong></td>
<td>Surgery in patients with additional risk factor present*, or surgery in patients aged 40-60 with no additional risk factor</td>
<td>Risk of calf DVT: 10-20 percent</td>
<td>Risk of fatal PE: 0.1-0.4 percent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of proximal DVT: 2-4 percent</td>
<td>Risk of clinical PE: 1-2 percent</td>
</tr>
<tr>
<td><strong>High risk:</strong></td>
<td>Surgery in patients &gt;60, or surgery in patients aged 40-60 with additional risk factor*</td>
<td>Risk of calf DVT: 20-40 percent</td>
<td>Risk of fatal PE: 0.4-1.0 percent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of proximal DVT: 4-8 percent</td>
<td>Risk of clinical PE: 2-4 percent</td>
</tr>
<tr>
<td><strong>Highest risk:</strong></td>
<td>Surgery in patients &gt;40 with multiple risk factors*, or hip or knee arthroplasty, hip fracture surgery, or major trauma, spinal cord injury</td>
<td>Risk of calf DVT: 40-80 percent</td>
<td>Risk of fatal PE: 0.2-5 percent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of proximal DVT: 10-20 percent</td>
<td>Risk of clinical PE: 4-10 percent</td>
</tr>
</tbody>
</table>

DVT: deep vein thrombosis; PE: pulmonary embolism.
* Additional risk factors include one or more of the following: advanced age, cancer, prior venous thromboembolism, obesity, heart failure, paralysis, or presence of a molecular hypercoagulable state (e.g., protein C deficiency, factor V Leiden). *Data from Geerts, WH, et al. Chest 2004; 126:3385.*
## Perioperative management of agents affecting hemostasis

<table>
<thead>
<tr>
<th>Name or class of drug</th>
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<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin and dipyridamole</td>
<td>Continuation may cause perioperative hemorrhage. Discontinuation may increase the risk of vascular complications.</td>
<td>Continue for surgeries where patients are at high risk for perioperative vascular complications and morbidity related to perioperative hemorrhage is not significant. Discontinue for surgeries where perioperative bleeding could be catastrophic as in CNS surgery. If decision is made to stop, discontinue aspirin 7-10 days before surgery and discontinue dipyridamole at least 2 days before surgery.</td>
<td>Resume with oral intake.</td>
</tr>
<tr>
<td>Thienopyridines (clopidogrel, prasugrel, or ticlopidine)</td>
<td>When used after cardiac stenting procedure, if discontinued can cause cardiac ischemia perioperatively. If continued can result in bleeding complications.</td>
<td>Ideally elective procedures should be delayed until the mandatory period of platelet inhibition with these agents is completed. When used for long term stroke prophylaxis, should be discontinued 7-10 days.</td>
<td>Resume with oral intake.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>See &quot;Management of anticoagulation before and after elective surgery-I&quot;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic antidepressants</td>
<td>Continuation may increase the potential for arrythmias. Abrupt withdrawal can lead to insomnia, nausea, headache, increased salivation and increased sweating.</td>
<td>Continue therapy up to and including day of surgery for patients on high doses. Patients on low doses and in whom perioperative arrythmia is likely should discontinue for 7 days prior to surgery.</td>
<td>Resume with oral intake. No parenteral substitution available.</td>
</tr>
<tr>
<td>Serotonin reuptake inhibitors</td>
<td>Increased risk of bleeding.</td>
<td>Discontinue therapy 3 weeks prior to surgery in patients undergoing high risk procedures (such as certain CNS procedures).</td>
<td>Resume with oral intake. No parenteral substitution available.</td>
</tr>
<tr>
<td>Monoamine oxidase inhibitors</td>
<td>If continued, and direct acting sympathomimetic agents like ephedrine are used during anesthesia, can result in severe HTN. If agents like meperidine or dextromethorphan are used can result in &quot;serotonin syndrome&quot;.</td>
<td>For emergency procedures a MAO-safe anesthetic technique should be used. For other surgeries, anesthesiologist and psychiatrist should collaborate and decide either to use MAO-safe anesthetic technique or discontinue the medication. If discontinued should be stopped for 2 weeks prior to surgery.</td>
<td>Resume with oral intake. No parenteral substitution available.</td>
</tr>
<tr>
<td>Lithium</td>
<td>Continuation may prolong the effect of muscle relaxants and due to impaired renal concentrating ability can cause hypovolemia and hyponatremia.</td>
<td>Continue therapy up to and including day of surgery with close monitoring of electrolytes and volume status.</td>
<td>Resume with oral intake. No parenteral substitution available.</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>No known adverse effects</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Resume with oral intake. A parenteral formulation (valproate sodium) is available.</td>
</tr>
</tbody>
</table>
## Perioperative management of psychotropic agents part 2

<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsychotics</strong></td>
<td>Some agents are associated with QT prolongation, and occasionally cause hypotension or arrhythmias. No recent data available.</td>
<td>Continue therapy up to and including day of surgery in patients with high risk of developing psychoses.</td>
<td>Continue therapy up to and including day of surgery. Parenteral formulations are available for haloperidol, chlorpromazine, aripiprazole, olanzapine, and ziprasidone. If prolonged NPO state is anticipated, depot formulations (eg haloperidol decanoate) could be considered, to begin well before surgery in consultation with psychopharmacologist.</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Abrupt withdrawal can result in agitation, HTN, delirium and seizures.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Parenteral diazepam, lorazepam and chlordiazepoxide are available for prolonged NPO state.</td>
</tr>
<tr>
<td><strong>Buspirone</strong></td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. No parenteral substitution available but parenteral diazepam, lorazepam or chlordiazepoxide can be used for prolonged NPO state.</td>
</tr>
</tbody>
</table>
**Monoamine oxidase inhibitors**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furazolidone (Furoxone)*</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Isocarboxazid (Marplan)*</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>Linezolid (Zyvox)</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Moclobemide (Manerix)*</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>Pargyline (Eutonyl)*</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>Pergolide (Permax)*</td>
<td>Parkinson disease</td>
</tr>
<tr>
<td>Phenelzine (Nardil)*</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>Procarbazine (Matulane)</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Rasagiline (Azilect)</td>
<td>Parkinson disease</td>
</tr>
<tr>
<td>Selegiline (Eldepryl)</td>
<td>Parkinson disease</td>
</tr>
<tr>
<td>Selegiline transdermal patch (Emsam)</td>
<td>Parkinson disease</td>
</tr>
<tr>
<td>Tranylcypromine (Parnate)*</td>
<td>Antidepressant</td>
</tr>
</tbody>
</table>

* Not available in US.
• Potent non-selective monoamine oxidase inhibitor requiring vigilant food and drug interaction monitoring or preferably discontinuation 2-3 weeks pre-operatively.
### Selected opioid analgesics for pain

<table>
<thead>
<tr>
<th>Drug (US trade names)</th>
<th>Equianalgesic (mg) doses*</th>
<th>Sample initial dose for opioid naïve adult* (mg)</th>
<th>Half-life (in hours)</th>
<th>Duration of analgesic effect (in hours)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10 IV/SQ/IMΔ</td>
<td>2-10 IV every 2 to 4 hours</td>
<td>2-3</td>
<td>3-4</td>
<td>Standard for comparison for opioids; multiple routes available (including tablet, rectal suppository, concentrated enteral liquid, parenteral infusion).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-10 SQ/IM every 3 to 4 hours</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>20-30 PO</td>
<td>10-30 PO every 4 hours</td>
<td>2-3</td>
<td>3-6</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Controlled-release morphine tablet (MS Contin®, Oramorph SR®)</td>
<td>◊</td>
<td>15 PO twice daily</td>
<td></td>
<td>8-12</td>
<td></td>
</tr>
<tr>
<td>Sustained-release morphine capsule (Kadian®)</td>
<td>◊</td>
<td>30 PO daily in one or two divided doses</td>
<td></td>
<td>12-24</td>
<td></td>
</tr>
<tr>
<td>Extended-release morphine capsule (Avinza®)</td>
<td>◊</td>
<td>30 PO daily</td>
<td></td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 IV/SQ/IM</td>
<td>0.3-1 IV every 2 to 4 hours</td>
<td>2-3</td>
<td>3-4</td>
<td>High potency (nearly seven times more potent per mg than morphine) and solubility may be beneficial for patients requiring high opioid doses and for subcutaneous administration. Multiple routes available (including tablet, rectal suppository, enteral liquid, parenteral infusion).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.3-1 SQ/IM every 3 to 4 hours</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>7.5 PO</td>
<td>2-4 PO every 3 to 4 hours</td>
<td>2-3</td>
<td>3-6</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Controlled-release</td>
<td>◊</td>
<td>3 PO every 12 hours</td>
<td></td>
<td>12-24</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>Formulation</td>
<td>Dose/Route</td>
<td>Frequency</td>
<td>Duration</td>
<td></td>
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<tr>
<td>---------------------------</td>
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<td></td>
</tr>
<tr>
<td><strong>Hydromorphone</strong></td>
<td>Extended-release hydromorphone</td>
<td>8 PO every 24 hours</td>
<td></td>
<td>24</td>
<td></td>
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<tr>
<td></td>
<td>(Hydromorph Contin®)</td>
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<tr>
<td><strong>Codeine</strong></td>
<td></td>
<td>200 PO</td>
<td>30-60 PO every 4 to 6 hours</td>
<td>2-4</td>
<td>4-6</td>
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<td></td>
<td>Codeine is not recommended for chronic pain management because adverse effects increase disproportionately to analgesic effects, as dose is increased. Polymorphic metabolism, drug interactions and risk of accumulation are also disadvantages of codeine.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td></td>
<td>15-20 PO</td>
<td>5-15 PO every 4 to 6 hours</td>
<td>2-3</td>
<td>3-6</td>
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</tr>
<tr>
<td></td>
<td>Oxycontin®</td>
<td>10 PO</td>
<td>10 PO twice daily</td>
<td>8-12</td>
<td></td>
</tr>
<tr>
<td><strong>Hydrocodone</strong></td>
<td></td>
<td>30 PO</td>
<td>5-10 PO every 6 hours</td>
<td>3-4</td>
<td>4-8</td>
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</tr>
<tr>
<td><strong>Oxymorphone</strong></td>
<td>0.5 IV every 4 to 6 hours</td>
<td>0.5 IV</td>
<td>5 every 4-6 hours (variable effect)</td>
<td>7-9</td>
<td>3-6</td>
</tr>
<tr>
<td></td>
<td>0.5-1.5 SQ/IM every 4 to 6 hours</td>
<td>5-10 every 4 to 6 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 PR§§</td>
<td>5 every 4-6 hours (variable effect)</td>
<td>4-6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 PO</td>
<td></td>
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</tr>
<tr>
<td><strong>Extended-release</strong></td>
<td></td>
<td>5 twice daily</td>
<td></td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Dose Formulations</td>
<td>Dosage Information</td>
<td>Note</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------------------------</td>
<td>--------------------</td>
<td>----------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Levorphanol</strong></td>
<td><strong>2 IV/SQ/IM§</strong></td>
<td>0.5-1 IV every 3 to 6 hours</td>
<td>0.5-1 SQ/IM every 6 to 8 hours</td>
<td>With long half-life, accumulation possible after beginning or increasing dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>11-16 4-8</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td><strong>4 PO</strong></td>
<td>2-4 every 6 to 8 hours</td>
<td>11-16 4-8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td><strong>10 IV/SQ/IM¥‡</strong></td>
<td>1.25-5 IV/SQ/IM every 4 to 8 hours</td>
<td>3-4 (initially) 6-8</td>
<td>Potency of commercially available formulation (a d,l racemic mixture) is presumably due to the d-isomer, which is an NMDA antagonist and can reverse tolerance and augment analgesia. May be far more potent than indicated in the table. As total daily dose of morphine increases, the estimated equianalgesic dose of methadone decreases progressively. Effects may be further altered by drug interactions involving CYP3A4. Due to its highly variable and prolonged half-life, methadone has the highest risk among opioids of overdose and accumulation during initial titration to effect (as steady state levels are approached) and during dose adjustment in chronic use.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>20 PO¥‡</strong></td>
<td>2.5-10 PO every 4 to 8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td><strong>50-100 micrograms IV/SQ</strong></td>
<td>10-50 micrograms IV/SQ every 1 to 2 hours</td>
<td>0.5-1 IV† 1-2 SQ†</td>
<td>Can be administered as a continuous IV or SQ infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid Product</td>
<td>IM Route</td>
<td>2 hours</td>
<td>Increases following repeated administration</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------</td>
<td>--------------------------------</td>
<td>-----------------------------------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Fentanyl transdermal system</td>
<td>-</td>
<td>12 to 25 micrograms every 72 hours</td>
<td>20-27 upon removal</td>
<td>48-72 per patch</td>
<td>Refer to topic Fentanyl: Drug information for oral and transdermal medication equianalgesic dosing guidelines. Not usually recommended for opioid naïve patients in currently available doses. Not recommended for acute pain.</td>
</tr>
<tr>
<td>Oral transmucosal fentanyl citrate lozenge (ACTIQ®)</td>
<td>-</td>
<td>NR</td>
<td>3.5-6 dose dependent</td>
<td>1-2</td>
<td>Not recommended for opioid naïve patients. Recommended starting dose for breakthrough pain, 200-400 micrograms, even with high &quot;baseline&quot; opioid doses.</td>
</tr>
<tr>
<td>Fentanyl citrate sublingual tablet (Abstral®)</td>
<td>-</td>
<td>NR</td>
<td>7</td>
<td>1-2</td>
<td>Not recommended for opioid naïve patients. Recommended starting dose for breakthrough pain, 100 micrograms, even with high &quot;baseline&quot; opioid doses.</td>
</tr>
<tr>
<td>Fentanyl buccal tablet (Fentora®)</td>
<td>-</td>
<td>NR</td>
<td>3.5-11 dose dependent</td>
<td>1-2</td>
<td></td>
</tr>
</tbody>
</table>

NMDA: N-methyl-D-aspartic acid; PO: orally; IV: intravenously; SQ: subcutaneously; IM: intramuscularly; PR: per rectum.

NR: Preparation not recommended for initial treatment of opioid naïve patients. The total daily dose requirement for long-acting formulation should be established first with the use of an appropriate immediate-release opioid analgesic. See text.

* Equivalence to a 10 mg dose of parenteral morphine sulfate.

- Dose reduction of approximately fifty percent required for older or debilitated adults or patients with low cardiac output or respiratory compromise.

Δ IM route not preferred due to pain at injection site.

◊ Opioids such as morphine and hydromorphone have the same equianalgesic potency whether administered in an immediate-release or a sustained or extended release form. To convert from oral immediate release to extended release, use sum of doses of immediate release preparation administered during usual interval for the extended release form. For example, morphine sulfate immediate release 30 mg every four hours (180 mg daily) converts to morphine sulfate controlled release 60 mg every eight hours (180 mg daily).

§ Not presently available in US.

¥ Variable.

‡ These conversion rates, which differ from those available in other tables and references, represent the recommendations of an expert panel convened to evaluate equianalgesic dosing (Knotkova H. J Pain)
† Bolus administration to opioid naïve patients.
### Perioperative management of chronic pain medications

<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>Abrupt withdrawal can cause yawning, abdominal cramps, nausea, vomiting, diarrhea, insomnia, anxiety and salivation.</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Rectal, transmucosal, transdermal and parenteral preparations available.</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Seizures, drug interactions.</td>
<td>Substitute another analgesic.</td>
<td>Substitute another analgesic until oral intake.</td>
</tr>
</tbody>
</table>
### Perioperative management of neurologic agents

<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipileptics</td>
<td>No known adverse effects.</td>
<td>Continue therapy up to and including day of surgery. For well controlled seizures can resume with PO intake. Parenteral phenytoin or phenobarbital should be administered in patients with difficult to control seizures.</td>
<td>Continue therapy up to and including day of surgery. Parenteral phenytoin or phenobarbital should be administered. These could be substituted for other antiepileptics with no parenteral substitute.</td>
</tr>
<tr>
<td>Levodopa/Carbidopa</td>
<td>Metabolite of Levodopa, dopamine can cause arrhythmias, hypotension or hypertension</td>
<td>Continue therapy up to the night before surgery and hold it the day of surgery.</td>
<td>Continue therapy up to the night before surgery and hold it the day of surgery. Resume with oral intake as soon as possible.</td>
</tr>
<tr>
<td>Dopamine agonists</td>
<td>Directly stimulate dopamine receptors and can cause arrhythmias or hypotension.</td>
<td>Continue therapy up to the night of surgery and hold it for at least 12 hrs before surgery.</td>
<td>Continue therapy up to the night of surgery and hold it for at least 12 hrs before surgery. Resume with oral intake as soon as possible.</td>
</tr>
<tr>
<td>Selegiline (selective MAO inhibitor)</td>
<td>At usual doses for Parkinson disease does not induce hypertension when tyramine containing foods are ingested.</td>
<td>Hold the medication the evening before surgery.</td>
<td>Hold the medication the evening before surgery. Resume with oral intake.</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>Can cause muscarinic side effects.</td>
<td>Continue therapy up to the night of surgery. For patients taking long acting preparations substitute short-acting preparations the night before surgery. Restart at half the usual dose when hemodynamically stable.</td>
<td>Continue therapy up to the night of surgery. For patients taking long acting preparations substitute short-acting preparations the night before surgery. Restart when hemodynamically stable. Parenteral substitutions are available. For IM substitution give 1/10th the usual oral dose and for IV substitution give 1/30th the usual dose.</td>
</tr>
</tbody>
</table>
## Perioperative management of rheumatologic agents

<table>
<thead>
<tr>
<th>Name or class of drug</th>
<th>Clinical considerations</th>
<th>Recommended strategy for surgery with brief NPO state</th>
<th>Recommended strategy for surgery with prolonged NPO state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal antiinflammatory drugs</td>
<td>Continuation may cause perioperative hemorrhage.</td>
<td>Hold for 3 days prior to surgery.</td>
<td>Resume with oral intake.</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Potential risk of bone marrow suppression</td>
<td>Continue therapy up to and including day of surgery. In patients with renal insufficiency, hold two weeks prior to surgery.</td>
<td>Continue therapy up to and including day of surgery. Resume with oral intake.</td>
</tr>
<tr>
<td>Sulfasalazine and azathioprine</td>
<td>Potential risk of bone marrow suppression</td>
<td>Hold for one week prior to surgery.</td>
<td>Hold for one week prior to surgery and resume with oral intake.</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Potential risk of bone marrow suppression</td>
<td>Hold for two weeks prior to surgery</td>
<td>Hold for two weeks prior to surgery and resume with oral intake</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Low risk of side effects</td>
<td>Continue therapy up to and including day of surgery.</td>
<td>Continue therapy up to and including day of surgery. Resume with oral intake.</td>
</tr>
<tr>
<td>Biologic response modifiers (etanercept, infliximab, anakinra, rituximab, adalimumab)</td>
<td>Risk of infection</td>
<td>Hold for one to two weeks prior to surgery and resume one to two weeks after surgery.</td>
<td>Hold for one to two weeks prior to surgery and resume one to two weeks after surgery or with oral intake.</td>
</tr>
<tr>
<td>Agents used in gout (colchicine, allopurinol, probenecid)</td>
<td>Abrupt discontinuation of allopurinol and probenecid may precipitate attack of acute gout. Probenecid interacts with numerous perioperative medications.</td>
<td>Continue therapy up to the night of surgery and hold the morning dose.</td>
<td>Continue therapy up to the night of surgery and hold the morning dose. Resume with oral intake. Parenteral ketorolac, intraarticular and systemic steroids are available for acute gouty flares in postop period.</td>
</tr>
</tbody>
</table>