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Perioperative medication management

[Visala Muluk, MD](#)[David S Macpherson, MD, MPH](#)

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INTRODUCTION — Medical consultants, anesthesiologists, and surgeons 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 recommendations made by anesthesiologists when queried about management of common medications [1]. For this reason, the recommendations in this review are to a large degree expert opinion, based in part on information from other reviews [2,3] and textbooks, along with clinical experience and theoretic considerations.

In generating these recommendations, we have used the following principles:

- Medications associated with known medical morbidity if withdrawn abruptly should be continued in the perioperative period. Substitute intravenous, transdermal, or transmucosal medicines should be used if absorption of these medications will be impaired because of loss of gastrointestinal function.
- Medications thought to increase the risk of surgical complications and not essential for short-term improvement in quality of life should be held through the perioperative period.
- Medications not meeting either of the above principles can be discontinued or continued based on individual physician judgment. If continued, the managing physician should remember that many other medications are administered perioperatively during a relatively short period that may interact with chronic medications. Furthermore, the metabolism and elimination of chronic medications and their metabolites may be altered during the perioperative period.

Discussion of every possible medication is beyond the scope of this topic review; only medications known to have perioperative effects or those in common use are discussed. The principles outlined above can be used for guidance about medications not discussed here, as it is unlikely that specific clinical studies will be available to guide decision making.

CARDIOVASCULAR MEDICATIONS — ([show table 1](#))

Beta blockers — Beta blockers may have a number of beneficial effects when taken perioperatively. In general, beta blockers reduce ischemia by decreasing myocardial oxygen demand due to increased stress and catecholamine release in the perioperative period. Most studies have found that beta blockers reduce perioperative ischemia in patients with underlying vascular disease; a number of small, nonrandomized studies and randomized studies have also found that beta blockers reduce the risk of perioperative myocardial infarction and death [4-6]. (See "[Management of cardiac risk for noncardiac surgery](#)", section on Beta blockers).

These findings have led to the recommendation to begin beta blockers perioperatively in most patients at high risk for cardiovascular disease who are undergoing surgery. Many patients who are taking beta blockers chronically have cardiovascular risk factors and are therefore also likely to benefit from perioperative beta blockade.

Potential adverse effects of perioperative beta blockade include bradycardia and hypotension, although in general these have not diminished the positive effects associated with these drugs. On the other hand, acute withdrawal of a beta blocker preoperatively can lead to substantial morbidity and even mortality, as can withdrawal postoperatively [7]. (See "[Management of cardiac risk for noncardiac surgery](#)" and see "[Major side effects of beta blockers](#)", section on Beta blocker withdrawal).

Recommendations — 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. Intravenous forms of beta blockade, such as [atenolol](#), [metoprolol](#), [propranolol](#), [labetalol](#), and [esmolol](#) should be given if the patient cannot take oral medications [8,9]. We have a slight preference for beta 1 cardioselective beta blockers (eg, atenolol, metoprolol, esmolol) 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.

Centrally acting sympatholytics (alpha 2 agonists) — Administration of centrally acting sympatholytic drugs such as [clonidine](#) may improve outcomes perioperatively, although the data are less conclusive than with beta blockers [10-16]. Abrupt withdrawal of these agents can precipitate rebound hypertension, 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]. (See "[Withdrawal syndromes with antihypertensive therapy](#)").

Other potential benefits of continuing alpha 2 agonists perioperatively include [18,19]:

- Decrease in the stress response to endotracheal intubation and surgery.
- These drugs reduce anesthetic requirements and possess sedative/anxiolytic, analgesic, and antishivering properties [18,19].

Recommendations — 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.

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.

Other centrally acting sympatholytic agents such as [methyldopa](#) or [guanabenz](#) are rarely used today. Withdrawal from abrupt discontinuation of these agents has been reported but is less common because of their slower onset of action [20,21]. For patients unable to take oral medications perioperatively, we recommend withholding methyldopa and guanabenz and using other parenteral hypertensive agents if

hypertension becomes a problem [10]. An intravenous form of methyldopa is available in the rare cases in which abrupt stoppage appears to be leading to a withdrawal syndrome.

Calcium channel blockers — There are limited data 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 on continuous [diltiazem](#) infusions [22], but studies large enough to demonstrate improved outcomes have not been conducted.

There are no serious interactions between calcium channel blockers and anesthetic agents; thus, they are safely administered in the perioperative period [23]. 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 [24].

Concerns have been raised about a possible association between calcium channel blockers and an increased risk of bleeding [25]. A randomized trial in valvular surgery patients found that, compared with placebo, patients receiving [nimodipine](#) had increased bleeding [26,27]. There have been reports that patients receiving calcium channel blockers have a greater fall in hemoglobin levels after hip surgery [28], but other studies have not confirmed this finding [29]. Two large trials in cardiac surgery patients did not find any association between bleeding risk and use of calcium channel blockers [30].

Recommendations — There are little data regarding the optimal management of calcium channel blockers during the perioperative period, but these agents appear safe and may have a theoretic benefit [31]; data regarding bleeding risk are contradictory. Thus, we recommend that they be continued in patients who are already taking them preoperatively [31]. 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 [see "Management of cardiac risk for noncardiac surgery"](#)).

ACE inhibitors — The management of patients who are taking angiotensin converting enzyme (ACE) inhibitors preoperatively is controversial. 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 vascular surgery who were on long-term ACE inhibitor therapy were randomly assigned to ACE inhibitor continuation or withdrawal [32]. 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 in the incidence of hypertensive episodes was noted between the two groups.
- 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 [33]. Similar to the previous study, patients who omitted their ACE inhibitors required less vasopressors during surgery. However, unlike the previous report, these patients required more vasodilators to control hypertension in the early postoperative period. There did not appear to be a net benefit of discontinuing ACE inhibitors preoperatively.

Recommendations — These findings suggest that continuing ACE inhibitors up to the time of surgery results in an increased incidence of hypotension perioperatively, but possibly a reduced incidence of postoperative hypertension. While the data do not lead to clear recommendations, we recommend continuing ACE inhibitors in patients who are taking them for the management of hypertension. On the other hand, it is reasonable to withhold ACE inhibitors on the morning of surgery in patients who are taking them for heart failure, particularly if the baseline blood pressure is low, to avoid significant hypotension during the induction of anesthesia [3].

Angiotensin II receptor blockers — 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 [34].

Recommendations — Based upon limited data, we recommend discontinuing ARBs on the day of surgery and resuming them postoperatively as long as the patient is not hypotensive and has normal renal function.

Diuretics — The two major physiologic effects of diuretics that are concerning in the perioperative period are hypokalemia and hypovolemia:

- Although hypokalemia can theoretically increase the risk of perioperative arrhythmia, observational studies of patients in whom arrhythmia might be most likely, that is those with structural heart disease, have failed to find such a relationship [35,36]. Furthermore, since depletion of potassium stores takes several weeks, a single dose of a diuretic is unlikely to markedly affect serum potassium levels.
- Systemic vasodilatation induced by anesthetic agents may cause hypotension in patients who are intravascularly depleted from diuretics.

Recommendations — These considerations have led some to recommend discontinuing diuretics for 48 hours prior to elective surgery. However, this is not practical for all patients, and there is no consensus on this issue [1]. 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. Intravenous preparations are available if necessary and are commonly used. For patients who require diuretics perioperatively, physicians should remain alert to the potential perioperative risks and should pay close attention to volume and potassium replacement.

GASTROINTESTINAL AGENTS — There are several potential advantages of continuing H2 blockers or proton pump inhibitors perioperatively in patients on chronic therapy. The stress of surgery coupled with other conditions (eg, prolonged intensive care unit stay and mechanical ventilation) can significantly 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 have been shown to decrease gastric volume and raise gastric fluid pH, thereby reducing the risk of chemical pneumonitis from aspiration [37,38]. (See "[Aspiration pneumonia](#)", 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.

Recommendations — 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. 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 ([show table 2](#)).

PULMONARY AGENTS — ([show table 2](#))

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

[complications](#)").

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 compliance with inhalation technique is likely to be poor.

Theophylline — There are no data investigating whether continuation of [theophylline](#) in the perioperative period decreases pulmonary complications. Since other modalities are more proven for this purpose, and because theophylline has the potential to cause serious toxicity at a level only slightly higher than the therapeutic range, we recommend it be discontinued the evening before surgery. (See "[Strategies to reduce postoperative pulmonary complications](#)").

Corticosteroids — Chronic [corticosteroids](#) in patients with pulmonary disease should be continued during the perioperative period to maintain optimal lung function and also to minimize the risk of adrenal insufficiency. (See "[Strategies to reduce postoperative pulmonary complications](#)" and see "[The surgical patient taking glucocorticoids](#)").

Leukotriene inhibitors — The leukotriene inhibitors [zileuton](#) (Zyflo), [zafirlukast](#) (Accolate), and [montelukast](#) (Singulair) help maintain control of asthma but are not used for acute therapy. (See "[Agents affecting the 5-lipoxygenase pathway in the treatment of asthma](#)"). Although the elimination half-life of these agents is relatively short, their effect on asthma symptoms and pulmonary function continues for up to three weeks after cessation of treatment [39]. There is no evidence of a withdrawal syndrome from abrupt stoppage of these agents and no evidence of worsening asthma. In addition, we are aware of no evidence of harmful interactions of these drugs with anesthetics.

Thus, we recommend that leukotriene inhibitors be given on the morning of surgery and resumed when the patient is tolerating oral medications. No parenteral substitution is available nor necessary given their long duration of action.

ENDOCRINE AGENTS — ([show table 3](#))

Glucocorticoids — The management of patients taking [corticosteroids](#) preoperatively is discussed in detail separately. (See "[The surgical patient taking glucocorticoids](#)"). In general, patients who have taken any dose of 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 on their usual dose of glucocorticoids perioperatively. In contrast, HPA axis suppression should be assumed to be present in patients taking [prednisone](#) at a dose greater than 20 mg/day for three weeks or more, and in patients with a Cushingoid appearance; these individuals may need an increased dose of corticosteroids perioperatively.

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 — Oral contraceptives are the most important cause of thrombosis in young women because of their widespread use. The risk of thrombosis increases within four months of the initiation of therapy and is unaffected by duration; the risk decreases to previous levels within three months of stopping treatment. (See "[Overview of the causes of venous thrombosis](#)", section on Oral contraceptives). The risk of venous thrombosis associated with oral contraceptives becomes particularly important perioperatively since surgery itself is a risk factor for thrombosis.

Oral contraceptives with greater estrogen content (>50 mg) have a higher risk of thromboembolism compared to preparations with lower estrogen content (30 mg). Nevertheless, even the lower estrogen content pills are associated with an increased risk of thrombosis [40,41].

Recommendations — 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 surgical patients who are at low risk for venous thrombosis. (See ["Prevention of venous thromboembolic disease"](#) for definitions of low, moderate, and high risk patients and procedures). In general, oral contraceptives should be discontinued six weeks prior to surgery in moderate or high risk patients. Other forms of contraception must be used to prevent unwanted pregnancy during this time. Oral contraceptives can be continued in moderate to high risk women who are likely to 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 women who have stopped oral contraceptives preoperatively.

Hormone replacement therapy — Although the estrogen content of preparations used for postmenopausal hormone replacement therapy (HRT) is much lower than in oral contraceptive pills, use of HRT, with either estrogen alone or estrogen plus a progestin, still appears to increase the risk of venous thromboembolism [42,43]. A case-control study that looked at the development of thromboembolism after hip or knee arthroplasty did not find an increased risk in women receiving HRT (odds ratio 0.66, 95% CI 0.35-1.18); however, the results may have been confounded by women at lower risk for thromboembolism being more likely to be prescribed HRT [44].

Since the risks associated with temporary discontinuation of hormone replacement briefly are minimal, it is recommended that women undergoing procedures at moderate or high risk for venous thromboembolism stop hormone replacement at least four to six weeks prior to surgery and resume treatment postoperatively. These agents can be continued for surgical procedures associated with a low risk of venous thrombosis. (See ["Prevention of venous thromboembolic disease"](#) for definitions of low, moderate, and high risk patients and procedures).

Selective estrogen receptor modulators — The indications for use of selective estrogen receptor modulators (SERMs) such as [tamoxifen](#) and [raloxifene](#) have expanded beyond breast cancer treatment to breast cancer chemoprevention and, at least for raloxifene, the prevention and treatment of osteoporosis. (See ["Selective estrogen receptor modulators for the prevention of breast cancer"](#) and ["Use of selective estrogen receptor modulators in postmenopausal women"](#)). Both tamoxifen and raloxifene increase the risk of venous thromboembolism [45,46]. Since brief discontinuation of SERMs being used for breast cancer prevention or for osteoporosis is unlikely to result in harm, we recommend the agents be discontinued for four weeks before surgeries associated with a moderate or high risk of venous thromboembolism; the drugs can be continued for low risk surgeries. For patients on SERMs for breast cancer treatment, the decision is more difficult and consultation with an oncologist is recommended.

Hypolipidemic agents — [Niacin](#), fibric acid derivatives ([gemfibrozil](#)), and HMG CoA reductase inhibitors ("statins") are known to cause myopathy and rhabdomyolysis. The risk is higher when these agents are used in combination, and surgery may also increase the risk of myopathy [47-51]. The risk of myopathy appears to be lowest with [pravastatin](#) and perhaps [fluvastatin](#). (See ["Muscle injury associated with lipid lowering drugs"](#)).

Temporary discontinuation of [niacin](#) and fibric acid derivatives perioperatively is likely to be safe since these agents are given for the goal of long-term reduction in vascular morbidity. Furthermore, the manufacturers of [atorvastatin](#) and [pravastatin](#) recommend discontinuing these agents in the perioperative period due to the risk of myopathy.

On the other hand, evidence is emerging that HMG CoA reductase inhibitors (statins), which may prevent vascular events through mechanisms other than cholesterol lowering (eg, plaque stabilization, reduction in inflammation, decreased thrombogenesis), may be of benefit in the perioperative period, and that this benefit might be lost if statins are discontinued:

- A small trial randomly assigned 100 patients scheduled to undergo elective vascular surgery and not previously treated with lipid lowering therapy to receive [atorvastatin](#) 20 mg daily for 45 days or placebo, without regard to cholesterol level [52]. Surgery was scheduled to be performed during the 45-day period and no sooner than two weeks after initiation of atorvastatin or placebo. The primary outcome was a composite cardiovascular endpoint of cardiac death, nonfatal myocardial infarction, unstable angina, or stroke during six months of follow-up. The rate of such an event was lower in patients treated with atorvastatin (8 versus 26 percent).
- A retrospective cohort study based on hospital discharge and pharmacy records of 780,591 patients ages 18 and older who underwent major noncardiac surgery found that 9.9 percent of patients were treated with lipid lowering therapy (91 percent of whom received statins) within the first two hospital days [53]. Treatment with lipid lowering therapy in the first two hospital days was associated with lower crude mortality than in patients treated later or who did not receive lipid lowering therapy (2.13 versus 3.05 percent) and in a multivariate model the risk of mortality was lower among treated patients (odds ratio [OR] 0.62, 95 CI 0.58-0.67). Patients treated with nonstatin lipid lowering therapy had a smaller, but still significant, reduction in mortality (OR 0.81, CI 0.70-0.95).
- A case-control study of patients undergoing major vascular surgery found a 78 percent reduction in the risk of perioperative mortality in patients who were being treated with statins (although this study did not look at whether statins were continued up until surgery) [54].
- A study of experimental one-hour cerebral artery occlusion in mice found that treatment with atorvastatin for 14 days reduced stroke volume by 40 percent; however, this protective effect was reduced once atorvastatin had been stopped for two days and eliminated after four days [55]. (See "[Mechanisms of benefit of lipid lowering in patients with coronary heart disease](#)" and see "[Initial assessment and management of acute stroke](#)").

Although both the benefit and the risk of continuing these agents remains to be demonstrated in large randomized clinical trials, based on the current evidence we recommend continuing statin therapy in patients undergoing surgery, particularly in patients at high risk for cardiovascular events. We currently favor discontinuing [niacin](#) and fibric acid derivatives at least one day before surgery.

Other lipid lowering agents such as [cholestyramine](#) and [colestipol](#) interfere with bowel absorption. We also recommend that these agents be discontinued before surgery to ensure absorption of other drugs needed acutely in the perioperative period [48]. 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.

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 dose should be approximately 80 percent of the patient's usual oral dose, as about this fraction of oral T4 is absorbed.

MEDICATIONS AFFECTING HEMOSTASIS — Many patients undergoing surgery are taking chronic medications that are intended to impair coagulation, such as [warfarin](#) and [aspirin](#), or take medications for another indication that have an unintended effect on hemostasis, such as nonsteroidal antiinflammatory drugs (NSAIDs) ([show table 4](#)).

Aspirin — The optimal perioperative management of patients who are taking [aspirin](#) is uncertain, and significant practice variation exists [1]. Aspirin irreversibly inhibits platelet cyclooxygenase, which may increase intraoperative blood loss and hemorrhagic complications [56-61]. 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) [62,63]. A similar risk has been noted in patients undergoing surgery for peripheral vascular disease [64]. (See "[Medical therapy to prevent perioperative complications after coronary artery bypass graft surgery](#)", section on Aspirin).

In addition to these perioperative risks, 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 [65,66]. (See "[Benefits of aspirin in cardiovascular disease](#)" and see "[Secondary prevention of stroke: Risk factor reduction](#)", section on Aspirin)

In patients undergoing cataract surgery the risk of ocular hemorrhage in patients taking [aspirin](#) is extremely low and similar to that in patients not taking aspirin [67]. (See "[Cataract](#)", section on Aspirin and NSAIDs).

[Aspirin](#) also may prevent venous thromboembolism [68]. However, other agents are more effective [69]. (See "[Prevention of venous thromboembolic disease](#)", section on Aspirin).

Recommendations — These findings suggest that 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. As noted above, this would include patients undergoing CABG or peripheral vascular surgery [62-64]. The usual recommendation in patients undergoing elective CABG is to discontinue aspirin three to five days before surgery. However, with increasing experience, some surgeons recommend continuation of aspirin throughout the preoperative period. A 2004 ACC/AHA task force recommended that aspirin should not be withheld before either elective or nonelective CABG after ST elevation MI [70].

The Seventh ACCP Consensus Conference on Antithrombotic Therapy recommended [aspirin](#) (325 mg) be started six hours after surgery [71]. Among stable patients, benefit may be seen with aspirin started one hour after surgery [72,73].

- On the other hand, 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](#)", section on Aspirin and NSAIDs). If the decision is made to stop aspirin, 5 to 10 days is necessary for new platelets to be formed. Use of the bleeding time to assess the effect of aspirin or NSAIDs on bleeding risk has fallen out of favor because it is a poor predictor of perioperative hemorrhage [74]. (See "[Preoperative assessment of hemostasis](#)").

Other antiplatelet agents — [Dipyridamole](#) has both vasodilator and antiplatelet activity. With the publication of the ESPS-2 trial [75], its use has become more common in patients with past stroke or transient ischemic attack (TIA). (See "[Treatment for specific causes of ischemic stroke and transient ischemic attack](#)"). The half-life of the modified-release preparation is reported as 10 hours. There are no data as yet on its safety if continued in the perioperative period. Like [aspirin](#), the factors to consider in deciding whether to continue or hold this medication reflect a balance between the risk of bleeding and risk of ischemic events. If the drug is discontinued, it should be stopped at least two days before surgery.

The thienopyridines, [clopidogrel](#) and the less frequently used ticlopidine, are platelet inhibitors used most often in patients who have had previous cerebrovascular events, recent acute coronary syndromes, or recent percutaneous coronary interventions with stenting [76]. While the exact risk of coronary artery stent thrombosis after the premature cessation of clopidogrel is unknown, the occurrence of thrombosis may be catastrophic. Whenever possible, elective surgery should be postponed until the minimum period of therapy with the thienopyridines is completed. (See "[Coronary artery stent thrombosis](#)", section on

Summary and recommendations).

Patients who take these agents chronically, for reasons other than the prevention of coronary artery stent thrombosis, are at increased risk for acute cardiovascular events when [clopidogrel](#) or ticlodipine is discontinued. However, these medications should probably be discontinued before surgery, and resumed as early as possible in the postoperative period.

The discussion of the timing of discontinuation and reinstatement of [clopidogrel](#) is discussed separately. (See "[Coronary artery stent thrombosis](#)", section on Risk of early noncardiac surgery).

Nonsteroidal antiinflammatory drugs — NSAIDs are normally held before surgical procedures because of their antiplatelet effects. The antiplatelet effects 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, amplifying the platelet response and leading to aggregation. (See "[NSAIDs: Overview of adverse effects](#)", section on Antiplatelet effects). While these antiplatelet effects lead to an increase in bleeding risk perioperatively, these same effects, like [aspirin](#), may reduce the risk of perioperative vascular events [77].

The selective COX-2 inhibitors such as [celecoxib](#), along with the nonacetylated [aspirin](#) preparations ([salsalate](#)), 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 see "[COX-2 selective inhibitors: Adverse cardiovascular effects](#)").

On balance, we recommend discontinuing NSAIDs, including selective COX-2 inhibitors, prior to surgery. For patients with dramatically decreased pain on COX-2 inhibitors, the agents can be continued.

The duration of cyclooxygenase inhibition varies by agent and does not correlate well 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 [78]. For most NSAIDs, platelet function can be expected to normalize within three days of discontinuation, suggesting that NSAIDs be discontinued at least three days before surgery. [Aspirin](#) should be used if a cardioprotective effect through platelet inhibition is desired (see "[Aspirin](#)" above).

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

PSYCHOTROPIC AGENTS — The perioperative management of patients taking psychotropic agents varies with the class of drugs used ([show table 5](#))

Tricyclic antidepressants — Tricyclic antidepressants inhibit the uptake of [norepinephrine](#) and serotonin at the synaptic uptake. (See "[Antidepressant medication in adults: SSRIs and heterocyclics](#)"). These agents may increase the potential for arrhythmias in combination with some volatile anesthetics and when sympathomimetic agents are used. On the other hand, abrupt withdrawal of tricyclic antidepressants can lead to insomnia, nausea, headache, increased salivation, and increased sweating [79].

There is little primary literature on how best to manage tricyclic agents perioperatively. For this reason, textbooks and other reviews vary in their recommendations, although most recommend continuing these agents in the perioperative period [1]. 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 perioperative arrhythmia is believed likely, the agents should be discontinued seven days before surgery. No parenteral substitution is available.

Serotonin reuptake inhibitors — SSRIs may increase the need for transfusions with surgery, perhaps because of their effects on platelet aggregation. (See "[Antidepressant medication in adults: SSRIs and heterocyclics](#)", section on Bleeding). A retrospective study of 520 patients undergoing orthopedic surgery found that the risk for transfusion was increased in patients on serotonergic antidepressants (most of

which were SSRIs) (OR 3.71, 95% CI 1.35-10.18) but not in patients on nonserotonergic antidepressants (OR 0.74, 95% CI 0.10-5.95) [80].

As the wash out period for SSRIs may be as long as three weeks, and reinitiation may not lead to clinical benefit for several weeks, stopping SSRIs could lead to exacerbation of mood and other disorders. Thus, the decision to withhold SSRIs perioperatively should balance the consequences of bleeding with the severity of the psychologic disorder being treated. Patients undergoing surgical procedures in which postoperative bleeding could lead to significant morbidity (such as certain central nervous system procedures) should have SSRIs discontinued several weeks prior to surgery, while patients with severe mood disorders should generally be maintained on SSRIs through surgery. In the rare patient with a severe mood disorder who is undergoing a procedure in which bleeding could lead to significant morbidity, consultation with a psychiatrist is recommended to consider alternative therapies during the perioperative period.

Monoamine oxidase inhibitors — Of all the antidepressant classes, monoamine oxidase inhibitors (MAO) require special attention preoperatively. These drugs are prescribed much less commonly than other antidepressants, but are still recommended in patients with refractory mood disorders in whom withdrawal and recurrent depression may be problematic.

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. In addition, administration of [dextromethorphan](#) and [meperidine](#) with MAO inhibitors can cause an excitatory reaction called the serotonin syndrome, manifested as agitation, headache, fever, seizures, coma, and death [81].

A MAO-safe anesthetic technique has been described and used in patients requiring emergency procedures [82]. This involves avoidance of [meperidine](#) and use of only direct acting sympathomimetic agents such as isoprenaline and [phenylephrine](#).

The decision to continue or withhold MAO inhibitors before surgery requires close collaboration with the anesthesiologist and psychiatrist.

- The drugs generally should be continued in cases in which the anesthesiologist is comfortable with use of MAO safe procedures and the psychiatrist believes temporary withdrawal of the agent is likely to exacerbate the mood disorder.
- Absent both of these conditions, we recommend discontinuing MAO inhibitors before surgery. Many MAO inhibitors are irreversible antagonists of MAO, 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.

Mood stabilizing agents — [Lithium](#) has a number of physiologic effects that may be important perioperatively.

- The effect of lithium mimics that of sodium, and thereby decreases release of neurotransmitters. This may prolong the effect of muscle relaxants.
- Nephrogenic diabetes insipidus has been described in up to 20 percent of patients taking lithium. (See "[Renal toxicity of lithium](#)"). Patients who have impaired renal concentrating ability can maintain euvolemia and a normal serum sodium through polydipsia. However, during the perioperative period, access to free water may be impaired and lead to volume depletion and hypernatremia.

- Chronic lithium use may have a multitude of effects on the thyroid. ([See "Lithium and the thyroid"](#)).

Despite these considerations, 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 if not recently done. Lithium must be held in patients who cannot take oral medications for a prolonged period since no parenteral substitution is available.

[Valproic acid](#) is another mood stabilizer that is increasingly being used in patients with bipolar disorder, although most of the experience with this agent is derived from patients who take it for seizure disorders. There are no reports demonstrating problems in patients continuing valproic acid perioperatively and we recommend it be continued. There are no parenteral forms available

Antipsychotics — Phenothiazines, butyrophenones, and the newer atypical antipsychotic medications ([olanzapine](#), [quetiapine](#), [risperidone](#), ziprazadone) are believed to be safe in the perioperative period. These drugs have antiemetic and sedative properties and some are used as part of usual anesthetic practice, although there is little experience with the use of many of the newer agents around the time of surgery. Some antipsychotics are associated with significant QT prolongation which may predispose to torsade de pointes. ([See "Psychotropic drug use in nursing homes"](#)). There are remote published reports of arrhythmia and hypotension associated with use of antipsychotics [83], but no more recent data.

Overall, given that the antipsychotics are effective in controlling psychoses that may be problematic perioperatively, and that they are relatively safe, they can be continued in patients believed at high risk for exacerbation of psychoses. For patients who cannot take oral medication for a prolonged period, parenteral antipsychotics, include [haloperidol](#) and thiorazine, are available, although they can be toxic if not used judiciously. Alternatively, in the unusual circumstance that a prolonged period of bowel rest related to surgery is anticipated in a patient with a difficult to control psychosis, the long acting parenteral form of haloperidol (haldol decanoate) can be started well before surgery.

Antianxiety agents — Patients on chronic therapy with benzodiazepines for antianxiety or sedative effects usually continue them throughout the perioperative period. These agents are commonly used in patients not on chronic benzodiazepine therapy to relieve preoperative anxiety. 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 for this reason withdrawal can occur several days to weeks after discontinuation. Thus, because these agents are safe in the perioperative period when patients are properly monitored and abrupt discontinuation can lead to withdrawal, we recommend they be continued perioperatively. If oral medication is not feasible, parenteral forms of benzodiazepines are available, including [diazepam](#), [lorazepam](#), and [chlordiazepoxide](#).

There are no data demonstrating either the safety or harm of [buspirone](#) in the perioperative period; we recommend it be continued perioperatively. Parenteral benzodiazepines can be substituted if the patient cannot take oral medications and anxiety is a significant problem.

CHRONIC OPIOID THERAPY — Patients taking long term opioids for the management of chronic pain need to continue these agents around the time of surgery ([show table 6](#)). Abrupt discontinuation of opioids may result in withdrawal symptoms including abdominal cramps, nausea, vomiting, diarrhea, insomnia, anxiety, irritability, temperature instability, diaphoresis, and salivation.

For patients unable to take oral medications, rectal, transmucosal, transdermal, and parenteral forms are available. ([See "Overview of the treatment of chronic pain"](#), section on Opioids). In general, parenteral doses equivalent to oral doses should be used ([show table 7](#)), 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 here ([show table 8](#)).

Antiepileptic drugs — There are very little data to guide the clinician regarding the perioperative management of antiepileptic drug therapy. Nevertheless, major motor seizures that occur during a surgical procedure can increase morbidity and mortality. Thus, patients with preexisting seizure disorders generally need to have anticonvulsant medications continued perioperatively. Pure absence seizures pose little threat perioperatively; it is not as vital to continue antiepileptic drugs in these patients. ([See "Perioperative care of the surgical patient with neurologic disease"](#)).

A number of options are available for patients who require antiepileptic drugs during the perioperative period and in patients who cannot take oral medications. [Phenytoin](#) and [phenobarbital](#) are available parenterally and are effective for most types of generalized seizures. ([See "Pharmacology of antiepileptic drugs"](#)). Valproate also can be administered parenterally, and some drugs are available in suspensions that can be administered via nasogastric tube. For patients who will not tolerate oral medications for only one or two days and in whom generalized seizures are infrequent, it is reasonable to hold the antiepileptic agent and simply resume when oral administration is feasible since the half-life of most of these agents is long.

Antiparkinson agents — Patients with Parkinson's disease represent many challenges related to medication management in the perioperative period. This includes challenges related to the effect of these drugs on [dopamine](#), resulting in potential perioperative hemodynamic and arrhythmogenic effects, along with the potential for abrupt withdrawal to lead to flares of Parkinson symptoms and the neuroleptic malignant syndrome [[84-86](#)].

In general, 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 practice reduces the risk of precipitating the neuroleptic malignant syndrome with medication withdrawal, while still controlling symptoms. [Levodopa-carbidopa](#) can be given the night before surgery (except for the long-acting preparation, which is held earlier in the day before surgery), while the [dopamine](#) agonists have a longer half-life and are discontinued the evening before surgery to avoid the potential cardiovascular effects of dopamine during the perioperative period. ([See "Perioperative care of the surgical patient with neurologic disease"](#)).

Agents used for myasthenia gravis — Perioperative management of patients with myasthenia gravis requires careful thought and planning and is best done by physicians who have experience with this disorder. Myasthenic crisis with respiratory failure is the most concerning complication in the perioperative period. ([See "Treatment of myasthenia gravis"](#), section on Myasthenic crisis). Furthermore, the medication regimen can be complex; patients with myasthenia usually are taking anticholinesterase medications such as [pyridostigmine](#), and may also be taking chronic immunosuppressive agents such as [corticosteroids](#), [azathioprine](#), or less commonly [cyclosporine](#).

[Pyridostigmine](#) can be held on the morning of surgery in patients with myasthenia to avoid muscarinic side effects and to decrease the need for muscle relaxants, but some physicians choose to continue it for psychological support [[87](#)]. Some patients take a long-acting preparation of pyridostigmine at bedtime (Mestinon Timespans); a short-acting form should be substituted the night before surgery. Anticholinesterase medications are usually restarted when the patient is hemodynamically stable at the patient's usual dose. Parenteral substitution also is available for these agents. When used intramuscularly 1/10th the usual oral dose is substituted; when used intravenously, 1/30th the usual oral dose is administered by slow IV push or a continuous infusion can be initiated at 2 mg/hour.

Since some patients with myasthenia gravis are on high doses of [corticosteroids](#), parenteral substitution is advised. ([See "The surgical patient taking glucocorticoids"](#)).

The onset of action of other oral immunosuppressive agents such as [azathioprine](#) or [cyclosporine](#) is usually several months. There are no published data to guide management of these drugs around the time of surgery. Although parenteral substitution is possible for both cyclosporine and azathioprine, they likely can be held on the morning of surgery given the long duration of effect. These agents can be resumed

when the patient is taking oral medication safely.

RHEUMATOLOGIC AGENTS

Rheumatoid arthritis drugs — 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 [see "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-1 ([etanercept](#), [infliximab](#), [adalimumab](#), [anakinra](#), and [rituximab](#)).

Only limited data have been published to guide perioperative management. A randomized trial in orthopedic patients found no increased rate of infection in patients who continued weekly [methotrexate](#) compared with those who discontinued methotrexate two weeks before surgery [88]. There are no available human data regarding other DMARDs in the perioperative period. Many DMARDs are renally excreted, and thus impaired kidney function can lead to buildup of DMARDs or their metabolites; this may lead to bone marrow suppression.

We recommend that in patients with normal renal function, [methotrexate](#) can be continued in the perioperative period. In patients with renal insufficiency, methotrexate should be held for two weeks. [Sulfasalazine](#) and [azathioprine](#) should be held for a week prior to surgery and resumed after surgery. [Leflunamide](#) should be held for two weeks before surgery and resumed after 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 two weeks prior to surgery and resumed one to two weeks after surgery.

Gout therapy — Surgery is known to precipitate acute gouty arthropathy [89]. The optimal management strategy for patients on chronic hypouricemic therapy or [colchicine](#) in the perioperative period is unknown. There is no parenteral substitution for [allopurinol](#) or [probenecid](#). Parenteral colchicine is available but it can cause myelotoxicity, as well as significant skin necrosis if infiltration occurs.

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 ([show table 7](#)). Should an acute gouty flare occur in a postoperative patient unable to tolerate oral medications, parenteral colchicine [90], rectal [indomethacin](#), parenteral [ketorolac](#) [91], intraarticular steroids, or systemic steroids can be used. ([See "Treatment of acute gout"](#)).

MEDICATIONS FOR BENIGN PROSTATIC HYPERTROPHY — Some patients treated with alpha-1-antagonists (eg, [terazosin](#), [doxazosin](#), [tamsulosin](#), [alfuzosin](#)) have developed intraoperative floppy iris syndrome (IFIS), a surgical condition involving intractable intraoperative iris prolapse with cataract surgery [92]. Patients should be asked about use of alpha-1-antagonists during the preoperative evaluation. These medications should generally be discontinued prior to surgery, although it is not known how long patients must be off alpha-1-antagonists to reduce the risk of IFIS. ([See "Cataract"](#)).

HERBAL MEDICATIONS — Herbal medications are frequently used by patients undergoing surgery [93]. Some of these agents have physiologic effects that could be deleterious in the perioperative period, including precipitation of clotting disorders and interactions with anesthetics. Many patients taking herbal medicines do not disclose this during the preoperative assessment; physicians should seek out a history of herbal medication use in presurgical patients.

Since there is no evidence that herbal medications improve surgical outcomes, and there are theoretic reasons that these agents may increase perioperative morbidity, we recommend they be stopped before surgery. A literature review that examined eight commonly used herbal remedies found the following [94]:

- 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 7 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 7 days prior to surgery.
- Kava may increase the sedative effect of anesthetics and should be discontinued at least 24 hours prior to surgery. The Food and Drug Administration has issued a safety alert about an association between kava use and fatal hepatotoxicity. ([See "Hepatotoxicity due to herbal medications"](#)).
- St. John's wort may diminish the effects of several drugs by induction of cytochrome p450 enzymes and should be discontinued at least 5 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 suppression. There are no data on preoperative discontinuation.

For simplicity and because the exact nature and purity of some herbal medications is unclear, we recommend that other herbal agents be stopped at least one week before surgery.

RECOMMENDATIONS — General recommendations for the management of a number of medications are found in the following tables:

- Cardiovascular agents ([show table 1](#))
- Gastrointestinal and pulmonary agents ([show table 2](#))
- Endocrine agents ([show table 3](#))
- Agents affecting hemostasis ([show table 4](#))
- Psychotropic agents ([show table 5](#))
- Rheumatologic agents ([show table 9](#))
- Opioids ([show table 7](#))
- Neurologic agents ([show table 8](#))

As mentioned in the introduction, many of these recommendations are derived from expert opinion, as there are few outcome data about the majority of medications taken in the perioperative period. The following principles were used in generating many of the recommendations, and can be applied to medications that are not discussed in this review:

- Medications associated with known medical morbidity if withdrawn abruptly should be continued in the perioperative period. Substitute intravenous, transdermal, or transmucosal medicines should be used if absorption of these medications will be impaired because of loss of gastrointestinal function.
- Medications thought to increase the risk of surgical complications and not essential for short-term improvement in quality of life should be held through the perioperative period.
- Medications not meeting either of the above principles can be discontinued or continued based on individual physician judgment. If continued, the managing physician should remember that many other medications are administered perioperatively during a relatively short period that may interact with

chronic medications. Furthermore, the metabolism and elimination of chronic medications and their metabolites may be altered during the perioperative period.

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GRAPHICS

Periop cardiovascular agents

Perioperative management of cardiovascular agents

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Beta blockers	Abrupt withdrawal can result in hypertension, tachycardia and myocardial ischemia. Perioperative use can prevent postoperative myocardial ischemic events.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Substitute IV labetalol, propranolol, metoprolol or esmolol during NPO state
Alpha 2 agonists	Withdrawal can cause extreme hypertension and myocardial ischemia	Continue therapy up to and including day of surgery	Continue therapy up to and including day of surgery. Substitute transdermal clonidine or rarely IV methyl dopa.
Calcium channel blockers	Conflicting evidence on whether there is an increased risk of bleeding	Continue therapy up to and including day of surgery	Continue therapy up to and including day of surgery. No IV substitution necessary unless poor hemodynamics (hypertension or arrhythmia)
Ace inhibitors and angiotensin receptor blockers	Continuation can result in hypotension.	Continue therapy up to and including day of surgery if using for hypertension. Discontinue on day of surgery if using for CHF and baseline	Continue therapy up to and including day of surgery if using for hypertension. Discontinue on day of surgery if using for CHF and baseline blood pressure is low. No IV form available. Consider parenteral beta blockers for perioperative hypertensive, and

		blood pressure is low.	nitrates/hydralazine for CHF
Diuretics	Continuation can result in hypovolemia and hypotension.	Continue therapy up to day of surgery but discontinue morning dose.	Continue therapy up to day of surgery but discontinue morning dose. Use parenteral forms as needed in postoperative period.

Periop GI pulmonary agents

Perioperative management of gastrointestinal and pulmonary agents

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
H2 blockers	No known adverse effects.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Substitute IV forms available for prolonged postoperative NPO state.
Proton pump inhibitors	No known adverse effects.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Substitute IV H2 blockers for prolonged postoperative NPO state.
Inhaled anticholinergics	No known adverse effects.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Use nebulized forms if patient unable to comply with inhalation maneuver.
Theophylline	No known adverse effects but very narrow range between therapeutic and toxic level.	Continue up to day before surgery. Discontinue the evening before surgery	Continue up to day before surgery. Discontinue the evening before surgery. Resume with PO intake. Use nebulized or inhaled beta agonist or anticholinergics
Leukotriene inhibitors	No known adverse effects.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery and resume when patient able to take oral medications.

Periop endocrine agents

Perioperative management of endocrine agents

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Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Oral contraceptives	Continuation may increase risk of venous thromboembolism. Stopping can result in unwanted pregnancies.	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 if OCP stopped.	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 if OCP stopped.
Hormone replacement therapy	Continuation may increase risk of venous thromboembolism.	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.	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.
Selective estrogen receptor modulators	Continuation may increase risk of venous thromboembolism.	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 being used for breast cancer treatment consult oncologist.	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 When SERMs are being used for breast cancer treatment consult oncologist.
Lipid lowering agents	Continuation may elevate the risk of myopathy; statins may provide cardiovascular protection.	Continue statins; discontinue other agents the day before surgery.	Continue statins up to and including the day of surgery; discontinue other agents the day before surgery. Resume with PO intake.
Oral hypoglycemics and insulin	See text	See text	See text
Corticosteroids	See text	See text	See text

Periop hemostasis agents

Perioperative management of agents affecting hemostasis

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Aspirin and dipyridamol	Continuation may cause perioperative hemorrhage. Discontinuation may increase the risk of vascular complications.	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 5-7 days before surgery and discontinue dipyridamol at least 2 days before surgery.	Resume with oral intake.
Ticlopidine and clopidogrel	When used after cardiac stenting procedure, if discontinued can cause cardiac ischemia perioperatively. If continued can result in bleeding complications.	Ideally elective procedures should be delayed until the mandatory period of platelet inhibition with these agents is completed (6 weeks). When used for long term stroke prophylaxis, should be discontinued 7-10 days.	Resume with oral intake.

Periop psychotropics I

Perioperative management of psychotropic agents part 1

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Tricyclic antidepressants	Continuation may increase the potential for arrhythmias. Abrupt withdrawal can lead to insomnia, nausea, headache, increased	Continue therapy up to and including day of surgery for patients on high doses. Patients on low doses and in whom perioperative arrhythmia is likely should discontinue for 7 days prior to	Resume with oral intake. No parenteral substitution available.

	salivation and increased sweating.	surgery.	
Serotonin reuptake inhibitors	Increased risk of bleeding.	Discontinue therapy 3 weeks prior to surgery in patients undergoing high risk procedures (such as certain CNS procedures).	Resume with oral intake. No parenteral substitution available.
Monoamine oxidase inhibitors	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 "serotonin syndrome".	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.	Resume with oral intake. No parenteral substitution available.
Lithium	Continuation may prolong the effect of muscle relaxants and due to impaired renal concentrating ability can cause hypovolemia and hypernatremia.	Continue therapy up to and including day of surgery with close monitoring of electrolytes and volume status.	Resume with oral intake. No parenteral substitution available.
Valproic acid	No known adverse effects	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Resume with oral intake. No parenteral substitution available.

Periop psychotropics II

Perioperative management of psychotropic agents part 2

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Antipsychotics (phenothiazines, butyrophenones,	Some agents are associated with QT prolongation, and	Continue therapy up to and including day of	Continue therapy up to and including day of surgery. Parenteral haldol and thorazine are available. Parenteral

olanzapine, respiradone)	occasionally cause hypotension or arrhythmias. No recent data available.	surgery in patients with high risk of developing psychoses.	(depo form) haldol should be started well before surgery if prolonged NPO state is anticipated ahead of time.
Benzodiazepines	Abrupt withdrawal can result in agitation, HTN, delirium and seizures.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Parenteral diazepam, lorazepam and chlordiazepoxide are available for prolonged NPO state.
Buspirone	No known adverse effects.	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. No parenteral substitution available but parenteral diazepam, Lorazepam and chlordiazepoxide can be used for prolonged NPO state.

Equivalent opioid doses

Equivalent opioid doses

Drug	Time to onset (minutes)	Oral dose (mg)	Parenteral dose (mg)
Morphine sulfate parenteral			10 q4 hr
Morphine sulfate oral (MSIR, Roxanol)	15 to 60	30 q4 hr	
Morphine sulfate controlled release (MS contin, Oramorph)		90 q12 hr	not available
Codeine	10 to 30	200 q4 hr	100 to 120 q4 hr
Oxycodone (Percocet, Percodan, Tylox)	15 to 30	15 to 20 q4 hr	not available
Oxycodone controlled release (Oxycontin)	15 to 30	45 to 60 q12 hr	not available
Hydromorphone (Dilaudid)	15 to 30	8 q4 hr	1.5-3.0 q4 hr
Levorphanol (Levodromoran)	30 to 90	4 q6 to q8 hr	2 q6 to q8 hr
Meperidine (Demerol)	10 to 45	300 q2 to q3 hr	100 q2 to q3 hr
Methadone (Dolophine)	30 to 60	20* q6 to q12 hr	10 q6 hr

* A dose ratio of 1:4 (1 mg of oral methadone = 4 mg of oral morphine) is used for patients receiving

less than 90 mg of morphine. Patients receiving 90 to 300 mg/day receive methadone at a ratio of 1:8. Finally, a ratio of 1:12 is used for patients receiving morphine doses greater than 300 mg/day.

Periop miscellaneous agents

Perioperative management of miscellaneous agents

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Opioids	Abrupt withdrawal can cause yawning, abdominal cramps, nausea, vomiting, diarrhea, insomnia, anxiety and salivation	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Rectal, transmucosal, transdermal and parenteral preparations available.

Periop neurologic agents

Perioperative management of neurologic agents

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Antiepileptics	No known adverse effects.	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.	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.
Levodopa/Carbidopa	Metabolite of Levodopa, dopamine can cause arrhythmias, hypotension or hypertension	Continue therapy up to the night before surgery and hold it the day of surgery.	Continue therapy up to the night before surgery and hold it the day of surgery. Resume with oral intake as soon as possible.
Dopamine agonists	Directly stimulate	Continue therapy up	Continue therapy up to the night of

(Pergolide, bromocryptine, pramipexole, and ropirinole)	dopamine receptors and can cause arrhythmias or hypotension.	to the night of surgery and hold it for at least 12 hrs before surgery.	surgery and hold it for at least 12 hrs before surgery. Resume with oral intake as soon as possible.
Selegiline (selective MAO inhibitor)	At usual doses for Parkinson's disease does not induce hypertension when tyramine containing foods are ingested.	Hold the medication the evening before surgery.	Hold the medication the evening before surgery. Resume with oral intake.
Pyridostigmine	Can cause muscarinic side effects.	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.	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.

Periop rheumatologic agents

Perioperative management of rheumatologic agents

Name or class of drug	Clinical considerations	Recommended strategy for surgery with brief NPO state	Recommended strategy for surgery with prolonged NPO state
Nonsteroidal antiinflammatory drugs	Continuation may cause perioperative hemorrhage.	Hold for 3 days prior to surgery.	Resume with oral intake.
Methotrexate	Potential risk of bone marrow suppression	Continue therapy up to and including day of surgery. In patients with renal insufficiency, hold two weeks prior to surgery.	Continue therapy up to and including day of surgery. Resume with oral intake.

Sulfasalazine and azathioprine	Potential risk of bone marrow suppression	Hold for one week prior to surgery.	Hold for one week prior to surgery and resume with oral intake.
Leflunamide	Potential risk of bone marrow suppression	Hold for two weeks prior to surgery	Hold for two weeks prior to surgery and resume with oral intake
Hydroxychloroquine	Low risk of side effects	Continue therapy up to and including day of surgery.	Continue therapy up to and including day of surgery. Resume with oral intake.
Biologic response modifiers (etanercept, infliximab, anakinra, rituximab, adalimumab)	Risk of infection	Hold for one to two weeks prior to surgery and resume one to two weeks after surgery.	Hold for one to two weeks prior to surgery and resume one to two weeks after surgery or with oral intake.
Agents used in gout (colchicine, allopurinol, probenecid)	No known side effects	Continue therapy up to the night of surgery and hold the morning dose.	Continue therapy up to the night of surgery and hold the morning dose. Resume with oral intake. Rectal indomethacin, parenteral ketorolac, intraarticular and systemic steroids are available for acute gouty flares in postop period.

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