Premedication and management of concomitant therapy

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Abstract

The management of a patient's co-existing illnesses, including decisions about their normal medication is an important part of their perioperative care. Adequate pre-assessment, preparation and liaison with other healthcare professionals is essential to decrease patient morbidity and mortality and prevent unnecessary surgical delay or suboptimal management. A full medication history including prescribed, over the counter and complementary medications is required, along with decisions regarding which medications should be omitted or have dose alterations. Medications may need to be prescribed in addition to the patient's normal medications, for example, thromboembolic prophylaxis. This article summarizes current recommendations with regard to premedication and concomitant medication.

Keywords Long term medication; premedication; surgery

Introduction

Numerous patients presenting for surgery take regular medications. Many of these have important interactions and effects on the nature and conduct of both anaesthesia and surgery. Historically, there has been a lack of standard management of perioperative medication, reflecting in part systemic inefficiencies and individual variation in medical decision making. Nowadays, most elective patients in Western societies attend pre-assessment clinics in advance of their surgical procedure, which allows for risk stratification and the standardization of many elements of care including medication. Day of surgery admission is more commonplace and this system allows time for the management of complex drug regimes in the perioperative period such as new oral anticoagulants.

In general, patients are fasted prior to elective surgery to reduce the risks of intraoperative regurgitation and pulmonary aspiration. Recommended fasting times are 6 hours for solid food, carbonated drinks and infant formula and 4 hours for breast milk. Adults may consume carbohydrate-rich drinks, clear non-particulate and non-carbonated fluids including tea/coffee with a small amount of milk up to 2 hours before surgery.[1] Clear fluids can be taken up to 1 hour before surgery in paediatric patients without an increased risk of aspiration.[2] Most medications can be taken with a small sip of water without compromising fasting.

Another important consideration is an appreciation of the effective clinical duration of each medication, and the consequences of continuing or halting administration in the perioperative period. So, a long-acting drug with unwanted perioperative effects (e.g. clopidogrel) should be stopped for a longer period than a short-acting drug with similar effects (e.g. oral anticoagulants). Some medications (e.g. β-blockers, antipsychotics) may be best continued in a different preparation if a patient is unable to manage oral intake.

Specific drugs used preoperatively

Anxiolytics

Sedative agents and anxiolytics are infrequently used as routine 'pre-meds'. Short-acting benzodiazepines (e.g. midazolam) may occasionally be prescribed by the anaesthetist for patients when reassurance alone does not allay their anxiety. This is more common in paediatric practice, cardiac surgery, or as part of a procedural sedation technique.

Prophylaxis against aspiration

The recommended fasting guidelines mentioned help reduce the risk of aspiration of gastric contents in elective surgery. Patients at increased risk are those who are pregnant, have a BMI>30, a history of symptomatic hiatus hernia or dyspepsia and those with diabetes mellitus. Patients who currently take acid suppressants such as ranitidine and lansoprazole should continue to take these drugs as normal. There is insufficient evidence to recommend the routine use of antacids, metoclopramide or H_2-receptor antagonists before elective surgery in non-obstetric patients, but an H_2-receptor antagonist should be given before elective caesarean section, with an intravenous H_2-receptor antagonist given prior to emergency caesarean section, supplemented with 30 ml of 0.3 mol l^{-1} sodium citrate if general anaesthesia is planned.[1]

Anti-sialagogues

Anti-sialagogues (e.g. atropine, glycopyrrolate) are used to decrease oropharyngeal secretions and are sometimes prescribed by anaesthetists particularly if an awake fibreoptic intubation is planned. This is commonly given intravenously or if anaesthesia or procedural sedation with ketamine is planned. Some cerebral palsy patients will take an anti-sialogue as part of their routine medication, and this should be maintained.

Analgesia

Patients who are in pain should be encouraged to take their normal analgesia or be prescribed suitable analgesia prior to theatre. Partial opioid agonists such as buprenorphine should be discontinued preoperatively because they can block the effects of other full opiates agonists commonly given at the time of surgery. Alternative opiates should be prescribed instead. However, if a patient presents for surgery and has not discontinued partial opioid analgesics, they should receive similar perioperative analgesia to any other patient. Such patients undergoing major surgery may have higher opiate analgesic requirements, particularly where regional analgesia is not used. Pre-emptive analgesia is the administration of analgesia prior to the onset of the

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painful stimuli. There is some evidence that this decreases pain receptor activation and the production and activity of pain neurotransmitters. In addition to simple analgesia, gabapentin is sometimes prescribed preoperatively. Increasingly, pre-emptive analgesia is used as part of enhanced recovery programmes, although overall, the evidence for long term benefit from pre-emptive analgesia is not compelling.[3]

Preoptimization

Iron deficiency anaemia should be corrected with oral iron before surgery in the elective patient. Intravenous iron should be offered to patients if they cannot tolerate, absorb or utilize oral iron, or if the urgency of surgery necessitates more rapid correction of anaemia than can be achieved with oral iron (e.g. cancer surgery).[4] Carbohydrate-rich drinks are used in enhanced recovery programmes.

Concomitant therapy

Cardiovascular medications

Up to half of all patients presenting for surgery take medication, the largest group of which are for cardiovascular disease.

ACE inhibitors (ACEI) and angiotensin II receptor blockers (AR2RB): Patients taking ACE1 and AR2RB drugs for hypertension are at risk of profound hypotension intraoperatively. These drugs are generally omitted on the day of surgery. In patients who take ACEI and AR2RB drugs as a treatment for heart failure, cessation may worsen cardiac function and this decision should be considered on a case-by-case basis.[5]

Beta blockers: Patients on long-term β-blockers should continue to take them. Beta blockers have a cardioprotective effect in those with cardiac disease but β-blockers may increase the rate of perioperative strokes.[6]

Calcium-channel blockers/nitrates/alpha-2 agonists: These classes of drugs should be continued preoperatively.

Statins may prevent vascular events through mechanisms including reduced inflammation and vascular plaque stabilization. There is evidence that statins may be cardioprotective, and current recommendations are that chronic treatment should continue, while patients having vascular surgery should have statins started 7–10 days preoperatively.

Anti-platelet drugs. Aspirin is an irreversible inhibitor of platelet cyclo-oxgenase. A large proportion of perioperative acute coronary syndromes have been attributed to abrupt cessation of aspirin, so as a general rule, this should be continued up until the day of surgery. For patients undergoing surgery where perioperative haemorrhage may be catastrophic, for example, neurosurgery, aspirin can be stopped for 7 days preoperatively. This risk/benefit judgement is made on a case-by-case basis with the surgical team. However, in many cases, even where high blood loss is anticipated, aspirin is now maintained until the day of surgery.

Clopidogrel and prasugrel are platelet P2Y12 receptor blockers and ticagrelor also acts via the P2Y12 receptor. These drugs are often administered following the insertion of coronary stents as part of dual antiplatelet therapy and clopidogrel is also used in the treatment of peripheral vascular disease. Dual anti-platelet therapy (DAPT) is often recommended for 12 months following percutaneous coronary interventions. Stopping DAPT within 6 weeks of bare metal stents or 12 months of drug eluting stents carries an increase in risk of stent thrombosis. Elective surgery should be postponed whenever possible until the minimum duration of therapy is completed. If DAPT must be stopped due to the risk of perioperative bleeding in more urgent cases (e.g. cancer) then seeking advice from a cardiologist regarding the risk of stent thrombosis is recommended. In such cases, aspirin is usually continued. Some stents now require a shorter duration of DAPT as the risk of thrombosis is lower. Clopidogrel, ticagrelor, and prasugrel should be discontinued for 7 days prior to surgery which allows regional anaesthetic techniques to be performed safely.

Dipyridamole is an agent with anti-platelet and vasodilator properties used for patients following Transient Ischaemic Attacks (TIAs) and strokes when clopidogrel cannot be taken. It is omitted on the day of surgery.

Non-steroidal anti-inflammatory drugs (NSAIDs): These are reversible inhibitors of cyclo-oxgenase which have anti-platelet effects due to reduced concentration of thromboxane A2. In patients at high risk of bleeding they should be stopped. Due to their potential for nephrotoxicity, they should be avoided in patients with evidence of renal impairment and NSAIDs also may cause gastric mucosal ulceration, and are perhaps best avoided after major surgery when significant fluid shifts and splanchnic hypoperfusion may occur.

Nephrotoxic drugs

ACE1, diuretics, gentamicin and intravenous contrast agents can be nephrotoxic and their use should be carefully considered perioperatively in patients at risk of renal impairment, particularly if co-administered with a NSAID.

Anticoagulants

Many patients take anticoagulants for a range of medical problems from cardiovascular disease to stroke prophylaxis. Continuing these medications is associated with an increased risk of perioperative bleeding but cessation may increase the risk of thromboembolism.

Warfarin is stopped 5 days preoperatively with the target INR of <1.5 on the day of surgery. It may be continued during minor procedures with a low risk of bleeding (e.g. dental or superficial skin surgery). Patients taking warfarin for atrial fibrillation are at relatively low risk for thrombosis when warfarin is withheld for surgery. Routine 'bridging' therapy with heparin in such patients is associated with a higher risk of major bleeding and cardiac events but no significant reduction in thromboembolic events.[7] Those with prosthetic heart valves, recent or recurrent thrombosis are at higher risk and bridging therapy with therapeutic low molecular weight heparin is often used perioperatively until warfarin can be recommenced. In the first month following the signature thromboembolic event, the chances of further thromboembolic events are much higher, so if possible elective surgery should be postponed until after this time. If surgery is urgent, vitamin K, prothrombin complex concentrates and fresh frozen plasma can be used to reverse the effects of warfarin rapidly.

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Dabigatran, rivaroxaban, apixaban and edoxaban are newer oral anticoagulants increasingly encountered in perioperative practice. They do not require routine monitoring as they have a predictable anticoagulant effect. Dabigatran is an oral direct thrombin inhibitor, and rivaroxaban, apixaban and edoxaban are direct factor Xa inhibitors. They are licensed for thromboembolic prevention and used in atrial fibrillation to reduce the chance of stroke. Idaricuzimab is a monoclonal antibody which binds avidly to dabigatran, reversing its anticoagulant effect. It is now licensed for this purpose in the UK. A factor Xa reversal agent, 'andexanet alfa' has been granted FDA approval in the US, but is not currently licensed for UK use. A 'universal' reversal agent is currently undergoing phase III clinical trials.[8]

Expert advice regarding monitoring and possible reversal of these agents in urgent surgical cases should be sought from a haematologist. For elective procedures, the length of discontinuation is determined by calculating the creatinine clearance. The dose of these oral anticoagulants must be checked in the first instance as the correct dose can be influenced by renal function, liver function and age. Dabigatran and rivaroxaban are generally stopped for between 2 and 4 days preoperatively. Apixaban and edoxaban are generally stopped for 48 hours preoperatively.

Low molecular weight heparin (LMWH) is commonly used as venous thromboembolic prophylaxis and treatment. Prophylactic LMWH has minimal effects on surgical bleeding, and is frequently administered at the time of surgery. If given at higher treatment doses it is recommended that the last dose be given 24 h before the surgery, especially if spinal or epidural anaesthesia is planned, given the increased risk of central neuraxial haematoma.

The half-life of intravenous unfractionated heparin is complex and dose dependant, but is in the order of 45 minutes. Patients receiving intravenous heparin before surgery should discontinue this 4 hours prior to the procedure. Monitoring activated partial thromboplastin time (APTT) is an easily available method to monitor dosing schedules.

A small number of patients have a significant risk of pulmonary embolism. Examples would include patients in the perioperative period who have established pulmonary embolus or proximal venous thrombosis, but who require major surgery, or those with heparin induced thrombocytopenia. There is currently a lack of clarity about which patient groups benefit most from IVC filter insertion, and the optimal duration of use. Again, local policies and expert advice should be consulted.

Oestrogen containing medications

The risk of thrombosis increases with the oral contraceptive pill (OCP) use but the decision to continue or stop the pill is a balance between the risk of thrombosis and the risk of pregnancy (also associated with an increase in thrombosis risk). Oral contraceptives are normally continued for those undergoing low-risk surgery. If not, the OCP should be discontinued 4 to 6 weeks prior to surgery. If the OCP is continued, drug interactions which may reduce the efficacy of oral contraceptives should be considered. Historically, examples include co-administration with enzyme-inducing drugs, e.g. rifampicin and broad-spectrum antibiotics altering gut flora and oral bioavailability. However, these drugs may have less effect on OCP efficacy than previously thought.[9] Occasionally, anaesthetists may use the drug sugammadex to reverse neuromuscular blockade at the end of surgery. In such cases, women should be advised to follow 'missed pill' advice, and women using non-oral hormonal contraceptives should be advised to use barrier contraceptives for 7 days.[10]

The oestrogen content of preparations used for postmenopausal hormone replacement therapy (HRT) is much lower but it is still associated with an increased risk of venous thromboembolism. As stopping HRT is unpleasant but with minimal risk it should be stopped at least 4–6 weeks prior to moderate- or high-risk surgery. Tamoxifen also carries a risk of thromboembolism and should be stopped 3 weeks prior to surgery when it is used as a secondary preventative therapy in breast cancer. Where tamoxifen is used as a sole primary treatment for oestrogen-sensitive breast cancer it may be appropriate to continue and accept the increased risk of thromboembolism.[11]

Diabetic drugs

There are 3.8 million people in the UK with diabetes and the incidence is increasing so the need to manage diabetic medications perioperatively is very common. The metabolic stress response from surgery leads to a catabolic state and inhibition of anabolic hormones, including insulin, resulting in hyperglycaemia in diabetic patients. The risk of postoperative complications is higher amongst diabetic patients and includes the risk of postoperative infection.

The management of the diabetic patient requires a multidisciplinary approach but guidance for pharmacological management is as follows. The aim is to keep the capillary blood glucose between 6 and 10 mmol/L, although 4–12 mmol/L is considered acceptable. For patient's undergoing elective surgery, the emphasis is now placed on trying to avoid a variable rate insulin infusion (VRIII, previously called a sliding scale). This can normally be achieved by ensuring only one meal is missed perioperatively by ordering patients first on theatre lists and by providing good analgesia and anti-emetics. Patients with type I diabetes should always have some form of insulin administered to avoid the development of diabetic ketoacidosis.[12]

Management changes to antihyperglycaemics as recommended by the Joint British Diabetes Societies guidelines are summarized in Table 1.[11]

For more major surgery, and for patients undergoing emergency surgery where it is anticipated that more than one meal will be missed, a variable rate intravenous insulin infusion (previously called a sliding scale) is needed. These may be a combined mixture designed to maintain normoglycaemia (e.g. 500 ml 10% dextrose with 10 mmol potassium and a variable amount of insulin added, typically 12–16 units initially, run at 80 ml/hr), or separate dextrose and insulin infusions. The former is inherently safer (since unopposed insulin infusion is not possible), although more cumbersome if blood glucose levels are not stable. Separate infusions are more common now and there is a shift towards the use of dextrose-saline-potassium solutions for maintenance (e.g. 0.45% saline/5% dextrose/0.15% potassium chloride), but each institution will have its own policy.

Increasingly, patients may have a continuous subcutaneous insulin infusion (CSII), or insulin pump, in place. This is a small self-contained pump with a range of programmable options, often delivering low basal rates of insulin, without the peaks and

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Perioperative management of diabetic medication: minor surgery

Drug	Management
Insulin	Long-acting preparations should be continued at 80% the normal dose Twice daily mixed insulins e.g. novomix 30 require 50% the normal morning dose on the day of surgery Basal bolus regimes require basal dose to be continued at 80% the usual dose. If morning theatre list omit the morning and lunchtime bolus and if afternoon theatre list omit lunchtime bolus
Non-insulin medications	
Metformin	Continue as normal (unless contrast media required and eGRF <50 ml/min)
Pioglitazone	Continue as normal
Sulphonyureas e.g. gliclazide	For a morning list, omit the morning dose if taken once or twice a day. For an afternoon list, take the previous evening's dose as normal (if taken twice a day), then omit the morning dose.
GLP-1 analogues e.g. Exenatide and DPP IV inhibitors e.g. Sitagliptin	Continue as normal
Acarbose and Meglitinide e.g.repaglinide	Omit morning dose for morning list but can be given as normal for afternoon listing
SGLT -2 inhibitors e.g. dapaglifozin	Continue as normal the evening prior to surgery. Omit the day of surgery

Table 1

troughs associated with larger intermittent dosing regimes. Perioperatively the pump can be continued with the patient's normal basal rate until they are eating and drinking normally if only one meal is likely to be missed. However, blood glucose measurement will need to be closely monitored as skin perfusion can decrease perioperatively with hypotension and dehydration. If the pump is stopped for any time then regular capillary blood glucose and electrolyte testing will be required as hyperglycaemia may occur after discontinuation. If more than one meal is to be missed the pump should be removed and a VRIII should be used. Bolus therapy can then be given as per the patient's normal regime once they are eating and drinking, the VRIII stopped 30 minutes later and the CSII restarted.

Respiratory drugs

Inhalers and oral medications for COPD and asthma should be continued as normal. Smoking has a wide range of effects on patients in the perioperative period, ranging from direct interactions with anaesthetic drugs through to increased rates of respiratory or postoperative wound complications. Abrupt cessation of nicotine intake may be harmful, so efforts to reduce smoking should take place around 2 months prior to surgery in order to be maximally effective. Perhaps counter intuitively, nicotine replacement therapy may increase complications and possibly even mortality rates, although adequately powered studies have yet to be completed.

Steroids

Chronic glucocorticoid therapy can suppress the hypothalamic-pituitary-adrenal (HPA) axis and, during times of stress including surgery, the adrenal glands may not appropriately secrete cortisol resulting in an Addisonian crisis. The degree of adrenal suppression depends on the dose and duration of steroid treatment. Patients who have been taking 5mg prednisolone or more long term should be regarded as potentially suppressed and managed with perioperative supplemental steroid cover, on a precautionary basis.[13] Inhaled steroids pose less risk, so only patients on very high doses (e.g. 1.5 mg beclometasone per day) need additional steroid administration. A recommended steroid replacement regime is shown in Table 2. The doses of hydrocortisone used are sufficient to provide some mineralocorticoid replacement as well, so obviating the requirement for separate fludrocortisone administration.

Thyroxine

Levothyroxine should be continued perioperatively. It has a long half-life so even if the oral route is unavailable it need only be given by intravenous or intramuscular administration after seven days. It then is given at 80% of the oral dose. The aim is to keep the patient clinically and biochemically euthyroid perioperatively.

Immunosuppressants

Disease modifying anti-rheumatic drugs (DMARDs) e.g. methotrexate and biological agents such as inhibitors of tumour necrosis factor (e.g. infliximab) are often used in rheumatoid arthritis and other chronic inflammatory diseases. The concerns

Perioperative steroid replacement

Surgery	Management
Minor surgery	Continue usual dose perioperatively. Additional 25 mg hydrocortisone intravenously intraoperatively
Moderate surgery	Continue usual dose of steroids preoperatively. Additional 25 mg of hydrocortisone intravenously (IV) intraoperatively, followed by 25 mg IV 8 hourly for 24 h prior to the patient's usual dose being recommenced.
Major surgery	Continue usual dose of steroids preoperatively. Additional 50 mg of hydrocortisone intravenously intraoperatively, followed by 50 mg IV every 8 h for 48–72 h. Once the patient is eating again the patient's usual dose can be recommenced

Table 2

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perioperatively include accumulation if renal function becomes impaired, with subsequent bone marrow suppression and increased risk of surgical site infection. There is little evidence of increased infection rate or poor wound healing associated with DMARDs continued at the time of surgery and thus methotrexate, hydroxychloroquine, lefluonomide, sulfasalzine and azathioprine can be continued.[14] Abrupt discontinuation can lead to a flare in arthritis which can in itself be problematic. TNF inhibitors should be stopped around 2 weeks prior to surgery (variable depending on the half-life of individual drugs) and resumed after satisfactory wound healing.[15]

Epileptic medication

Antiepileptic drugs should be continued perioperatively. The oral bioavailability of different manufacturers preparations, and different formulations of the same drug may vary significantly, and many of these drugs including phenytoin and phenobarbitone have a narrow therapeutic index. Thus, regular plasma monitoring of drug levels may be required, and named product prescribing may be preferable to generic prescribing for some patients. Many antiepileptic drugs are also enzyme inhibitors and drug interactions should be considered. For patients unable to take oral medications there are parenteral alternatives of several of the drugs and many formulations are compatible with nasogastric tube administration.

Anti-parkinsonian medications

Parkinson's disease is common, and carries higher risks in the perioperative period of complications such as aspiration pneumonitis and a range of infections. Symptoms may also deteriorate through suboptimal management of drug therapy. Many patients have irregular and frequent drug regimes, and it is imperative that these are maintained to prevent the development of life-threatening Parkinsonian crises. If drug regimens cannot be adhered to due to surgery or poor enteral absorption, options include administration of alternative preparations of the same drug (e.g. via nasogastric tubes), or adding agents such as apomorphine or rotigotine to established medications.[16] In general, expert advice should be sought.

Psychotropic medications

Decisions regarding cessation of agents need to consider the risk of psychiatric consequences against the risk of potential side effects and interaction with anaesthetic agents. As a general rule, these drugs should be continued wherever possible, and abrupt withdrawal should be avoided. Tricyclic antidepressants should be continued unless there is a high risk of arrhythmias. Selective serotonin reuptake inhibitors (SSRIs) may increase bleeding particularly in those on anti-platelet therapy. In general, they should only be stopped if postoperative bleeding may cause severe morbidity and the risk outweighs the risk of worsening psychiatric illness. Cessation of SSRIs requires slow reducing doses over weeks and introduction of alternative agents. Monoamine oxidase inhibitors (MAOI) interfere both with sympathomimetic agents often given during anaesthetics and enzymes involved with opiate metabolism, so if possible should be discontinued and alternative medication started 2 weeks before surgery after discussion with the patient's psychiatry team.

Older patients

Older patients commonly present for surgery, and this will only increase as our population ages. A comprehensive medicines history is imperative in this patient group, as they are more prone to polypharmacy and adverse drug interactions. Antipsychotic medication (e.g. haloperidol 0.5–5 mg orally/IM, as required) should only be considered in the management of delirium if patients present a risk to themselves or others. These drugs should not be given to patients with Parkinson's disease or Lewy-Body dementia, as acute Parkinsonian crises may ensue.

Herbal medications

Many are associated with an increased risk of bleeding and can interact with anaesthetic agents so it is recommended that all herbal medications are stopped at least 1 week prior to surgery. Some herbal and complementary medicines can be directly toxic, or fatal (renal, hepatic or cardiac impairment), thus highlighting the importance of a comprehensive drug history and appropriate advice to patients.

Conclusion

Perioperative drug management is an important part of overall patient care. Despite an often scanty evidence base, local policies and procedures should be established and used to facilitate efficient and safe management for individuals. Good management may make the difference between a short, safe and uneventful hospital stay, and one with unnecessary complications. ◆

REFERENCES

1 Smith I, Kranke P, Murat I, et al. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. *EJA* 2011; **28:** 556–69.
2 Thomas M, Morrison C, Newton R, Schindler E. Consensus statement on clear fluid fasting for elective pediatric general anaesthesia. *Paediatr Anaesth* 2018; vol. 28**:** 411–4.
3 Niraj G, Rowbotham DJ. Persistent postoperative pain: where are we now? *BJA* 2011; **107:** 25–9.
4 Blood Transfusion. 2015. The National Institute for Health and Care Excellence. Available from: https://www.nice.org.uk/guidance/ng24/chapter/Recommendations#alternatives-to-blood-transfusion-for-patients-having-surgery-2 (accessed 3 January 2019).
5 Priebe HJ. Preoperative cardiac management of the patient for non-cardiac surgery: an individualized and evidence-based approach. *Br J Addict* 2011; vol. 107**:** 83–96.
6 POISE Study Group. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008; **371:** 1839–47.
7 Douketis JD, Spyropoulos AC, Kaatz S, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. *NEJM* 2015; **375:** 823–33.
8 McIlmoyle K, Tran H. Perioperative management of oral anticoagulation. *BJA Education* 2018; **18:** 259–64.
9 Archer JSM, Archer DF. Oral contraceptive efficacy and antibiotic interaction: a myth debunked. *J Am Acad Dermatol* 2002; **46:** 917–23.
10 Bridion sugammadex dosing considerations. 2018. Merck, Sharp & Dohme Corp. Available from: https://www.merckconnect.com/

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static/pdf/bridion-sugammadex-dosing-considerations.pdf (accessed 4 January 2019).
11 Management of adults with diabetes undergoing surgery and elective procedures: improving standards. Joint British Diabetes Societies for Inpatient Care, September 2015.
12 Hussain T, Kneeshaw P. Stopping tamoxifen peri-operatively for VTE risk reduction: a proposed management algorithm. *Int J Surg* 2012; **10:** 313–6.
13 ADSHG surgical guidelines, 2017.
14 Ledingham J, Gullick N, Irving K, et al. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. *Rheumatology* 2017; **56:** 865–8.
15 Ding T, Ledingham J, Luqmani R, et al. BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. *Rheumatology* 2010; **49:** 2217–9.
16 Brennan KA, Genever RW. Managing Parkinson's disease during surgery. *BMJ* 2010; **341:** c5718.

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