

Peri-operative Drug Management Guidelines

Policy Title:	Peri-operative Drug Management Guidelines		
Executive Summary:	This policy provides guidance on which drugs should be given peri-operatively and which drugs should be temporarily withheld.		
Supersedes:	New policy		
Description of Amendment(s):	N/A		
This policy will impact on: Drug management for all patients admitted for elective surgery			
Financial Implications: Limited financial impact. Resources required in the form of policy writers will have to review their policies to ensure that they meet the guidance contained in this document.			
Policy Area:	Trust Wide	Document Reference:	
Version Number:	1.1	Effective Date:	Sept 2009
Issued By:	Chair of Medicines Management	Review Date:	Sept 2011
Author: (Full Job title)	Lead Surgical Pharmacist Consultant Anaesthetist	Impact Assessment Date:	
APPROVAL RECORD			
	<u>Committees / Group</u>	<u>Date</u>	
Consultation: All Consultants	Medicines Management Group		
Approved by Director:	Director of Finance and Performance		
Received for informatio:	OMT		

Introduction

Evidence collected by the National Confidential Enquiry into Peri-operative Deaths (NCEPOD) suggests that peri-operative drug management is not currently optimal and omission of important medication may contribute to post operative mortality. Omission of regular drug therapy may cause exacerbation of the underlying pathology or withdrawal symptoms which may compromise patient outcome. NCEPOD suggests that patients do not receive essential medication pre-op owing to staff misinterpreting the term “nil by mouth”(NBM).¹

What does NBM mean?

- Clear fluids (water/squash) – none in 2 hours prior to surgery (except for 30mL to administer medication).
- Food (includes milk) – none in the 6 hours prior to surgery.
- Medicines –regular medication should be administered up to 1 hour prior to surgery with 30mLs of water unless they need to be withheld.

(If in any doubt please ask anaesthetist, surgeon or pharmacist)

Pre-admission clinic/admitting doctor’s responsibilities:

Peri-operative pharmaceutical management decisions should not be made on the morning of surgery. It is important that planning begins earlier at the pre-op assessment stage so that certain drugs which require discontinuation for longer periods of time pre-op can be managed effectively. Owing to potential interactions with anaesthetic agents and regular drugs, a thorough drug history must be completed so that the anaesthetist is aware of all drugs, including herbal medicines and supplements, which the patient is taking. Any drugs discontinued within the previous three months must also be documented for the anaesthetist’s attention. This must be documented in the medical notes/front of drug chart. It is mandatory that an accurate and complete drug chart is written pre-operatively for the anaesthetist’s attention. Please refer to the following guideline to decide on a pharmaceutical management plan for the patient.

East Cheshire NHS Trust
Summary of Peri-operative Drug Management

Drug	Stop?	When to restart?
<u>Aspirin</u>	Minor surgery: continue Major surgery or high risk of bleeding post-op: stop 7 days before surgery	Give when risk of bleeding no longer significant (usually ~3-4 days post-op)
<u>Potassium-sparing diuretics</u> (Spironolactone, amiloride)	Omit morning dose on day of surgery	Give morning dose next day
<u>NSAIDs</u>	Controversial whether any benefits from stopping. Short-acting agents e.g ibuprofen, diclofenac: stop 1 day pre-op Long-acting agents e.g piroxicam, naproxen: stop 4 days pre-op For major orthopaedic surgery stop 4-7 days pre-op according to Consultant preference.	Give when risk of bleeding no longer significant (usually ~3-4 days post-op)
<u>COX II inhibitors</u> (Celecoxib, Etoricoxib)	Continue	Continue
<u>Clopidogrel and ticlopidine</u>	Clopidogrel: stop 7 days pre-op Ticlopidine: stop 7-10 days pre-op See Appendix 2 for patients with coronary stents	Give when risk of bleeding no longer significant (usually ~3- 4 days post-op)
<u>Dipyridamole</u>	Stop 24 hours pre-op	Give when risk of bleeding no longer significant (usually ~3-4 days post-op)
<u>Diuretics (thiazide + loop)</u>	Continue	
<u>"Old" MAOI</u> (phenelzine, isocarboxazid, tranylcypromine)	INFORM ANAESTHETIST May decide to use MAOI "safe" anaesthesia or to stop 2/52 pre-op with careful discussion with psychiatrist	48 hours post-op If continuing need to avoid opioids during post-op period
<u>Reversible MAOI</u> (Moclobemide)	INFORM ANAESTHETIST May decide to use MAOI "safe" anaesthesia or to stop 24 hours pre-op	24 hours post-op If continuing need to avoid opioids during post-op period
<u>Corticosteroids</u> (Prednisolone, dexamethasone)	Give morning dose as usual and supplement with i/v hydrocortisone if necessary as per guidelines(see below)	Restart next day if not NBM
<u>Lithium</u>	INFORM ANAESTHETIST Omit 24 hours before major surgery Check U+Es pre-op May decide to stop 24 hours pre-op or continue with close monitoring of fluid balance and U+E's as lithium toxicity may develop in patients with deranged electrolytes.	ASAP post-op but will require close monitoring of fluid balance and U+E's post-op to avoid lithium toxicity
<u>HRT</u> (including patches, tablets, implants, gel)	Continue with s/c heparin prophylaxis and TEDS	Continue
<u>Tamoxifen</u> <u>Anastrozole</u>	Breast cancer: Tamoxifen confers a higher risk of developing VTE. Refer to Consultant for decision with regards to when to stop and possible alternative treatment pre-op if necessary. Anovulatory infertility: Stop 6/52 pre-op	If stopped re-start once fully mobilising

Drug	Stop?	When to restart?
<u>Insulin</u>	<p><u>Minor day case surgery</u> (See Appendix 3 for types of insulin) <i>Evening before surgery</i> – usual diet & insulin Diet Last full meal before midnight Last light snack before 0230 hr Last clear fluid before 0630 hr Insulin Long acting insulin – no reduction Intermediate acting insulin – to reduce by 1/3 (i.e 2/3 of evening insulin dose)</p> <p><i>On morning of surgery</i> – Omit breakfast & all SC insulin 1) Short procedure + early morning Delay insulin regime 2) Short procedure + afternoon Diet Light breakfast before 7 am Clear fluids until 11am Basal bolus regime – 1/3 of morning dose of short acting insulin morning with light breakfast Insulin bd regime - 1/2 total morning dose with light Breakfast</p> <p><u>Intermediate & major surgery</u></p> <p><u>Morning list</u> <i>On evening before surgery</i> – usual diet & insulin Diet No food after midnight Sips of water if necessary before 0630 Insulin Long Acting Insulin – no reduction Intermediate acting insulin – to reduce dose by 1/3 (i.e give 2/3 of evening insulin dose)</p> <p><i>On morning of surgery</i> – No food or insulin <i>Start IV soluble insulin & glucose at 0630 hr or on admission for same day surgery</i></p> <p><u>Afternoon list</u> <i>During the night before surgery</i> – usual insulin dose Diet Light breakfast before 0700 hr <i>Start IV soluble insulin & glucose at 0700 hr or admission to ward</i> If you need further information, please refer to peri-operative diabetes guidelines and contact diabetes team (SpR bleep 1005 or Ext 1349) or in reach Diabetes Specialist Nurses (when available on 07699 7335111).</p>	<p>Give patient usual meal (similar Carbohydrate amount) with usual insulin dose</p> <p>Start patients on insulin dose 10% higher than their usual doses & readjust.</p> <p>Continue IV insulin & glucose infusions for one further hour after giving the first dose of short acting insulin <u>Or</u> <u>4 hours after giving the first dose of intermediate acting insulin</u></p>

Drug	Stop?	When to restart?
<p><u>DMARDs and immunosuppressants</u> e.g methotrexate, cyclophosphamide</p>	<p>For RA patients on methotrexate:</p> <ul style="list-style-type: none"> • Check renal function within 6 weeks of any planned operation • If the eGFR is > 30 ml/min then methotrexate should be omitted the week before and the week after surgery. Renal function should be checked again post-operatively and if it has not changed then the same dose of methotrexate can be re-started if the patient is making satisfactory progress. • If the eGFR is ≤ 30ml per minute, then all medications should be discussed with the rheumatologist prior to surgery. • Patients should not stop their methotrexate for more than two weeks without good reason. The rheumatologist should be consulted in this situation. • Patients should be informed in writing at the time of their pre-operative assessment when they should omit their methotrexate. They should also be informed that any stop of treatment is only short-term and that they should expect to be taking the same dose of methotrexate when they go home as when they came into hospital. They should continue to take their folic acid in the usual prescribed dosage throughout. <p>If for other conditions e.g post transplant: will need to continue- discuss with relevant consultant before withholding therapy</p>	<p>See guidance opposite</p>

Drug	Stop?	When to restart?
<u>Oral diabetic medication</u>	<p><u>Sulphonylureas:</u> Omit on morning of minor surgery (unless the patient is on long acting such as Glibenclamide or Chlorpropamide which should be stopped 48 hours before)</p> <p><u>Metformin:</u> Omit on morning of surgery if the patient is expected to eat & drink post-operatively or to stop 48 hours pre-operatively if the patient is unlikely to be eating & drinking within first 24 hours following surgery. (caution : to consider stopping 48 hours before and 72 hours following surgery if alteration in renal function is expected as it may potentiate development of lactic acidosis and replace with short acting oral hypoglycaemic agent such as gliclazide)</p> <p><u>Glitazones:</u> Omit on morning of minor surgery</p> <p><u>Gliptins:</u> Omit on morning of minor surgery</p> <p><u>Exenatide :</u> Omit on morning of minor surgery</p> <p>If capillary blood glucose is > 12 units, to consider using intravenous insulin infusion & glucose as per peri-operative diabetes guidelines.</p>	Restart oral hypoglycaemics once patient is eating and drinking.
<u>Combined oral contraceptives</u> (e.g Loestrin, Logynon, Microgynon, Ovran, Marvelon, Minulet, Brevinor, Cilest)	Continue unless surgery has high thrombotic risk e.g major joint surgery/prev VTE. If to be discontinued refer to relevant consultant surgeon and advise patient to use other methods of contraception. Ensure patient is prescribed LMWH prophylaxis and TEDS	Assess
<u>Progestogen-only pills and contraceptive depot injections</u> (Femulen, Micronor, Microval, Neogest, Norgeston, Noriday, Depo Provera, Noristerat)	Continue	Continue
<u>Drugs for dementia</u> (Donepezil, rivastigmine, galantamine)	INFORM ANAESTHETIST May decide to proceed and monitor neuromuscular blockade or to withhold these drugs pre-op (donepezil needs to be stopped 2-3/52 pre-op and rivastigmine/galantamine 24 hrs pre-op)	If stopped re-start ASAP post-op
<u>Drugs of abuse</u>	ENSURE ANAESTHETIST IS AWARE IF ILLICIT DRUG USE IS STRONGLY SUSPECTED	---
<u>Herbal medicines</u> (e.g Garlic, Ginseng, Gingko, St Johns Wort)	REFER TO SEPARATE TABLE If in doubt stop herbal preparations pre-op due to potential interactions with conventional medicines and an increased risk of bleeding	On discharge
<u>Oral anticoagulants</u> (Warfarin, phenindione, acenocoumarol)	PLEASE SEE FLOWCHART FOR PERI-OPERATIVE ANTICOAGULATION IN APPENDIX 1	

This sheet is intended as a summary of the guidelines for the management of drug therapy in the peri-operative period
For further guidance please refer to these guidelines or contact your pharmacist

Drugs that should be stopped

a) Diuretics

Potassium-sparing diuretics e.g. spironolactone or amiloride should be omitted on the morning of surgery. Tissue damage and reduced kidney perfusion immediately post-operatively may contribute to the development of hyperkalaemia which may be additive with concurrent potassium-sparing diuretics ².

b) Aspirin

Aspirin induces an irreversible inactivation of platelet cyclo-oxygenase. This inhibition lasts the life of the platelet (~ seven to ten days on average in circulation). The result is impairment of thromboxane-dependent platelet aggregation and prolongation of the bleeding time. Concern surrounding the continuation of aspirin pre-operatively focuses on the effects on platelet function, associated with increased tendency to bleeding and development of epidural haematoma when spinal or epidural anaesthetic techniques are used ³. Aspirin is known to increase the bleeding time significantly but there is a lack of data regarding the clinical significance of this when patients have been taking doses of only 75-150mg per day ^{3,4}.

Patients undergoing minimally invasive surgery should continue taking their aspirin as the benefits of treatment are far greater than any risk of increased bleeding. Aspirin should be stopped when the risks of post-operative bleeding are high, such as during major surgery, or where the consequences of even minor bleeding are significant, particularly those patients receiving epidural anaesthesia or analgesia. This must be balanced against precipitating thromboembolic complications if aspirin is stopped, particularly in those patients with unstable angina. If aspirin is to be stopped where possible, it should be done seven to ten days before surgery to allow recovery of adequate platelet function ^{3,5}.

c) NSAIDs

Other NSAIDs inhibit cyclo-oxygenase in a dose-dependent but reversible process, unlike aspirin. The duration of this inhibition depends on the agent used. Although preoperative bleeding time does not seem to predict surgical bleeding, several studies have suggested that the use of NSAIDs in the pre-operative period does lead to significantly increased peri-operative blood loss ^{8,9}.

NSAIDs should be stopped in time to allow recovery of adequate platelet function. This usually occurs within one day for short-acting drugs e.g ibuprofen, diclofenac and within three days for long-acting drugs e.g naproxen, piroxicam ^{6,7,8}. Withholding NSAIDs for longer periods than this is inappropriate, and frequently results in patients being admitted for their procedure with poorly controlled pain. Analgesia during this period can be maintained with paracetamol and/or a weak opioid.

The COX II-selective inhibitors (meloxicam, rofecoxib, celecoxib and etoricoxib) do not inhibit COX I, therefore platelet aggregation is not inhibited.

These agents do not need to be routinely withheld pre-operatively ¹⁰

d) Clopidogrel and Ticlopidine

Clopidogrel is an inhibitor of ADP-induced platelet aggregation. It acts by irreversibly modifying the platelet ADP receptor. Consequently, platelets exposed to clopidogrel are affected for the remainder of their lifespan. If a patient is to undergo elective surgery and an anti-platelet effect is not desired, clopidogrel should be discontinued 7 days before surgery¹¹.

Ticlopidine blocks ADP-induced platelet aggregation and possibly interferes with platelet adhesions which may lead to prolongation of bleeding times. This agent should be stopped 7-10 days before surgery to ensure adequate platelet recovery has been achieved.

e) Dipyridamole

Dipyridamole is both a vasodilator and an inhibitor of platelet function. Dipyridamole reduces platelet adhesion and aggregation. Dipyridamole alone has not been found to increase post-operative bleeding compared to a control group¹². However, dipyridamole is commonly used in conjunction with other agents known to prolong post-operative bleeding such as aspirin and warfarin, and combinations of these drugs have additive effects on platelet function. Therefore, when used in conjunction with aspirin, clopidogrel or warfarin, dipyridamole should also be withheld pre-operatively. Stopping dipyridamole 24 hours pre-operatively is sufficient for adequate platelet recovery^{12,13}.

f) Monoamine Oxidase Inhibitors (MAOI)

MAOI interact with certain drugs used in anaesthesia, including pethidine, dopamine, ephedrine and phenylephrine producing unpredictable effects on blood pressure and even death¹⁴. It is possible to continue taking MAOI if the anaesthetist avoids using these interacting drugs. This would be necessary in the case of emergency surgery or if there was some concern regarding the patient's mental stability if the drug was discontinued.

If it is decided to discontinue these agents then the standard MAOIs (phenelzine, isocarboxazid and tranylcypromine) need to be discontinued two weeks pre-operatively with the close co-operation of the patient's psychiatrist. Moclobemide (a reversible MAOI) only needs to be discontinued 24 hours pre-operatively^{14 15}.

g) Lithium

It is not essential that lithium treatment is stopped before surgery, but close monitoring of fluid and electrolytes is essential due to the narrow therapeutic index of lithium and the usual changes in electrolyte levels post-operatively. Low If it is decided to stop lithium treatment as a precaution then 24 hours pre-operatively is usually sufficient. Close monitoring of fluid balance and electrolytes is essential and a lithium level obtained if possible symptoms of toxicity develop^{15 16}. Concurrent treatment with NSAIDs should be avoided.

h) Oral Contraceptives

Oral progestogen-only contraceptives (Femulen, Micronor, Microval, Neogest, Norgeston, Noriday) may be continued as there is no increased risk of

thromboembolism. This also applies to the progestogen-only depot contraceptives (Depo-Provera, Noristerat).

Stopping the combined oral contraceptive (COC) before major surgery is a controversial issue. The risk of postoperative VTE increases from 0.5-1 % for pill users versus non users. This small excess risk in COC must be balanced against the risks of stopping the pill 4-6 weeks prior to surgery, including unwanted pregnancy, the effects of surgery and anaesthesia on a pregnancy, and the risk of a subsequent termination.¹⁷

j) Hormone Replacement Therapy (HRT)

Taking HRT is likely to increase the risk of post-operative venous thromboembolism but this risk has not been well quantified. Current advice regarding continuing or stopping HRT is conflicting, with the BNF advising stopping HRT¹⁹ and specialist groups advising continuing²⁰. Most women on HRT are likely to have additional risk factors for thromboembolism which in themselves necessitate use of peri-operative thromboprophylaxis. Withdrawing HRT also may precipitate the recurrence of menopausal symptoms at an already stressful time.

Therefore, women may continue their HRT with thromboprophylaxis in addition. If however, the risks of continuing are considered to exceed the benefits then it should be stopped four weeks before elective surgery.

j) Tamoxifen

Tamoxifen is an oestrogen receptor antagonist that is used to treat oestrogen receptor positive breast cancer and anovulatory infertility. The IBIS study recently confirmed that tamoxifen-treated women have approximately a 2.3 fold higher risk of venous thromboembolism (VTE) than those treated with placebo. Approximately 40% of these cases occurred within 3 months of surgery or following immobility. The Committee of Safety of Medicines (CSM) has subsequently considered how the risk of VTE should be managed¹⁸. It advised that patients taking tamoxifen for breast cancer should not stop taking their tamoxifen before surgery unless the risk of tamoxifen-induced thrombosis clearly outweighs the risk of interrupting treatment. They should be prescribed prophylactic heparin. Although no specific advice is currently available for other agents such as anastrozole, similar procedures should be followed. In patients taking tamoxifen for anovulatory infertility tamoxifen should be stopped at least 6 weeks before surgery and only re-started when the patient is fully mobile.

k) Warfarin

See appendix for peri-operative anticoagulation for patients admitted on anticoagulation undergoing elective surgery. For emergency surgery please contact anaesthetist.

l) Insulin

See table for guidelines

m) Oral Diabetic Medication

The only oral hypoglycaemic drug that is essential to stop pre-operatively is chlorpropamide, but this is seldom used now. Metformin may cause lactic acidosis when renal function is impaired, and should be withdrawn 48-72 hours before surgery and procedures involving radio-contrast media. For minor surgery that is unlikely to affect renal function, metformin can be continued^{22 23}. If metformin is stopped it should not be re-started until renal function returns to normal. All other oral hypoglycaemic drugs need to be omitted on the morning of surgery. For minor surgery, they can be re-started once the patient is eating again. For more major surgery and where glycaemic control is very poor patients need to be treated like insulin-dependent diabetics and changed to a sliding scale regime of insulin. Patients may then require subcutaneous insulin for a short period post-operatively whilst they recover from the physiological stresses of surgery. Intensive monitoring of blood glucose levels will be required during this period^{22 23}.

n) DMARDs and Immunosuppressants

For all patients on methotrexate for Rheumatoid Arthritis see appendix 4 for further details.

Other medications frequently used in patients with rheumatic conditions include hydroxychloroquine, sulfasalazine, azathioprine, leflunomide and cyclophosphamide. Little data exist on the use of these agents in the peri-operative period. There is currently no evidence that these agents adversely affect post-operative recovery, although if there are specific concerns regarding the haematological or renal effects of these agents adversely affecting post-operative recovery then they can be withheld several days before surgery and resumed a few days post-operatively⁷. If any of these agents are being used for other conditions, particularly haematological conditions or post-transplantation then the advice of the relevant specialist must be obtained before discontinuing any immunosuppressant therapy

o) Donepezil, Rivastigmine & Galantamine

The acetylcholinesterase inhibitors, donepezil (Aricept), rivastigmine (Exelon) & galantamine (Reminyl®) are used to improve cognitive function in Alzheimer's disease. Through their effects on acetylcholinesterase these agents are likely to exaggerate the muscle relaxation during anaesthesia produced by suxamethonium, hence prolonging neuromuscular blockade. Although not formally studied, these effects have been noted in clinical practice^{27 28}. The relevant pharmaceutical manufacturers recommend discontinuation of both of these agents pre-operatively to avoid these effects. Eisai stated that donepezil is needed to be withdrawn 2-3 weeks prior to surgery as the half life of this drug is in excess of 70 hours. It can then be re-started at the starting dose of 5mg daily promptly after surgery. However, the company also states that should donepezil be discontinued for 3-6 weeks and then re-started then the patient will not obtain the original level of function that they did initially on treatment²⁹. Galantamine activity at the receptor site ceases after 24 hours so a stoppage time of 24 hours can be recommended. Also rivastigmine has a much shorter half-life so the company only recommends omitting the dose the night before

surgery and re-starting therapy immediately post-operatively ³⁰. If there is not the opportunity to withhold these agents for the above time periods then the anaesthetist must be made aware of the potential for prolonged neuromuscular blockade.

p) Drugs of Abuse

There is only limited information regarding the potential for drugs of abuse to interact with drugs used in the peri-operative period. This may be due to a lack of suspected incidents or a lack of awareness of patients' illicit drug use before surgery. There have been case reports of grand mal seizures ³² and severe psychomotor agitation ³² during anaesthesia in cocaine users. There are no documented interactions between cannabis or Ecstasy and drugs commonly used during anaesthesia. It is important for the anaesthetist to be made aware of any pre-operative illicit drug use as there is only minimal information of the effects of these drugs during anaesthesia and it may assist in the management of any unexplained complications.

q) Herbal Medicines

A number of anaesthetists have reported significant changes in heart rate and blood pressure in those patients taking certain herbal preparations. This has led to the American Society of Anaesthesiologists advising all patients to stop taking their herbal preparations at least two weeks before elective surgery ^{33 34}. Increasing usage of these agents in the general population have resulted in the need for more detailed guidelines in the use of these agents in the peri-operative period. These are in preparation at present and will be launched later in 2003. Some of the potential problems that may be associated with herbal products include:

36

Echinacea	Preferably discontinue as far in advance as possible before surgery.	Increases risk of allergic reactions, may increase risk of infection.
Ephedra	Preferably discontinue at least 24 hours before surgery as may increase heart rate and blood pressure.	Increased risk of MI and stroke. Increased risk of ventricular arrhythmias in patients anaesthetised with halothane
Garlic tablets	Preferably discontinue at least 7 days prior to surgery	Increased risk of bleeding secondary to anti-platelet effect
Ginkgo	Preferably discontinue at least 36 hours before surgery.	Increased risk of bleeding secondary to anti-platelet effect.

East Cheshire NHS Trust

Ginseng	Preferably discontinue at least 7 days before surgery	May increase risk of hypoglycaemia, and bleeding.
St John's Wort	Preferably discontinue at least 5 days before surgery	Inhibits neurotransmitter uptake
Valerian	Preferably reduce dose gradually over several weeks before surgery.	Could increase sedative effect of anaesthetics. Long term use may increase doses of anaesthetic required.

Drugs that should be CONTINUED

It is essential that certain medicines be continued throughout the peri-operative period to prevent the relapse of the treated condition or to avoid the effects of drug withdrawal. Continuation may necessitate that the drug is given by an alternative route or changed to an alternative drug with a similar action. The most important drugs have been mentioned below.

Medication	Recommendations	Comments	Alternative route if oral unavailable
Antihypertensives (Beta-blockers, calcium channel antagonists, ACE inhibitors)	Continue as usual	Rebound hypertension can occur if stopped abruptly. Monitor BP closely post-op.	Injections are available of some drugs only- may need to be changed to an alternative drug if oral route not possible
Antacids and ulcer-healing drugs (H ₂ blockers, proton pump inhibitors, antacids)	Continue as usual	Essential prior to anaesthesia	Ranitidine, pantoprazole and omeprazole available as injections.
Antianginals (Nitrates, nicorandil, calcium channel antagonists)	Continue as usual	May precipitate chest pain if withheld.	Convert nitrates to patch and use buccal for chest pain. Alternative agents may be required as few are available as injections.
Antiarrhythmics (Amiodarone, digoxin, flecainide)	Continue as usual	Possibility of recurrence of arrhythmias if stopped. Check digoxin levels.	Intravenous forms available- require careful monitoring.
Anticonvulsants (Phenytoin, sodium valproate, carbamazepine)	Continue as usual	Possibility of precipitating convulsions if stopped. Ensure prn diazepam Rx.	Intravenous and rectal forms available- not all bioequivalent.
Antidepressants (Tricyclics, SSRIs) NOT MAOIs	Continue as usual	Withdrawal symptoms can occur if stopped abruptly.	Monitor for withdrawal symptoms- no alternative forms commercially available.
Antipsychotics (Haloperidol, Chlorpromazine)	Continue as usual	Withdrawal symptoms can occur if stopped abruptly plus severe agitation.	IV forms available. May also need prn doses prescribing.
Benzodiazepines (Diazepam, lorazepam)	Continue as usual	Withdrawal symptoms can occur if stopped abruptly.	Rectal and IV forms available.
Bronchodilators (Salbutamol, ipratropium, theophylline)	Continue as usual	May precipitate bronchospasm if withheld.	Use nebulas. Can convert oral to iv amionophylline if necessary.
Corticosteroids (Dexamethasone, prednisolone)	Continue as usual	Increased risk of Addisonian crisis if stopped.	SEE GUIDELINES BELOW*
Parkinsons medication (Madopar, Sinemet)	Continue as usual	Movement disturbances will return on withdrawal of treatment.	Apomorphine injection available but for specialist use only- very emetic.
Thyroid medication (Thyroxine, carbimazole)	Continue as usual	Both have 3-4/7 half-life. After this time need replacing.	Thyroxine → IV liothyronine (not bioequivalent). No commercially available pr or IV carbimazole.

***Corticosteroids³⁵**

Current dose <10mg/day
Current dose >10mg/day

Assume normal HPA response
Minor surgery
Moderate surgery

Major surgery

High-dose immunosuppression

Additional steroid cover not required
25mg hydrocortisone at induction
25mg hydrocortisone at induction + 100mg per day for 24 hours
25mg hydrocortisone at induction + 100mg per day for 48-72 hours
Give usual immunosuppressive doses during peri-operative period
Treat as if on steroids
No peri-operative steroids necessary

Stopped taking steroids

<3 months ago
>3 months ago

Peri-operative anticoagulation for patients admitted on anticoagulation undergoing elective surgery

Pre-op target
INR <1.5
or Surgeon / anaesthetist discretion
(check for specialist instructions in notes)

Low Risk Patient

5 Days before Surgery
Stop Oral Anticoagulation

- Routine thromboprophylaxis should be initiated as normal in patients and continued until oral anticoagulation is within therapeutic range
- Evening of surgery
Restart oral anticoagulation unless NBM, has epidural or at surgeon/anaesthetic discretion
1.5 x normal dose for 2 days
- Check INR day 3
- If less than or within therapeutic range recommence normal anticoagulant dose
- If INR above therapeutic range seek advice.

Arrange earliest anticoagulant clinic appointment on discharge

High Risk Patient

5 Days before Surgery
Stop oral anticoagulation. Commence Tinzaparin 175 iu/kg each morning 4 days prior to surgery (if CrCl < 30ml/min use clexane 1mg/kg each morning)

Morning of Surgery
Check INR.
Omit Tinzaparin dose
Administer prophylactic enoxaparin dose four hours post-op

- Commence oral anticoagulant on evening of surgery unless NBM, has epidural or at surgeon/anaesthetic discretion.
- Day Following Surgery restart therapeutic dose of Tinzaparin and continue until INR within therapeutic range.
- Dose 1.5 x normal for two days. Check INR day 3. If within therapeutic range recommence normal anticoagulant dose
- If INR above or below therapeutic range seek advice.

Arrange earliest anticoagulant clinic appointment on discharge

Clot Low Risk

eg; Atrial fibrillation

Clot Risk High

Prosthetic (mechanical) heart valve
All DVT/PE on anticoagulation

NB - ENSURE YELLOW ANTI-COAGULANT RECORD BOOK IS UPDATED

**If in doubt seek advice – Consultant Haematologist - Dr John Hudson ext. 1801 or switchboard
Pharmacy Medicines Information - ext 1268 or 3835**

Anticoagulation Policy Working Party:

Dr J Hudson	-	Consultant Haematologist
Dr M Rothwell	-	Consultant Anaesthetist
Mr P Denn-	Associate	Specialist Orthopaedics
Mr K R Ratnam	-	Associate Specialist Orthopaedics
Dr R Egdell	-	Consultant Cardiologist
Mrs P Rowan	-	Peri-operative Specialist Practitioner
Ms C Lloyd	-	Peri-operative Specialist Practitioner
Mrs A Littlewood	-	Medicines Management Pharmacist
Miss E Oliver	-	Clinical Pharmacist

NB 4 days of tinzaparin supplied from hospital pharmacy. Patient attends admitting ward for daily administration of tinzaparin. Case notes sent to ward from pre-op assessment clinic. If patient unable to attend arrange with district nurse.

Approved by MMG
Date; February 2007
Review date: February 2011
Adapted from North Cheshire Hospital
NHS Trust Guidelines

Effective date Sept 2009 Review Date Sept 2011

ines Version 1

Appendix 2

East Cheshire NHS Trust Surgical Business Unit Policy for patients having elective surgery who are taking anti-platelet agents *and* who have a coronary stent.

Summary:

- Clopidogrel increases bleeding and should be stopped 10 days before any elective surgery **UNLESS THE PATIENT HAS AN INTRACORONARY STENT**, when doing so can greatly increase the chance of stent thrombosis with a high mortality. At the moment we are only seeing a small number of patients presenting with a stent and taking clopidogrel.
- Clopidogrel *should be continued perioperatively* in these patients unless the surgeon or anaesthetist feels that it would be a significant risk to do so. Such cases should be referred to Dr Egdell, Consultant Cardiologist.
- The risk of stopping clopidogrel in these circumstances is very variable, dependant on many risk factors and opinion is evolving. Appropriate courses of action, as well as continuing or stopping the drug, may include deferring or cancelling surgery or even performing it in another facility.

Clopidogrel:

Clopidogrel is a potent irreversible antiplatelet agent. Restoration of platelet function relies on the patient making new platelets, which takes a week. Bleeding can be treated by platelet transfusion because the plasma half life (as opposed to the effect) of clopidogrel is short. Since its introduction, it has become clear that clopidogrel causes significant bleeding and it is usual practise to stop it one week before elective surgery. Clopidogrel has many indications. For nearly all of these it is clear that it should be stopped during the perioperative period even for minor surgery. The one situation where this is not the case is if the patient has a coronary stent.

Clopidogrel is increasingly prescribed with aspirin following the 90% of percutaneous coronary interventions which now involve stents. PCI causes trauma to the vessel wall, activating platelets and causing coronary thrombosis if antiplatelet drugs are not used. There is increasing evidence that stopping clopidogrel *even for a short time* is a bad idea, particularly in the context of the perioperative hypercoagulable state. Perioperative LMWH alone doesn't solve the problem.

This is not a minor issue. Non-cardiac surgery following stenting has been associated with a cardiac complication rate of up to 45% and a mortality of 5-20% in two recent major studies. The treatment for suspected stent thrombosis is urgent PCI, which is a difficult, risky procedure with a higher mortality than major bleeding.

Aspirin:

Aspirin is a lifelong therapy which should never be stopped after a coronary or cerebrovascular event. It may be stopped seven days prior to surgery if it is for primary prevention only. Neuraxial blocks are safe with up to 300mg per day of aspirin.

Weighing up the risks:

The decision to stop antiplatelet therapy, particularly clopidogrel, depends on the balance of what the surgeon feels the risks and consequences of bleeding are if you

don't, and what the cardiologists think the risk of stent thrombosis is if you do. Anaesthetists must play a role in balancing these concerns.

Risks of stopping clopidogrel and causing stent thrombosis:

- Cessation of antiplatelet therapy is the major independent predictor of late stent thrombosis. This in turn has a 50% incidence of acute MI and a 20% mortality.
- Although operating on patients taking clopidogrel increases bleeding considerably, it doesn't seem to increase morbidity, mortality, or surgical outcome. There is now good evidence that stopping it does.
- The risk is greater:
 - the more recently the stent was implanted
 - with drug eluting stents as opposed to bare metal stents
 - if the patient has other risk factors for stent thrombosis which are:
 - renal failure
 - diabetes mellitus
 - low ejection fraction
 - PCI involving bifurcation lesions or multiple drug eluting stents

Risks of continuing clopidogrel and causing excessive bleeding:

- In non-cardiac surgery, patients on aspirin and clopidogrel have 25-40% increased risk of bleeding. Some studies however, have failed to show any difference.
- Clopidogrel is an absolute contraindication to regional or neuraxial block. Neuraxial blocks are used extensively at ECNHS Trust for lower limb joint replacements and laparotomies. They provide superior pain relief and confer a morbidity / mortality advantage on high risk surgical patients. Not doing them may increase risk to the patient.
- Consideration should be given to stopping clopidogrel if there is risk of bleeding into a closed space, for example neurosurgery or posterior chamber eye surgery.

At ECNHS Trust we have no immediate on-site access to either platelets to treat clopidogrel-induced bleeding, or PCI to treat stent thrombosis. It may be that patients where this balance is very controversial should have their surgery in institutions where these are available.

Type of stent and timing of insertion:

There are two main types of stent; bare metal stents and drug eluting stents.

Bare metal stents:

BMS fail by being occluded with scar tissue. The risk is 12-20% within six months. Late re-stenosis is rare. Clopidogrel is normally only given until the stent is epithelialised, which takes about 6-12 weeks. Stopping it after that time is probably low risk.

Drug eluting stents:

These are coated with an antiproliferative drug to prevent scarring. However, the drug elution prevents them epithelialising rendering them *more* prone to thrombosis, especially on stopping clopidogrel. DES fail by stent thrombosis. The risk is 5% within 6 months. Clopidogrel is therefore used for a year and the trend is to use it for even longer. 80% of stents inserted are now of this type.

With both types, aspirin therapy is usually for life.

The European Society of Cardiologists recommend that if it is known that the patient will have non-cardiac surgery soon, a BMS should be used.

Examples of possible scenarios:

1. Patient listed for elective knee replacement.

Serious consideration should be given to deferring the surgery until the clopidogrel would normally have been stopped. This would not normally be for more than a year.

2. Patient requiring emergency surgery with a high risk of bleeding.

Order platelets as well as cross matching blood. Do not use a neuraxial block. Restart antiplatelet therapy as soon as team confident that risk of bleeding is low

3. Patient for an urgent planned laparotomy for colorectal cancer.

Potentially the most difficult because the timing of surgery is restricted. Anaesthetist will have to try to quantify how much of a survival benefit an epidural could afford, which will depend on how "high risk" the patient is. Many may have to be done with a PCA.

If the decision is to continue clopidogrel; platelets should be available in the hospital.

If clopidogrel is stopped:

aspirin should be continued.

the patient should have enoxaparin 40mg once a day at night for three days afterwards

It should be restarted as soon as possible. This may be:

the same day unless there is a reason not to

as soon as the patient can eat and drink

after an epidural catheter has been removed at 48-72 hours post-op.

An initial loading dose of 300mg should be given.

In all cases, the decision about what to do with a stented patient's antiplatelet therapy should be discussed with them during the consent process.

References:

Review Article- Coronary artery stents and non-cardiac surgery

Howard-Alpe G, de Bono J et al

British Journal of Anaesthesia 98(5):560-574 (2007)

Editorial- Coronary stents and perioperative anti-platelet regimen: dilemma of bleeding and stent thrombosis

Spahn D, Howell S et al

British Journal of Anaesthesia 96(6):675-677 (2006)

Coronary artery stenting and non-cardiac surgery- a prospective outcome study

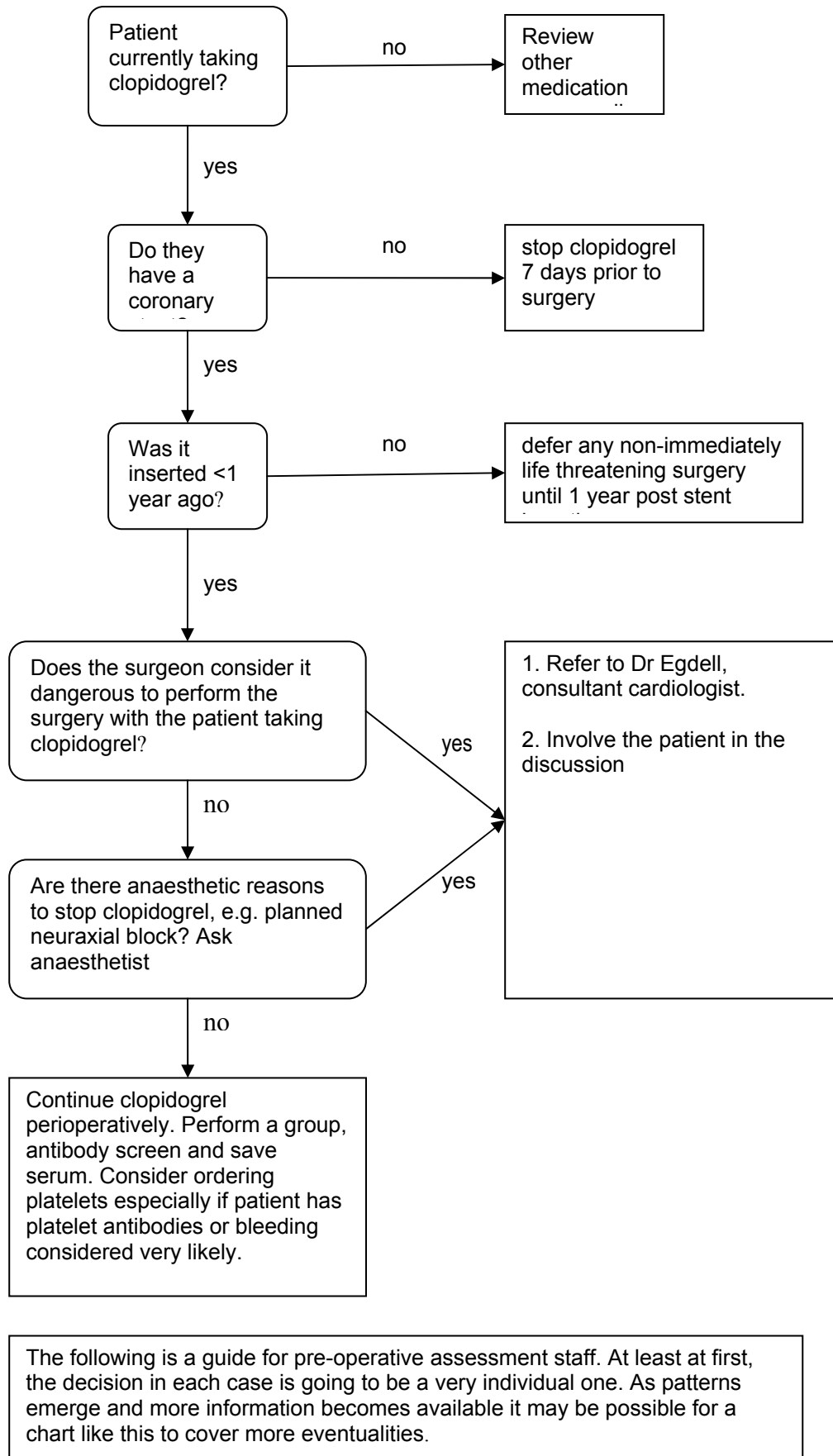
Vicenzi M, Meislitzer T et al

British Journal of Anaesthesia 96(6):686-693 (2006)

Dr David Banks

Consultant Anaesthetist

June 2007



Appendix 3

List of Insulins

Short Acting Insulins

Actrapid
Humulin S
Novorapid
Apidra
Humalog

Intermediate Acting Insulin

Humalog Mix 25
Humalog Mix 50
Mixtard 30
Humulin M3
Novomix 30

Long Acting Insulin

Lantus
Levemir
Insulatard

For further information see current BNF

Appendix 4

EVIDENCE-BASED MEDICINE: PERIOPERATIVE USE OF METHOTREXATE IN PATIENTS WITH INFLAMMATORY JOINT DISEASE

Deborah PM Symmons

Honorary Consultant Rheumatologist
East Cheshire NHS Trust
Victoria Road
Macclesfield SK10 3BL

Director
Arthritis Research UK Epidemiology Unit
Manchester Academic Health Sciences Centre
Stopford Building
University of Manchester
Oxford Road
Manchester M13 9PT

Telephone: +44 161 275 5044

Fax: +44 161 275 5043

e-mail: deborah.symmons@manchester.ac.uk

Methotrexate is the “anchor” disease modifying anti-rheumatic drug (DMARD) used in the treatment of rheumatoid arthritis (RA). It is also extensively used in patients with psoriasis and psoriatic arthritis (PsA). Methotrexate is a structural analogue of folic acid which competitively inhibits the binding of dihydrofolic acid to folate-dependent enzymes such as dihydrofolate reductase (DHFR). Methotrexate decreases the amount of intracellular folinic acid and affects the metabolic pathways within the cell that are folinic acid dependent. Despite its known site of action, the exact mechanism by which methotrexate improves the signs and symptoms of RA is unclear. It appears to have only marginal effects on humoral and cellular immune responses. Many of its therapeutic effects in RA may be due to anti-inflammatory activity.

Methotrexate is used in a wide range of doses: most commonly between 7.5mg and 25mg weekly. It may be administered either orally or by subcutaneous injection. Patients usually also take oral folic acid on at least one other day of the week in order to reduce the risk of side effects.

Methotrexate is absorbed rapidly and completely at the dosages used to treat RA. After absorption 50-70% is bound to plasma proteins, mainly albumin. Methotrexate is primarily cleared by the kidneys and 80-90% is excreted unchanged in the urine. Any impairment of renal function will result in increased serum levels of methotrexate which may increase the possibility of bone marrow, liver and other toxicities (see below). Methotrexate use in RA is contraindicated if the estimated glomerular filtration rate (eGFR) is less than 30ml per minute. In patients with an eGFR of 30-59 ml per minute, the dose should be reduced.

Side effects of methotrexate

Adverse reactions to methotrexate are common but usually minor. These include gastrointestinal problems such as nausea, diarrhoea and stomatitis. Patients may also complain of headache, fatigue or impaired ability to concentrate. Predisposing factors for toxicity are higher dose, advanced age, renal insufficiency and concomitant use of other antifolates (such as trimethoprim). Major side effects include

1 Hepatotoxicity

Methotrexate may cause direct damage to hepatocytes or may enhance viral damage in patients with concomitant hepatitis B or hepatitis C. Patients on long-term methotrexate therapy should have regular monitoring of their transaminase levels and serum albumin.

2 Myelosuppression

Methotrexate is frequently associated with a macrocytosis which is usually of no clinical significance. However, it may also be associated with leucopenia, thrombocytopenia and pancytopenia. Regular monitoring of the full blood count should detect this. Myelosuppression is more likely if renal function is impaired or if methotrexate is accidentally taken daily instead of weekly.

Infection and methotrexate

The risk of infection in patients receiving methotrexate has not been well established. Infections seem to be more common in patients who are receiving glucocorticoids in addition to methotrexate, but there is no clear evidence that methotrexate alone increases the risk of infection. However there are case reports of opportunistic infections such as pneumocystis jirovecii pneumonia and cytomegalovirus occurring in patients exposed to methotrexate.

Perioperative use of methotrexate

Patients with inflammatory disorders who are taking methotrexate may have to undergo emergency or elective surgery. In particular, they may require orthopaedic surgery such as total joint replacement. There are a number of theoretical concerns with regards to the perioperative use of methotrexate. Concern has been expressed that methotrexate may delay wound healing, increase the risk of perioperative infections or that methotrexate toxicity may be more likely in the perioperative period because of impaired renal function secondary to temporary dehydration or the use of additional drugs. This short paper reviews the available guidelines for the perioperative use of methotrexate as well as the evidence on which they are based.

Current guidelines

The British Society for Rheumatology Guidelines currently state, "Therapy can be continued. Caution for early detection of infection and complications."**(1)** A recent multi-national panel of rheumatologists, in a consensus study funded by Abbott, made a series of recommendations **(2)**. Recommendation 9 out of 10 stated, "Methotrexate can be safely continued in the perioperative period in RA patients undergoing elective orthopaedic surgery." Both these sets of guidelines advocate the careful monitoring of patients on methotrexate, in particular with respect to renal function, in the routine situation. It seems strange, therefore, that both sets of guidelines should recommend continuing methotrexate throughout the perioperative period without any mention of the need to check renal and liver function preoperatively and in the immediate post-operative period. Both sets of guidelines are based on a limited number of relevant publications which are summarised below.

A review of the literature on which the guidelines are based

The first relevant paper was published in 1991. From the University of Birmingham, Alabama diagnostic index of around 300 patients with RA who had started methotrexate between 1981 and 1989, Bridges et al identified 38 patients who had undergone elective orthopaedic surgery. They divided the patients into two groups according to whether or not they had received a dose of methotrexate within four weeks of surgery. The mean weekly dose of methotrexate in both groups was 8mg. There were 4 complications (prosthetic joint infection, wound dehiscence or infection) in the 19 patients who underwent surgery within 4 weeks of receiving a dose of methotrexate. There were no complications in the 25 patients who were not taking methotrexate at the time of surgery. 41% of the procedures in this second group were performed before methotrexate was ever started. Six patients were included in both groups for different procedures. These results were statistically

significantly different and the authors concluded that methotrexate may play a role in early post-operative complications in patients with RA. **(3)**. In 1993, Sany et al published the first randomised study of methotrexate withdrawal in patients with RA undergoing orthopaedic surgery. In this unblinded study, 64 patients were randomised either to have their methotrexate discontinued one to two weeks before surgery and re-started one month later (a total of approximately six weeks off methotrexate) or to continue the methotrexate. The mean weekly methotrexate dose in both arms was 10mg. No post operative infections occurred in either arm. Delayed wound healing was observed in 10% of the procedures in which methotrexate was continued and 12% of the procedures in which it was discontinued. These differences were not statistically significant. All the patients who discontinued their methotrexate for more than four weeks experienced a flare in their RA. The authors concluded that interruption of methotrexate was not required in patients with RA, although they did recommend that a larger study be conducted **(4)**. In 1995, Escalante and Beardmore in San Antonio, Texas conducted an audit of 204 patients with RA who had undergone a total of 367 orthopaedic operations. Their aim was to identify risk factors for the occurrence of early wound complications following surgery. In a multivariate model, the only significant predictors of complications were Hispanic ethnicity and operative blood loss. Complications were less frequent amongst patients given methotrexate than those on other DMARDs but the difference was not significant **(5)**. The mean weekly dose of methotrexate was not given. In a study of 32 patients at the Fitzsimons Army Medical Centre, Colorado, the orthopaedic surgeon and/or rheumatologist assigned patients either to withhold the methotrexate the week prior to and the week of surgery (n=19) or to maintain methotrexate throughout the perioperative period (n=13) **(6)**. The mean weekly dose of methotrexate was 12.5mg (with an upper limit of 20mg). Four post-operative infections occurred in the group who continued their methotrexate while none occurred in the group who stopped their methotrexate for two weeks. These differences were statistically significant. All infections occurred within one month post-operatively. There were no disease flares. Perhala et al **(7)** found no significant difference in complications between 61 RA patients who withheld methotrexate 1-4 weeks before total hip or knee replacement and 60 patients who continued methotrexate throughout the perioperative period (5.5% versus 8.7% of procedures with complications). Nevertheless, it is the group who continued the methotrexate who had the higher complication rate. The mean weekly dose of methotrexate in this study was 8.2mg.

By far the most influential paper is the randomised controlled trial undertaken at Wrightington Hospital by Grennan et al **(8)**. They studied three groups of patients with RA undergoing elective orthopaedic surgery. Group A were patients who had been taking methotrexate for at least 6 weeks before surgery was undertaken and who continued their methotrexate treatment throughout. Group B were patients in whom methotrexate treatment was stopped two weeks prior to surgery and restarted two weeks after surgery. Group C were patients who were not on methotrexate at the time the decision was made to operate. Sample size calculations indicated that 400 subjects were needed in each of Group A and Group B in order to detect a doubling of the complication rate in Group A vs Group B with

80% power and a 5% significance level. The initial protocol allowed for an interim analysis at two years, although no stopping rules were stated. Patients were randomly allocated to either Group A or Group B by the study co-ordinator who attempted to match subjects for type of surgery and who used a block of 10 randomisation design. No one was blinded to treatment allocation. By the time of the interim analysis, 88 patients had been recruited to Group A, 72 to Group B and there were 228 in Group C. Thus, whilst this is often quoted as being a large trial of 388 patients, in fact, there were only 160 patients in the two treatment arms. The mean weekly dose of methotrexate was 10mg in Group A and 7.5mg in Group B. Group A experienced 2 complications (one wound discharge and one wound dehiscence). There were 11 complications in Group B (4 wound redness, 4 wound discharge, 1 wound dehiscence and 2 other complications (not further clarified). Combining all these post-operative events, the rate of complications was higher in the group who continued their methotrexate than in those that discontinued it. Interestingly, when Groups A, B and C were combined, methotrexate in any dose and whether continued or discontinued before surgery did not increase the risk of surgical complications, suggesting that the differences observed were due to the differences in other co-morbidities and drugs. For example, there was a higher prevalence of diabetes, hypertension, bronchitis and steroid use in the group who temporarily stopped their methotrexate. Six weeks after surgery, none of the patients in Group A and 6 (8%) in Group B had evidence of flare of their RA. There was no statistically significant difference in disease activity at 6 months and 12 months after surgery. The authors concluded that there is no need to stop methotrexate in the perioperative period. **(8).**

A further retrospective study was published in 2005 from Japan where methotrexate is only licensed in doses up to 8mg weekly. It is debatable whether the results of this study can be generalised to European Caucasian patients. The study comprised 77 procedures in patients who continued methotrexate, 21 procedures in patients who discontinued methotrexate at least one week preoperatively and 103 procedures in patients who were not taking methotrexate in the relevant time period. The mean weekly dose of methotrexate was under 5mg. No mention is made as to when the patients restarted their methotrexate. At 4 weeks post-operatively, arthritis flares were seen in 14.3% of the group who discontinued their methotrexate and 3.9% of patients who continued. Poor wound healing was observed more frequently in the group who discontinued their methotrexate but the differences were not statistically significant **(9).**

Perioperative use of methotrexate					
Evidence for stopping			Evidence for continuing		
Reference	Continued MTX Number (complications)	Stopped MTX Number (complications)	Reference	Continued MTX Number (complications)	Stopped MTX Number (complications)
Bridges et	19 (4)	25 (0)	Sany et al	32 (3)	32 (4)

al			*		
Carpenter et al *	13 (4)	19 (0)	Perhala et al	60 (5)	61 (3)
			Grennan et al *	88 (2)	72 (11)
			Murata et al **	77 (4)	21 (3)
Total	32 (8) (25%)	44 (0) (0%)		257 (14) (5.4%)	186 (21) (11.3%)
* randomised ** very low dose methotrexate in Japanese					

Summary

The major concern in all these studies was whether methotrexate therapy influences the risk of post-operative wound infections following elective orthopaedic surgery. All the studies are small and group all severities of complication together. The largest number of complications in any treatment group in a single study is 11. The studies were mainly conducted in the era when methotrexate doses were substantially lower than those in use today. Nevertheless, in controlled situations, it would seem that wound infections are not increased in patients who continue their methotrexate therapy and that there is a significant risk of disease flare in RA patients who stop their methotrexate for four weeks or more. The only study which stopped methotrexate for a period of two weeks **(6)** found no increase in disease flares. None of these studies addressed the issue of monitoring renal function around the period of surgery and no serious post-operative complications or deaths are reported in any of these studies. However, it is quite likely that such complications may have been systematically missed in the retrospective cohort studies.

It would seem unwise for the BSR and the international guidelines to recommend that methotrexate should be continued throughout the perioperative period without any mention of the need to monitor renal function. These guidelines are easily accessible and may be consulted and followed by surgical teams with little background knowledge of the risks and benefits of methotrexate. The international guidelines do not indicate that there is no published information on the perioperative safety of methotrexate for other forms of surgery, in particular gastrointestinal surgery. When so much emphasis is placed upon monitoring renal function in the stable condition, especially in the elderly, it seems only logical that it should be monitored even more closely in the perioperative situation where it may become impaired. Elective orthopaedic operations are often performed on elderly patients with multiple co-morbidities and so at high risk of impaired renal function.

Recommendations

It would seem, therefore, that the safest option is to advocate the following:

- 1 All patients on methotrexate should have their renal function checked within 6 weeks of any planned operation.
- 2 If the eGFR is > 30 ml/min then methotrexate should be omitted the week before and the week after surgery. Renal function should be checked again post-operatively and if it has not changed then the same dose of methotrexate can be re-started if the patient is making satisfactory progress.
- 3 If the eGFR is ≤ 30 ml per minute, then all medications should be discussed with the rheumatologist prior to surgery.
- 4 Patients should not stop their methotrexate for more than two weeks without good reason. The rheumatologist should be consulted in this situation.
- 5 Patients should be informed in writing at the time of their pre-operative assessment when they should omit their methotrexate. They should also be informed that any stop of treatment is only short-term and that they should expect to be taking the same dose of methotrexate when they go home as when they came into hospital. They should continue to take their folic acid in the usual prescribed dosage throughout.
- 6 The rheumatology nurse is always available to provide advice to patients on their methotrexate dosage and monitoring

References

- 1 Chakravarty K, McDonald H, Pullar T et al *BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Society of Dermatologists* Rheumatology 2008
- 2 Visser K, Katchamart W, Loza E et al *Multi national evidence based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative*
Ann Rheum Dis. 2009 Jul;68(7):1086-93
- 3 Bridges EL, Lopez-Mendez A, Han KH, Tracy IE, Alarcon GS *Should methotrexate be discontinued before elective orthopaedic surgery in patients with rheumatoid arthritis?* J Rheumatol 1991 18: 98—8
- 4 Sany J, Anaya J-M, Canovas F et al *Influence of methotrexate on the frequency of postoperative infectious complications in patients with rheumatoid arthritis* J Rheumatol 1993; 20: 1129-33
- 5 Escalante A and Beardmore TD *Risk factors for early wound complications after orthopedic surgery for rheumatoid arthritis.* J Rheumatol 1995; 22:1844-51
- 6 Carpenter MT, West SG, Vogelgesang SA, Caset Jones DE *Postoperative joint infections in rheumatoid arthritis patients on methotrexate therapy* Orthopaedics 1996; 19: 207-10
- 7 Perhala RS, Wilke WS, Clough JD, Segal AM *Local infectious complications following large joint replacement in rheumatoid arthritis patients treated with methotrexate versus those not treated with methotrexate* Arthritis Rheum 1991; 34: 146-52
- 8 Grennan DM, Gray J, Lowden J et al *Methotrexate in early post-operative complications in patients with rheumatoid arthritis undergoing elective orthopaedic surgery.* Ann Rheum Dis 2001 60:214-7
- 9 Murata K, Yusuda T, Ito H et al *Lack of increase in post-operative complications with low dose methotrexate therapy in patients with rheumatoid arthritis undergoing elective orthopaedic surgery.* Mod Rheumatol 2006 16; 14-19

Suggested form of leaflet to give to rheumatology patients who are listed for surgery. This could include other medication as well:

You have been listed to have an orthopaedic operation. Some of the medication that you take for your arthritis may need to be stopped shortly before surgery and restarted again afterwards.

1. Anti-inflammatory drugs such as

Appendix 5

Equality and Human Rights Policy Screening Tool

Policy Title: Peri-operative Drug Management Guidelines				Directorate: Trust wide			
Name of person/s auditing / authoring policy: Lead Surgical Pharmacist							
Policy Content: <ul style="list-style-type: none"> For each of the following check whether the policy under consideration is sensitive to people of a different age, ethnicity, gender, disability, religion or belief, and sexual orientation? The checklist below will help you to identify any strengths and weaknesses of the policy and to check whether it is compliant with equality legislation. 							
1. Check for DIRECT discrimination against any minority group of PATIENTS:							
Question: Does the policy contain any statements which may disadvantage people from the following groups?		Response		Action required		Resource implication	
		Yes	No	Yes	No	Yes	No
1.0	Age?		X		X		X
1.1	Gender (Male, Female and Transsexual)?		X		X		X
1.2	Learning Difficulties / Disability or Cognitive Impairment?		X		X		X
1.3	Mental Health Need?		X		X		X
1.4	Sensory Impairment?		X		X		X
1.5	Physical Disability?		X		X		X
1.6	Race or Ethnicity?		X		X		X
1.7	Religious Belief?		X		X		X
1.8	Sexual Orientation?		X		X		X
2. Check for DIRECT discrimination against any minority group relating to EMPLOYEES:							
Question: Does the policy contain any statements which may disadvantage employees or potential employees from any of the following groups?		Response		Action required		Resource implication	
		Yes	No	Yes	No	Yes	No
2.0	Age?		X		X		X
2.1	Gender (Male, Female and Transsexual)?		X		X		X
2.2	Learning Difficulties / Disability or Cognitive Impairment?		X		X		X
2.3	Mental Health Need?		X		X		X
2.4	Sensory Impairment?		X		X		X
2.5	Physical Disability?		X		X		X
2.6	Race or Ethnicity?		X		X		X
2.7	Religious Belief?		X		X		X
2.8	Sexual Orientation?		X		X		X
TOTAL NUMBER OF ITEMS ANSWERED 'YES' INDICATING DIRECT DISCRIMINATION = 0							

3. Check for INDIRECT discrimination against any minority group of PATIENTS:							
Question: Does the policy contain any conditions or requirements which are applied equally to everyone, but disadvantage particular people because they cannot comply due to:		Response		Action required		Resource implication	
		Yes	No	Yes	No	Yes	No
3.0	Age?		X		X		X
3.1	Gender (Male, Female and Transsexual)?		X		X		X
3.2	Learning Difficulties / Disability or Cognitive Impairment?		X		X		X
3.3	Mental Health Need?		X		X		X
3.4	Sensory Impairment?		X		X		X
3.5	Physical Disability?		X		X		X
3.6	Race or Ethnicity?		X		X		X
3.7	Religious, Spiritual belief (including other belief)?		X		X		X
3.8	Sexual Orientation?		X		X		X

4. Check for INDIRECT discrimination against any minority group relating to EMPLOYEES:							
Question: Does the policy contain any statements which may disadvantage employees or potential employees from any of the following groups?		Response		Action required		Resource implication	
		Yes	No	Yes	No	Yes	No
4.0	Age?		X		X		X
4.1	Gender (Male, Female and Transsexual)?		X		X		X
4.2	Learning Difficulties / Disability or Cognitive Impairment?		X		X		X
4.3	Mental Health Need?		X		X		X
4.4	Sensory Impairment?		X		X		X
4.5	Physical Disability?		X		X		X
4.6	Race or Ethnicity?		X		X		X
4.7	Religious, Spiritual belief (including other belief)?		X		X		X
4.8	Sexual Orientation?		x		X		X

TOTAL NUMBER OF ITEMS ANSWERED 'YES' INDICATING INDIRECT DISCRIMINATION = 0							
--	--	--	--	--	--	--	--

Signatures of authors / auditors:

Date:

Equality and Human Rights Compliance / Percentage Calculation

Number of 'Yes' answers for DIRECT discrimination.	(A)0
Number of 'Yes' for INDIRECT discrimination.	(B)0
Total answers for POLICY CONTENTS discrimination.	(A+B)0
Percentage content non compliant	= 0 (Divide a+b by 36 x 100)

REFERENCES

1. Phillips S, Hutchinson S, Davidson T. Pre-operative drinking does not affect gastric contents. *Br J Anaesth* 1993; 70:6-9
2. Dawson J, Karalliedde L. Drug Interactions and the clinical anaesthetist. *Eur J Anaesthesiol* 1998; 15: 172-89
3. Drugs in the peri-operative period: 1- stopping or continuing drugs around surgery. *Drugs Ther Bull* 1999; 37: 62-4
4. Chui PT, Chung DCW. Medications to withhold or continue in the pre-operative consultation. *Curr Anaesth Crit Care* 1998; 9 :302-6
5. Drugs in the peri-operative period: 4- Cardiovascular drugs.; *Drugs Ther Bull* 1999; 37: 89-92
6. Stafford-Smith M, Muir M, Hall R. Peri-operative management of drug therapy. *Drugs* 1996; 51: 238-259
7. Kelley JT, Conn DL. Perioperative management of the rheumatic disease patient. *Bulletin on the rheumatic diseases* 2002; 51(6): 1-7
8. Connelly CS, Panush RS. Should nonsteroidal anti-inflammatory drugs be stopped before elective surgery? *Arch Intern Med* 1991; 151: 1963-6
9. Robinson CM, Christie J, Malcolm-Smith N. Non-steroidal antiinflammatory drugs, peri-operative blood loss, and transfusion requirements in elective hip arthroplasty. *J Arthroplasty* 1993; 8: 607-10
10. Reuben SS, Fingerioth R, Krushell R, Maciolek H. Evaluation of the safety and efficacy of the peri-operative administration of rofecoxib for total knee arthroplasty. *The Journal of arthroplasty* 2002; 17(1): 26-31
11. Personal communication. Medical Information department, Sanofi-Synthelabo Ltd. December 2002.
12. Nuutinen LS et al. The effect of dipyridamole on the thrombocyte count and bleeding tendency in open heart surgery. *J Thorac Cardiovasc Surg* 1977; 74: 295-298
13. Personal communication. Information services department, Boehringer Ingelheim Ltd. December 2002.
14. Stack CG, Rogers P, Linter SPK. MAOI and anaesthesia. *Br J Anaesth* 1988; 60: 222-7
15. Motalebzadeh R. Surgery in patients with psychiatric disorders. *Surgery* 1999; 17: 53-55
16. Using lithium safely. *Drugs Ther Bull* 1999; 37: 22-4
17. SIGN Guidelines 62, Prophylaxis of Venous Thromboembolism, Section 10 Oral Contraceptives and hormone replacement therapy.
18. CSM and MCA .Current problems in Pharmacovigilance 2002; 28: 10
19. Sridhar R, Grigg AP. The perioperative management of anticoagulation. *Australian Prescriber* 2000; 23: 13-16
20. Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery. *NEJM* 1997; 336: 1506-1511
21. Bass S. Peri-operative management of anticoagulants, corticosteroids and immunosuppression. *Surgery* 1999; 17:83-86
22. Sced A, Davies NJH. Peri-operative management: diabetes. *Surgery* 1999; 17: 106-9
23. Hirsch IB, McGill JB, Cryer PE, White PF. Perioperative management of the diabetic patient. *Anesthesiology* 1991; 74: 346-59
24. Bridges SL Jr, Lopez-Mendez A, Han KH. Should methotrexate be discontinued before elective orthopaedic surgery in patients with rheumatoid arthritis? *Journal of Rheumatology* 1991; 18: 984
25. Perhala RS, Wilke WS, Clough JD, et al. Local infectious complications following knee joint replacement in rheumatoid arthritis patients versus those not treated with methotrexate. *Arthritis Rheum* 1991; 34: 146
26. Grennan DM, Gray J, Loudon J, et al. Methotrexate and early postoperative complications in patients with rheumatoid arthritis undergoing elective orthopaedic surgery. *Ann Rheum Dis* 2001; 60: 214-7
27. Sprung J, Castellani WJ, Srinivasan V, Udayashankar S. The effects of donepezil and neostigmine in a patient with unusual pseudocholinesterase activity. *Anesthesia and Analgesia* 1998; 87(5): 1203-1205
28. Heath ML. Donepezil: Alzheimer's disease and suxamethonium. *Anaesthesia* 1997; 52(10): 1018
29. Personal communication. Medical Information department, Novartis Pharmaceuticals UK Ltd. January 2003.

30. Personal communication. Medical Information department, Eisai Ltd. January 2003.
31. Hendley BJ. Convulsions after cocaine and propofol. *Anaesthesia* 1990; 45: 788-9
32. Bernards CM, Teijeiro A. Illicit cocaine ingestion during anaesthesia. *Anesthesiology* 1996; 84: 218-220
33. Larkin M. Surgery patients at risk for herb-anaesthesia interactions. *Lancet* 1999; 354: 1362
34. Assemi M. Herbal preparations: Concerns for operative patients. *Anaesthesia Today* 1999; 10: 17-23
35. Nicholson G, Burrin JM, Hall GM. Peri-operative steroid supplementation. *Anaesthesia* 1998; 53: 1091-1104
36. Editor's comment. Use of herbal medicines could pose risk to patients undergoing surgery. *Pharmaceutical Journal* 2001;267:75-9