Safer Prescribing Workbook
Section 3 – High Risk Drugs

Written by: Michelle Cerrato
Education and Training Pharmacist
SUHT
Section 3

High Risk Drugs and Regimens

This section will look at the following areas:

3.1 Anticoagulation therapy
3.2 Insulin therapy
3.3 Opioids and equivalence in prescriptions
3.4 Chemotherapy – outline only
3.5 Immunosuppressants
3.6 Drug interactions and adverse drug reactions

Potassium is a high-risk drug, but see section 4 on infusion fluids and additives for detailed information about this. Antibiotics are also high-risk drugs but will be covered in section 6 on Therapeutic Drug Monitoring.

The main aim of this section is to make you aware of the high-risk drugs that you will encounter during your practice and specify how to avoid making common mistakes. Available Trust guidelines have been highlighted for you to refer to where necessary. You should also check in the BNF for information on dosing, side effects and interactions and contact your ward pharmacist if you are not sure about prescribing or monitoring response to a high-risk drug or any other medication.

3.1 Anticoagulation therapy

The objectives of this section are:

- To be able to write prescriptions according to local anticoagulation guidelines
- To be able to demonstrate awareness of possible drug interactions with warfarin
- To understand the need for adequate monitoring of various anticoagulants

3.1.1 Introduction

Warfarin, heparin and related anticoagulants are frequently involved in serious medication errors. Most patients are treated safely with anticoagulants. However, if therapy is not monitored properly, or the patient’s clinical condition/concurrent drug therapy changes then over or under anticoagulation can result with potentially fatal consequences.

Safe anticoagulation is a multidisciplinary team process involving healthcare professionals in both primary and secondary care.

Example
Fatal outcome of azapropazone/warfarin interaction

A 66-year old man was treated with warfarin for atrial fibrillation. He developed acute arthritis, diagnosed as gout by his general practitioner. He was prescribed the anti-inflammatory drug azapropazone. The dose was subsequently increased in response to an exacerbation of his arthritis. The patient then developed signs of bleeding. The general practitioner arranged for a full blood count, but did not check the INR. Before the results were available the patient suffered a massive intracranial haemorrhage, was admitted to hospital and died. His INR on admission was greater than 10.


3.1.2 Prescribing anticoagulation

Heparin

If an IV heparin infusion is required for your patient the heparin should be prescribed using the Trust heparin chart (see below), following the Trust heparin guideline. IV heparin should also be cross-referenced on the main drug chart so that everyone is aware that the patient is prescribed it on a separate chart.

The Trust heparin guidelines can be obtained from the following link: http://suhranet/index.cfm?articleid=3050
In most cases an IV bolus of 5,000 units should be given and then an IV infusion should be started using heparin at a concentration of 20,000 units in 20ml, usual starting rate of 1.4ml/hour (some high care areas may use lower starting rates due to previous adverse incidents with high APTRs, check before prescribing). The APTR should be monitored 4 - 6 hours after starting or changing the rate, and then every 24 hours when stable.

- **Task**
  On a ward round the decision is made to commence your patient on heparin thromboprophylaxis. The consultant asks you to prescribe twice daily heparin. Write a prescription for this patient

---

**Enoxaparin**

Enoxaparin is a low molecular weight heparin that requires less monitoring than IV heparin, although it is as effective. Remember to check that you have prescribed the correct dose for the indication:

- **Task**
  - Dose and route of enoxaparin for ACS = ........................................................
  - Dose and route of enoxaparin for DVT/PE = ..................................................

For patients with renal impairment (CrCl < 30ml/min) the dose of enoxaparin (being used for treatment of ACS) should be reduced to 1mg/Kg OD due to the high risk of bleeding. In some specialities, the patient would be changed to an IV heparin infusion instead, so check what the practice is where you are working. The patient should be accurately weighed in order to give a correct dose and treatment should be reviewed daily.

Enoxaparin is also used for thromboprophylaxis; see case studies at the end of this section.
**Warfarin**

Warfarin has a long half-life, which means that it takes approximately three days before reaching therapeutic levels and also takes three days for any effect to wear off. This is very important and must be considered when prescribing warfarin. Adequate anticoagulation must be given while the patient is loaded with warfarin.

- All patients should have a yellow anticoagulation book with an appointment to be seen in the anticoagulation clinic at Southampton or at their local clinic/GP surgery. The pharmacy department will supply the yellow book to the patient, ward staff should arrange appointments.

- The pharmacy department in Southampton only supply **1mg & 3mg** warfarin tablets.

- Warfarin should be prescribed on the Trust anticoagulation prescription card (see below) and cross-referenced on the main inpatient drug chart.

- On the anticoagulation prescription card, there is a checklist of counselling points and a place to sign once you have given the patient information about their warfarin. The ward pharmacist and the nurse can also counsel patients about their warfarin and should sign the chart to say what they have done.

- It is essential that all patients are fully counselled about their warfarin before discharge, and that appropriate follow up arrangements have been made.

- Please discuss the points on the checklist with your patients. If you are short of time the salient points all warfarin patients should be told are:
  - The different strengths of warfarin
  - The dose of warfarin to take on discharge
  - The need for regular blood tests & when and where the next blood test will be

- The bottom of the warfarin chart should be completed and then faxed to the GP surgery – liaise with the nurses and ward clerks to arrange this.

- If you are unsure of any matter relating to the discharge of patients prescribed warfarin or have any anticoagulation queries please contact your ward pharmacist, the medicines information department (x6908/6909) or the on-call pharmacist via switchboard out of hours.

*The Trust warfarin guidelines can be found using the following link:*  
Southampton Hospitals NHS Trust Anticoagulation Prescription Card

Surname: 
First Name: 
Ward: 
Unit No.: 
D.O.B.: 
Consultant: 

Reason for anticoagulation:  
Pre-op warfarin dose, if applicable  
INR Target Range: to  
Concurrent interacting Drugs

<table>
<thead>
<tr>
<th>Date</th>
<th>Prothrombin Ratio (INR)</th>
<th>Dose</th>
<th>Nurses Signature (when given)</th>
<th>Doctor’s Signature of Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAB. WARFARIN mg. at pm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discharge information to the GP:
On a weekday please ensure this anticoagulation prescription card is faxed to the GP on the day the patient is discharged. If patient is to be discharged on weekends, please fax it first thing Monday morning.

Dose on discharge: __________________________ Date next INR due: __________________________

Duration of treatment: __________________________ Who will stop the warfarin? __________________________


Please contact the medical team if this patient’s INR goes above ______ or falls below ______ and we will consider admission.

Please ensure that the Yellow Anticoagulation booklet is FULLY completed.

6
INFORMATION CHECKLIST FOR PATIENTS DISCHARGED ON WARFARIN:

Please ensure all the following information on the checklist is given to the patient/carer verbally, initially by the doctors, and then reinforced by doctors and pharmacists to ensure patient has understood the information while in hospital. Nurses should also reinforce information at the time of discharge and ensure that written information is supplied.

<table>
<thead>
<tr>
<th>Information - please sign relevant box</th>
<th>Doctor</th>
<th>Pharmacist</th>
<th>Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLEASE SIGN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Why warfarin has been prescribed? including relative risk/benefit
- How warfarin works?
- How much is needed? What is INR? Tablets colour and strength Blood test needed
- Risk of poor warfarin control
  - Recurrent clots
  - Risk of severe bleeding (inc intra and extra cranial bleeding)
  - How to recognise / minor / major bleed and what to do if these occur
- Who to contact in an emergency?
- Importance of telling other health professionals: dentist, pharmacist, physiotherapist, etc about being on warfarin
- Taking warfarin at the same time each day (usually 6pm)
- What should you do if you miss a dose?
- Length of time for treatment
- Who will stop the medication?
- Dietary advice with information sheet
- Not consuming more than 1 to 2 units of alcohol in a day
- Starting new or stopped current medication
- Hobbies and leisure

**Information to patient/carer at the time of discharge**

- Importance of not missing the blood test and contacting the GP
- Dose to take in mg. on discharge
- How many of which colour tablets to take.
- Check patient has yellow book and information leaflets and that yellow book has been FULLY completed
- Details on treatment card faxed to the GP
- On discharge, check patients understanding of all the above

TO BE FILED IN MEDICAL NOTES
**Task**

Using the guidelines for initiating warfarin therapy, specify the dose of warfarin you would prescribe for the following patient and what the target INR is:

Mr AB, 75 years old.
Diagnosed with heart failure 10 years ago. Now needs to start warfarin due to chronic AF. The patient is also taking the following medication:
- Amiodarone 200mg BD for 4 days then reduce to 200mg OD
- Furosemide 40mg OD
- Aspirin 75mg OD
- Ramipril 5mg OD
- Bisoprolol 1.25mg OD

**Day 1** – dose of warfarin = ……………………………

**Day 2** – dose of warfarin = ……………………………

**Target INR** = ……………………………

Comment on the above choices:…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………

Mr AB has blood taken at 9.30am on day 3 and his INR is measured as 2.9

**Day 3** – dose of warfarin = ……………………………

Mr AB’s INR on day 4 is 4.1

Comment on what you would do and the possible reasons for this INR result:
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
Alternative oral anticoagulation

For the rare situations where patients are unable to tolerate warfarin (drug of choice), alternative oral anticoagulation is available:
- Acenocoumarol (nicoumalone) [Sinthrome®]
- Phenindione
The same procedures apply as with warfarin and the INR must be monitored closely. Make sure that it is very clear on the drug chart that the patient cannot take warfarin and that the alternative anticoagulant is clearly prescribed.

3.1.3 Drug interactions with warfarin

The list below contains the drugs that are most likely to interact with warfarin according to available evidence, however it is prudent to check the INR within 5 days of starting any new drug in a patient who is already on warfarin. For patients who are being loaded on warfarin and who are also taking interacting drugs, it is sometimes appropriate to use lower loading doses (see Trust guideline on initiating warfarin for further details). See the latest edition of the BNF for further information on drugs that interact with warfarin.

- **Increased INR**
  - Amiodarone
  - Fluconazole (and other azoles)
  - Ciprofloxacin (and other quinolones)
  - Erythromycin/clarithromycin
  - SSRIs e.g. sertraline
  - Isoniazid
  - Metronidazole
  - Cotrimoxazole
  - Alcohol
  - Cranberry

- **Increased bleeding risk** → avoid use with warfarin if possible
  - Antiplatelets-aspirin, clopidogrel
  - NSAIDs
  - COX II Inhibitors e.g. celecoxib

- **Reduced INR**
  - Rifampicin
  - Carbamazepine
  - Trazadone
  - Penicillins
  - St John’s Wort
  - Phenytoin
  - Sucralfate
3.1.4 Case Study 1: Treatment of DVT/PE

Admission

Mr VT a 55-year old man, weighing 85kg, admitted via the emergency department with a red and swollen leg, SOB and chest pain

PMH Nil
Allergies penicillin
OE pulse regular
SOB Left leg inflamed, swollen at calf and painful

Diagnosis Proximal DVT and PE (confirmed by CTPA)

Rx Enoxaparin sc 85mg bd
Warfarin loading dose-prescribed on chart as 10mg day 1, 10mg day 2, 5mg day 3

Questions

1. Why does Mr VT need both enoxaparin and warfarin?

2. Is the dose of enoxaparin appropriate for Mr VT?

3. What monitoring is required with enoxaparin therapy?

4. Is the loading regime of warfarin appropriate?

5. Why is it important to take a complete drug history from Mr VT?

Day 3 INR = 2.1

Questions

6. What dose of warfarin would be appropriate for day 3?
7. How long should Mr VT continue enoxaparin?

8. How long should Mr VT continue on warfarin?

9. How often should the INR be monitored when it is in range?

3.1.5 Case Study 2: Prevention and management of over anticoagulation

Mr JQ, 62 years old, weight 39kg

PC Painful cyanotic foot

Tx Angioplasty followed by bypass graft

PMHx Right above knee amputation, high alcohol intake

DHx simvastatin, aspirin, enoxaparin sc 60mg daily, ciprofloxacin

U&Es Albumin 26g/L (35-48g/L)

**Day 1 post graft**

Warfarinised as follows: 10mg day 1, 10mg day 2, 5mg day 3

Enoxaparin sc 60mg daily until INR in therapeutic range

**Day 3**

INR = 8.3

**Questions**

1. What actions would you take?
2. Why did this happen?

3. What would have been a more appropriate way of loading this patient with warfarin?

3.1.6 Case Study 3: Management of warfarin patients at discharge

Mrs KP 85 years old
PC Palpitations, SOB
PMHx Diabetes
Hypertension
Confusion
ECG shows atrial fibrillation
Started on warfarin as follows: 10mg day 1, 5mg day 2, 5mg day 3, 3mg day 4
Other medication: Metformin 500mg BD
Gliclazide 80mg BD
Ramipril 5mg OD
Simvastatin 40mg ON
Aspirin 75mg OD

Questions
1. The patient is ready to be discharged. Who would you need to contact regarding continued monitoring of her warfarin therapy?
2. What particular details would it be important to pass on to the team taking on her warfarin management?

3. What information would you need to give to the patient before they are discharged with warfarin?

3.1.7 Thromboprophylaxis Case Studies

Case 1
Mr RL is an 80-year old patient admitted for a knee replacement as a result of osteoarthritis. He has no other past medical history.

1. Would you classify this patient as low, medium or high risk and why?

2. What prophylaxis would you recommend?

Case 2
Mr DF is a 34-year old patient admitted for an elective cholecystectomy. He has no past medical history, however clerking reveals that his father died of a stroke aged 40, his brother had a non-fatal thrombotic stroke at the age of 19 and his sister had a PE post partum.

1. Would you classify this patient as low, medium or high risk?

2. What prophylaxis would you recommend?
Case 3

Mrs VL aged 79, has been admitted following a fall in which she sustained a fractured neck of femur. She has a past medical history of hypertension and CCF.

1. Would you classify this patient as low, medium or high risk?

2. What prophylaxis would you recommend?

Case 4

Mr TP is a 65-year old patient on an acute medical ward. He has been admitted with an exacerbation of COPD, he is unable to mobilise due to SOB.

1. What thromboprophylaxis would you recommend for Mr TP?

Case 5

Mrs ST is a 60-year old diabetic patient who weighs 120 kg. She has been admitted with worsening renal failure and is fairly immobile. Her CrCl is 20ml/min.

1. What thromboprophylaxis would you recommend for this patient?

See the Trust guidelines on thromboprophylaxis for medical and surgical patients for further information available using the following link: http://suhtranet/index.cfm?articleid=4819T
3.2 Insulin therapy

The objectives of this section are:

- To gain a better understanding of the pharmacological properties of the different insulins prescribed.
- To understand the rationale for prescribing insulin regimes
- To be able to avoid making common insulin prescribing mistakes on the ward
- To understand how to prevent and treat hypoglycaemia safely and effectively in patients with diabetes
- To understand how to manage glycaemic control pre-, peri- and post-operatively

3.2.1 Introduction

There are a wide variety of insulins and delivery devices available, allowing regimens to be tailored to individual need. This also means that there is a high risk of error, so prescribing needs to be accurate and clear. There are numerous guidelines available to guide the management of diabetic patients.

NICE guidance 2004 on insulin therapy suggests the following:

- Use an insulin regimen that allows the patient optimum wellbeing
- Use glargine/detemir insulin when nocturnal hypoglycaemia or morning hyperglycaemia are a problem
- If serious hypoglycaemic episodes persist consider using an insulin pump.
- For late post prandial hypoglycaemia, use rapid acting insulin analogues

The onset and duration of action, and the peak effect are determined by the insulin type and by the physical and chemical form of the insulin. Neutral or soluble insulin is the quickest and shortest acting, appearing in the circulation within 10 minutes after sc injection. Recombinant insulin analogues closer resemble the action of physiological insulin. Isophane insulin is a suspension of protamine with insulin, giving an onset of action of 1 – 2 hours and peak effect at 4 – 8 hours. This is usually given twice a day. There are a wide range of mixed insulins containing isophane and soluble/aspart/lispro insulin in different proportions (known as biphasic insulin) now available e.g. Mixtard 30. Long acting analogue insulins e.g. insulin glargine provide a fairly constant basal insulin supply similar to that of basal insulin secretion in non-diabetics, which have improved the management of type I diabetes.

Insulin should be prescribed using the Trust adult diabetes prescription chart (pink chart). A copy of this chart is shown below. Page 1 and 4 should be used when prescribing intravenous insulin infusions and pages 2 and 3 should be used for regular subcutaneous insulin injections. The insulin prescription should be cross-
referenced on the main inpatient drug chart and all other medication for diabetic patients should be prescribed on the inpatient chart.

Southampton University Hospitals NHS

ADULT DIABETES PRESCRIPTION CHART

Please indicate on main prescription chart that the patient has a diabetic prescription chart

<table>
<thead>
<tr>
<th>Allergies:</th>
<th>Address Label</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ward:</th>
<th>Sheet No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consultant:</th>
<th>Name:</th>
<th>Hospital No:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address:</th>
<th>Date of Birth:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Intravenous Insulin Infusion Protocol**

Can be used for DKA but fluid prescription required - see protocol. In pregnancy ask diabetes team for advice.

**Continuous Insulin Protocol. Review need for insulin infusion every 24 hours**

### Human Actrapid 50 units in 50mls 0.9% Saline.
Infuse according to scale below.

<table>
<thead>
<tr>
<th>Blood Glucose (mmol/L)</th>
<th>initial insulin infusion rate (U/hour)</th>
<th>Amended infusion rate (U/hour) (if required)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2.4</td>
<td>See Hypoglycaemia guidance</td>
<td>See Hypoglycaemia guidance</td>
</tr>
<tr>
<td>2.5 - 4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1 - 7.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>7.1 - 10</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>10.1 - 14.9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Dr sign for continuation of insulin infusion every 24 hours</th>
<th>Nurses signature for administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date/nurses initials</td>
<td>Date/nurses initials</td>
</tr>
<tr>
<td></td>
<td>Date</td>
<td>Dr sig</td>
</tr>
</tbody>
</table>

### Intravenous fluid guidance (prescribe on IV fluid chart)

- IV fluid requirements are dependent on clinical condition of patient e.g. renal or cardiac failure.
- In medical patients we suggest co-infusion of 5% dextrose at 100 ml/hour, assuming normal cardiac and renal status.
- In surgical patients consider 1 litre of dextrose/saline with 2 grams of KCl at 80 ml/hour.
- If patient eating and drinking consider why i.v. insulin required as opposed to conventional s/c insulin
- IF ON I.V. INSULIN CHECK Plasma K+ and Na+ DAILY.

### Hypoglycaemia guidance

- If blood glucose is 2.5 to 4
  - Asymptomatic
  - Symptomatic

- If blood glucose is less than 2.5
  - Treat with 25mls of 50% dextrose i.v.

### Monitoring Instructions for intravenous insulin (for record see back page)

The capillary blood glucose concentration should be measured every hour, at least until the patient is stable.

If the blood glucose is stable between 5 and 11mmol/L for 3 consecutive hours the blood glucose should be measured every 2 hours thereafter.

If blood glucose more than 15mmol/L for 2 hours and ketonuria is present call cover doctor to amend iv infusion rate. (probably need more insulin).
## Pre admission diabetes treatment

Please indicate on main prescription chart that the patient has a diabetic prescription chart.

### INSULIN PRESCRIPTION

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Time</th>
<th>Dose (Units)</th>
<th>Date</th>
<th>2.5.05</th>
<th>3.5.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novomix 30</td>
<td>08.00</td>
<td>10</td>
<td>12</td>
<td>sig</td>
<td>sig</td>
</tr>
<tr>
<td>Sub cutaneous 5/C</td>
<td>12.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td>18.00</td>
<td>8</td>
<td>10</td>
<td>sig</td>
<td>sig</td>
</tr>
<tr>
<td></td>
<td>22.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dr Signature: Dr R Smith
Date: 02.05.05
RS: 3.5.05

---

### Missed Dose Codes
1. Patient not available
2. Drug not available
3. Patient refused
4. Request by Doctor
5. Nil by Mouth
6. Clinical reason

### Insulin presentation:
(Please tick)
- 10ml vial
- Penfill 3ml

---

Stop Metformin if Creatinine > 150 micromol/L, acute pulmonary oedema, hepatic failure and with X ray contrast. Insulin treatment may be the best option if hyperglycaemia persists.
<table>
<thead>
<tr>
<th>Date</th>
<th>Before Breakfast</th>
<th>Before Lunch</th>
<th>Before Dinner</th>
<th>Before Bed</th>
<th>Other/Hypos</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Simple monitoring advice:**

- Instructions for iv insulin infusion on front page and monitoring record on back page.
- Patients being treated with subcutaneous insulin should have their capillary blood glucose tested at least once a day during their hospital stay.
- If unstable, test 3-4 times a day until stable for 2 days. (Vary times of testing each day)
- Patients being treated with oral anti-diabetic agents: If unstable, test twice a day until stable for 2 days, then test before breakfast for 3 days. Then test every 2 days.
- Patients treated with diet: If unstable test twice a day until stable, then test every third day prior to breakfast and 2 hours after breakfast.

Stable blood glucose 5 – 11mmol/L
Unstable blood glucose < 5mmol/L or > 11mmol/L
<table>
<thead>
<tr>
<th>Time</th>
<th>0100</th>
<th>0200</th>
<th>0300</th>
<th>0400</th>
<th>0500</th>
<th>0600</th>
<th>0700</th>
<th>0800</th>
<th>0900</th>
<th>1000</th>
<th>1100</th>
<th>1200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin (u/hr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sign Initials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>1300</th>
<th>1400</th>
<th>1500</th>
<th>1600</th>
<th>1700</th>
<th>1800</th>
<th>1900</th>
<th>2000</th>
<th>2100</th>
<th>2200</th>
<th>2300</th>
<th>2400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin (u/hr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sign Initials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Additional records**

<table>
<thead>
<tr>
<th>Time</th>
<th>0100</th>
<th>0200</th>
<th>0300</th>
<th>0400</th>
<th>0500</th>
<th>0600</th>
<th>0700</th>
<th>0800</th>
<th>0900</th>
<th>1000</th>
<th>1100</th>
<th>1200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin (u/hr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sign Initials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>1300</th>
<th>1400</th>
<th>1500</th>
<th>1600</th>
<th>1700</th>
<th>1800</th>
<th>1900</th>
<th>2000</th>
<th>2100</th>
<th>2200</th>
<th>2300</th>
<th>2400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin (u/hr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sign Initials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Instructions for ‘taking down’ an intravenous insulin infusion:**

- Confirm the patient is able to eat and drink.
- Give s/c insulin as prescribed prior to meal.
- Stop i.v. insulin infusion after meal.
- Ensure capillary glucose concentration is monitored QDS for at least 24 hours after i.v. insulin infusion has been stopped.

Diabetes Nurse Specialist - Ext 3761/ Bleep 1199/ Bleep 1536/ Bleep 1535
Diabetes SpR 9203
**Task 1**
Starting with the fastest acting, put these insulins in order of action:

<table>
<thead>
<tr>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Mixtard 30</td>
</tr>
<tr>
<td>Glargine</td>
</tr>
<tr>
<td>NovoMix 30</td>
</tr>
<tr>
<td>Humalog</td>
</tr>
<tr>
<td>Humulin S</td>
</tr>
<tr>
<td>Determir</td>
</tr>
<tr>
<td>Novorapid</td>
</tr>
<tr>
<td>Human Insulatard</td>
</tr>
</tbody>
</table>

1.  
2.  
3.  
4.  
5.  
6.  
7.  
8.  
**Task 2**

A patient on your ward is normally on the regime shown.

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Time</th>
<th>Dose(Units)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. Acrapid</td>
<td>08.00</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Sub cutaneous</td>
<td>12.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td>16.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dr Signature: [Signature]
Date: 14/8/107

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Time</th>
<th>Dose(Units)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. Mixard 30</td>
<td>08.00</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Sub cutaneous</td>
<td>12.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td>18.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dr Signature: [Signature]
Date: 14/8/107

What is wrong with this regime?
**Task 3**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Time</th>
<th>Dose (Units)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Mixtard</td>
<td>08.00</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Sub cutaneous</td>
<td>12.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td>18.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.00</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

1. Identify the problem with this prescription

2. What could be the consequence of this error?

3. What would you do differently and why?
Task 4

During an evening on-call, a nurse bleeps you to say Mr A, is feeling sweaty & dizzy. He is complaining of hunger even though he ate a full meal only an hour ago.

1. What would you ask the nurse to do pending your review?

You arrive on the ward 10 minutes later the patient is now drowsy & tremulous with a BP160/95 mmHg, HR 100 bpm, O2 Sats 100% on air, RR 25 breaths/minute. He is pushing the nurses away when they try and help him. On quick review of the notes he is a Type I diabetic on twice-daily Mixtard 30, 12 units in the morning & 6 units in the evening.

2. Here is his insulin chart. What do you think?

3. What would be the order of your actions?

4. Would he still require his morning insulin?

5. How can you prevent this happening again?
Task 5

Mr C has Type II diabetes. His present medication is gliclazide 80 mg bd. His glycaemic control is optimal. He is to be admitted to your ward on 2/9/07 with surgery planned for the following morning. He will be nil by mouth from midnight 2/9/07.

1. Should his gliclazide be stopped, and if so, when?

2. Does this gentleman require an IV insulin sliding scale?

3. If so, when should the IV insulin sliding scale be discontinued?

4. Describe the process of converting a patient from an IV insulin sliding scale to oral therapy
3.3 Opioids

The objectives of this section are:

- To be able to prescribe opioids safely and correctly
- To understand some of the main side effects of their use and manage these appropriately
- To be able to swap between different opioids when necessary and still maintain adequate pain relief for the patient.

3.3.1 Introduction

Opioids as a group of drugs can be separated into two types – weak opioids e.g. codeine and dihydrocodeine and strong opioids e.g. morphine, fentanyl, oxycodone.

Morphine is the standard strong opioid analgesic. It is available in a variety of formulations to be administered by various routes. Morphine’s duration of action is approximately four hours.

To obtain rapid control of acute pain an intravenous dose of 2.5 -5mg of morphine should be given, titrated to pain relief. For control of chronic pain caused by malignancy, a first line choice would be oral morphine liquid 5 -10mg every four hours or as often as necessary to control pain. After control is achieved it is then advised to change to an oral sustained release preparation given every twelve hours, with immediate release morphine prescribed when required for breakthrough pain. Morphine is metabolised by the liver to an active metabolite, which should be considered in those with renal impairment.

Oxycodone and hydromorphone are synthetic opioids available as standard and sustained release oral preparations. Some patients may tolerate these agents better than morphine, although morphine is still first line. Fentanyl is available as a transdermal patch for long term use to treat chronic pain. The patch is designed to release the drug continuously for 3 days, after which the patch should be replaced. Take care when prescribing to ensure that the patch is not administered daily.

Task

Your patient Mr DJ has been taking morphine SR capsules 40mg BD but is now unable to swallow. Prescribe a fentanyl patch for him on the drug chart below that will give equivalent pain control. Consult the following website to assist you with prescribing: www.emc.medicines.org.uk
When starting a fentanyl patch, existing analgesic therapy should be continued for the first 12 hours until therapeutic levels are achieved.

The main adverse effects of opioids are respiratory depression (reversed by naloxone), sedation, nausea and vomiting (antiemetics should be prescribed routinely), constipation (suitable regular laxatives should be prescribed), tolerance to the analgesic effect with chronic use (although addiction is rare when prescribed for pain relief), and smooth muscle spasm causing biliary colic and urinary retention.

Due to the many routes by which morphine and other strong opioids can be administered, there is a huge risk of error when prescribing. Care should be taken to make sure that the drug has been prescribed by the correct route and at the correct frequency. Opioids are all controlled drugs and are therefore subject to prescribing restrictions – see section 1 for further details.

Case Study 1

Mrs. AW has metastatic lung cancer. On the ward round the consultant asked you to refer her to the palliative care team for assessment of her pain control. The palliative care team have recommended the following:

- regular morphine at a dose of 10mg
- additional PRN morphine for breakthrough pain
- regular paracetamol
- a PRN antiemetic
- regular lactulose and PRN senna

1. Choose an appropriate formulation of morphine and write prescriptions for the above on Mrs. AW’s drug chart below:
<table>
<thead>
<tr>
<th>DRUG (print approved name)</th>
<th>Dose</th>
<th>Additional info and/or dose/kg</th>
<th>Date</th>
<th>Route</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>05.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>21.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DRUG (print approved name)</th>
<th>Dose</th>
<th>Additional info and/or dose/kg</th>
<th>Date</th>
<th>Route</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>09.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>21.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DRUG (print approved name)</th>
<th>Dose</th>
<th>Additional info and/or dose/kg</th>
<th>Date</th>
<th>Route</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>09.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>21.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A week later the palliative care team have reviewed Mrs. AW again. In addition to her regular morphine (now 60mg BD), she has been having 3 to 4 additional doses a day for breakthrough pain. The palliative care team have recommended that she be switched to an equivalent dose of fentanyl patch and to continue with morphine prn for breakthrough pain. The lactulose and senna seem to be causing her colic so they have recommended regular co-danthramer instead.

2. Write a prescription for the fentanyl patch, PRN morphine and co-danthramer on the drug chart below:

The following resources may be useful to you:
- BNF
- [www.emc.medicines.org.uk](http://www.emc.medicines.org.uk)
<table>
<thead>
<tr>
<th>DRUG (print approved name)</th>
<th>Dose</th>
<th>Additional info and/or dose/kg</th>
<th>Date</th>
<th>Route</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Route</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Print name &amp; designation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table continues as follows...**
## AS REQUIRED MEDICATION (FOR VARIABLE DOSES SEE REVERSE OF CHART)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Date</th>
<th>Time</th>
<th>Signature</th>
<th>Bleep</th>
<th>Given by</th>
<th>Print Name</th>
<th>Additional Information/Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg</td>
<td>microgram</td>
<td>ml</td>
<td>units</td>
<td>Max Freq/dose</td>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Patients Name:**

**Month:**

**Year:**
Four days later Mrs. AW has deteriorated and the palliative care team have advised that she be switched to a subcutaneous infusion of morphine via a syringe driver, and that cyclizine be added to the syringe driver also. Her pain has been well controlled with the fentanyl patch.

3. What would be an appropriate dose of s/c morphine to be prescribed over a 24-hour period?

The following guideline may be useful to you:

‘The use of morphine sulphate in syringe drivers’, available from the following link: http://suhtranet/index.cfm?articleid=4176

4. Why is morphine preferred to diamorphine at present?

5. What would be an appropriate dose of s/c cyclizine to be prescribed over a 24-hour period?

Later that day Mrs. AW’s blood results are reviewed on the ward round. She has a calcium level of 3.5mmol/L corrected. The consultant decides she needs a bisphosphonate and asks you to prescribe one.

6. Which bisphosphonate will you prescribe, at what dose and how should it be administered? Prescribe the bisphosphonate on the drug chart below:
A few minutes later the SHO comes back. Mrs. AW has a serum creatinine of 150µmol/L and he wants you to check whether the bisphosphonate requires any dose reduction in view of this. She weighs 50Kg.

7. What dose of the bisphosphonate will you now prescribe? Are there any other precautions?
3.4 Chemotherapy

The objectives of this section are:

- To have an awareness of the need for careful prescribing of chemotherapy agents
- To have an understanding of the national guidelines in place to restrict the prescribing, dispensing and administration of intrathecal chemotherapy to prevent serious errors occurring.
- To be aware of the national guidance available to support the prescribing and use of methotrexate.

3.4.1 Introduction

Chemotherapy literally means “treatment with drugs”. It is usually shorthand for “cytotoxic chemotherapy” which means treatment with cell-killing drugs. There are about 60 chemotherapy agents currently available although new advances in treatment means that this number is growing all the time. These drugs are commonly divided into 5-6 classes by mode of action and virtually all work on DNA replication/cell division i.e. basic cellular processes.

Cytotoxic drugs are therefore not very selective, have severe side-effects and present a health hazard to those handling them.

Toxicity to patients
- Nausea and vomiting
- Hairloss
- Infertility
- Bone marrow suppression i.e. anaemia, infection, bleeding and mucositis

Cytotoxic drugs are not selective, but cancer cells are more vulnerable. By using pulses of treatment, the effect is cumulative versus the tumour. Combination chemotherapy is often used due to the following reasons:
- Drugs from different classes may be synergistic
- Drugs from different classes avoid resistance mechanisms
- Avoids toxicity associated with full doses of drugs

The main limitations of chemotherapy are lack of efficacy and toxicity. Efficacy can be improved by overcoming resistance to the drug or giving a higher dose. Toxicity can be improved by developing more selective drugs and finding ways to protect normal tissues.
3.4.2  **Intrathecal Chemotherapy**

**Definition:** anticancer drugs that are injected into the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord.

It is useful in those malignancies where cancerous cells are likely to be harboured in the central nervous system. These include leukaemia and lymphoma.

The main drugs that are given via the intrathecal route are:

- Methotrexate
- Cytarabine
- Dexamethasone / hydrocortisone
- Antibiotics in neuro patients although unlicensed

**Vinca alkaloids** must **ONLY** ever be given by the intravenous route. Severe neurotoxicity results when injected into the CNS, that is normally fatal. The vinca alkaloids are listed below:

- Vinblastine
- Vincristine
- Vindesine
- Vinflunine
- Vinorelbine

Since 1985 at least 13 patients have died or been paralysed as a result of the accidental intrathecal administration of vincristine intended for intravenous administration. All vinca alkaloids have the potential to do this. The most recent incident occurred in Nottingham and an external enquiry published various recommendations in 2001 (Toft Report). Other publications on the subject of intrathecal chemotherapy are as follows:

- Jan 2001 – Toft Report (external inquiry)
- April 2001 – Woods Report (CMO)
- Nov 2001 - National Guidance, to be implemented by 31 December 2001
- Local Policy

“By 2001, reduce to zero the number of patients dying or being paralysed by maladministered spinal injections”

Taken from: *An Organisation with a Memory 2000*

…the adverse incident that led to the patient’s death was not caused by one or several human errors but by a far more complex amalgam of human, organisational, technical and social interactions…

Taken from: *Toft Report 2001*

**Key requirements of the national guidance**

Each NHS Trust must have the following:

- A certified register of staff who have been adequately trained, deemed competent to manufacture, dispense, supply and administer intrathecal chemotherapy
- A formal induction programme
- Regular training programmes
- A written protocol

Implications – Prescribing
- A register must be maintained of those competent to prescribe intrathecal chemotherapy.
- Only members of medical staff whose names are on the register may prescribe intrathecal chemotherapy.
- Prescribing is restricted to consultants and registrars only.
- There must be a separate prescription chart for intrathecal chemotherapy

Implications - Dispensing
- A register must be maintained of all those deemed competent to dispense and release intrathecal chemotherapy.
- All intrathecal chemotherapy must be labelled with “For intrathecal use only” in capital (highlighted) letters.
- Intrathecal chemotherapy must only be released where there is written evidence that all intravenous therapy for that patient has been given.
- For adults vincristine must be dispensed at a concentration of 0.1mg/ml.
- Vincristine must be dispensed in a 10ml syringe as a minimum.
- Vincristine must be labelled as “For intravenous use only. Fatal if given by other routes.”

Implications - Delivery
- Intrathecal chemotherapy must only be released from pharmacy to a designated doctor or taken to the ward by a designated member of pharmacy staff.
- If taken to the ward the intrathecal chemotherapy must be issued directly to the doctor administering the treatment, or placed in a designated refrigerator.
- In both cases the member of pharmacy staff should sign release of the drugs, identifying to whom the drugs were released or that they have been lodged in the relevant refrigerator. Where the doctor does not take direct receipt of the drugs, they must check the drugs and sign on retrieval from the refrigerator.

Implications - Storage
- In pharmacy, intravenous and intrathecal chemotherapy must be stored in separate areas.
- On the ward intrathecal chemotherapy must be stored in a dedicated refrigerator reserved for this purpose alone. This must be kept locked.
- Only a doctor on the register of designated personnel should remove the intrathecal chemotherapy from the refrigerator.

Implications - Administration
- Intrathecal chemotherapy must be administered in an area where no other cytotoxic drugs are being given or stored.
- Medical staff must use a formal checking procedure to ensure the right drug and dose is given to the correct patient by the correct route.
- A chemotherapy trained nurse on the designated register must be involved in checking the intrathecal chemotherapy during administration.
• Senior House Officers may do the lumber puncture but **CANNOT** be involved in the administration of intrathecal chemotherapy at any stage of the process.

**Implications – Out of Hours**

• Under normal circumstances intrathecal chemotherapy should only be administered within **normal working hours**.

**Implications - Challenge**

• All staff involved with care of cancer patients must be encouraged to challenge colleagues if, in their judgement, either protocols are not being followed or their actions may increase risk to the patient.
• This should not be seen as adversarial.

3.4.3 **Methotrexate**

Methotrexate is one of the most commonly used chemotherapy agent. It is also used in the treatment of rheumatoid arthritis, psoriasis and inflammatory bowel disease. You will be required to prescribe it for these other conditions. Methotrexate can be given orally, IV, IM or SC but as you will remember from your induction, regardless of the route it is always given **ONCE A WEEK**. Methotrexate can cause severe side effects such as hepatic fibrosis, liver toxicity, severe alveolitis and bone marrow suppression. Patients have been harmed when methotrexate has been inappropriately prescribed or taken daily in error. National guidance has been issued to try to avoid such harm from occurring. **The NPSA guidance on methotrexate can be obtained from the following link:**

[http://www.npsa.nhs.uk/health/display?contentId=5085](http://www.npsa.nhs.uk/health/display?contentId=5085)

Patients should always take their methotrexate on the same day each week. The prescriber should ensure that doses not due are crossed through on the inpatient drug chart to avoid inadvertent administration.
3.5 Immunosuppressants

The objectives of this section are:

- To be aware of the main immunosuppressants used and the common errors that can occur when prescribing.

3.5.1 Introduction

Immunosuppressants are used to prevent tissue rejection after organ transplantation and to treat autoimmune and collagen diseases. Examples of immunosuppressive agents include steroids, ciclosporin, tacrolimus, mycophenolate and azathioprine. All of these drugs have the potential to cause serious side effects and so should be prescribed with care, ensuring that adequate monitoring of the patient is undertaken.

3.5.2 Corticosteroids

Glucocorticoids (usually prednisolone) are used to suppress inflammation (e.g. in asthma, ulcerative colitis and inflammatory eye and skin conditions), allergy and immune responses (to prevent rejection following tissue transplantation). Steroids are very effective but with long term use, serious adverse effects can occur e.g. adrenal suppression, increased susceptibility to infections, diabetes, muscle wasting, growth retardation in children, osteoporosis and peptic ulceration.

Prednisolone is the most commonly prescribed steroid. It is used in high doses e.g. 40mg OD in exacerbations of asthma or COPD. It may also be continued long term at lower doses for conditions such as polymyalgia rheumatica. Some long-term asthma and COPD patients are steroid dependent and so if the patient is given a high dose on admission to treat an exacerbation, then the dose should be weaned down slowly to prevent adrenal suppression. It is widely accepted that patients can have up to 3 weeks of treatment with steroids without the need to wean them off at the end.
**Task 1**

Mrs FD, 65 years old, admitted for an exacerbation of her COPD. Prescribed: prednisolone 30mg OM, salbutamol nebs 2.5mg QDS, ipratropium nebs 500mcg QDS, doxycycline 200mg OD

The patient has improved sufficiently to be able to be discharged.

What other information would you need to find out before writing this patient’s discharge prescription?

..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................
..............................................................................................................................................................

**Task 2**

Mr GT, 75 years old with chronic COPD. He is usually on a maintenance dose of prednisolone 10mg OD (taken for the last 5 years). He was admitted with an exacerbation of his COPD 5 days ago. His prescription is as follows:

- Prednisolone 30mg OM for 4 days, now reduced to 25mg OM
- Formoterol inhaler (Atimos Modulite) 10.1mcg BD
- Tiotropium inhaler 18mcg OD
- Co-amoxiclav IV 1.2g TDS for the last 5 days
- Salbutamol nebs 2.5mg PRN

Using the discharge prescription below, prescribe the medication for Mr GT to take home.
CONFIDENTIAL

Patient Address

Tel No
Date of Birth:  Sex:
Hospital No:
NHS No:
Discharge date:
Admit date:
Admit method/type:
Discharge to:
Discharge From:

<table>
<thead>
<tr>
<th>DIAGNOSES/MAIN PROBLEMS</th>
<th>OPERATION/PROCEDURE</th>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1.</td>
<td>1.</td>
</tr>
<tr>
<td>2.</td>
<td>2.</td>
<td>2.</td>
</tr>
<tr>
<td>3.</td>
<td>3.</td>
<td>3.</td>
</tr>
<tr>
<td>4.</td>
<td>4.</td>
<td>4.</td>
</tr>
<tr>
<td>5.</td>
<td>5.</td>
<td>5.</td>
</tr>
<tr>
<td>6.</td>
<td>6.</td>
<td>6.</td>
</tr>
</tbody>
</table>

- CLINICAL RECOMMENDATIONS:

OTHER RELEVANT INFORMATION:

Please record ALL DRUGS that the patient is taking and indicate with a TICK those which you require to be dispensed.

<table>
<thead>
<tr>
<th>DRUG (APPROVED NAME)</th>
<th>DOSE AND FREQUENCY</th>
<th>NO OF DAYS</th>
<th>PHARMACY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Continuation Sheet used YES ☐ NO ☐ PHARMACIST CLINICAL CHECK: DISPENSED BY: CHECKED BY: DATE:

OTHER DRUG INFORMATION:

INFORMATION GIVEN TO PATIENT:

FOLLOW UP ARRANGEMENTS:

RESULTS AWAITED:

Signature: Patient’s Ward: Date:
Name:
Designation:
Responsible Consultant:
Copies to:
3.5.3 Ciclosporin

Ciclosporin is a calcineurin inhibitor. It is a potent immunosuppressant but can also be very nephrotoxic. Care should be taken when prescribing ciclosporin to ensure that the correct brand is used due to differences in bioavailability. Care should also be taken when converting a patient from oral ciclosporin to IV due to differences in dosage depending on the route used.

Task 3

Mr AS had a kidney transplant 3 years ago. He is taking ciclosporin capsules (Neoral®) 75mg BD as part of his immunosuppressant regimen. The patient has been admitted for a GI surgical procedure and it is expected that he will remain nil by mouth for the next 2 days. He therefore needs to be converted to IV ciclosporin to ensure adequate immunosuppression.

Using the following reference sources to help you, prescribe the IV ciclosporin on the drug chart below.

- BNF
- www.emc.medicines.org.uk

<table>
<thead>
<tr>
<th>DRUG (print approved name)</th>
<th>Dose</th>
<th>Additional info and/or dose/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature</td>
<td>mg</td>
<td></td>
</tr>
<tr>
<td>Print name &amp; designation</td>
<td>microgram</td>
<td>units</td>
</tr>
<tr>
<td></td>
<td>Date</td>
<td>Route</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How would you monitor Mr GT with regard to his ciclosporin treatment?

-------------------------------------------------------------------------------------------------------------------------------------
-------------------------------------------------------------------------------------------------------------------------------------
-------------------------------------------------------------------------------------------------------------------------------------
-------------------------------------------------------------------------------------------------------------------------------------
-------------------------------------------------------------------------------------------------------------------------------------
-------------------------------------------------------------------------------------------------------------------------------------


3.5.4 Tacrolimus

Tacrolimus is also a calcineurin inhibitor. It is not chemically related to ciclosporin but has a similar mode of action. It is thought that there is a greater incidence of neurotoxicity and nephrotoxicity with tacrolimus, but hypertrichosis appears to be less compared with ciclosporin. Tacrolimus is mainly used in immunosuppression regimens after kidney and liver transplantation, usually in patients intolerant of ciclosporin. The main points to be aware of when prescribing tacrolimus is that it interacts with many other medicines, so care must be taken and blood levels monitored closely. The dose also depends on the route used i.e. in established patients the IV dose is approximately one fifth of the oral dose, adjusted according to levels e.g. 6mg bd PO = 2.4mg IV over 24 hours (if a patient is immediately post transplant and unable to take oral medication, the IV dose is increased to one third of the oral dose). When converting back to oral dosing, give the first oral dose 8-12 hours after the infusion is stopped. It is very rare to need to prescribe this IV though as it is well absorbed orally.

Task 4

Mrs LT, 57 years old, weight 65Kg
Admitted with acute diarrhoea and vomiting, and abdominal pain
Renal transplant 2 years ago

Drugs on admission:
- Tacrolimus 1mg mane 1.5mg nocte
- Mycophenolate 500mg bd
- Prednisolone 7.5mg mane
- Omeprazole 20mg mane
- Novomix 30 - as per BMs
- Atenolol 25mg mane
- Furosemide 40mg mane

Using the reference sources below to assist you, answer the following questions
- BNF
- www.emc.medicines.org.uk

The patient developed unexplained sepsis with a possible ischaemic bowel, therefore antibiotics were started (meropenem 1g OD IV). A tacrolimus level was checked and found to be high (20.3ng/ml)

1. What would you do?
2. What are the recommended blood levels to aim for?

   The patient was then found to have yeasts in blood cultures, therefore fluconazole 400mg OD IV was started.

3. What is the potential problem with the addition of this drug?

4. How would you manage this situation?
3.6 Drug Interactions and Adverse Drug Reactions

The objectives of this section are:

- To understand what an adverse drug event is
- To understand how adverse drug reactions are reported
- To understand the Trust procedure for reporting medication errors
- To gain an understanding of the mechanisms by which drug interactions occur

3.6.1 Introduction

An adverse drug event (ADE) is any event that causes, or has the potential to cause patient harm. Adverse drug reactions (ADRs) and medication errors are both ADEs.

**Adverse Drug Reactions (ADRs)**

An adverse drug reaction (ADR) has been defined by the World Health Organisation (WHO) as: "Any response to a drug which is noxious, unintended and occurs at doses used for prophylaxis, diagnosis or therapy."

Actual and suspected ADRs must be reported to the Committee on the Safety of Medicines (CSM) via the yellow card reporting scheme. For ‘black triangle’ drugs any suspected ADR should be reported regardless of severity. Black triangle drugs are those that are new to the market, or have been formulated into a new delivery system or have been newly licensed for a different route of administration (designated black triangle in the BNF).

For older drugs all unusual reactions should be reported. Serious reactions should be reported even if they are well recognized e.g. gastrointestinal bleeding with NSAIDs. Serious reactions include those that are fatal, life threatening, disabling and that result in or prolong hospitalization e.g. drug induced renal impairment, electrolyte disorders, skin reactions.

<table>
<thead>
<tr>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using the BNF would you report the following ADRs?</td>
</tr>
<tr>
<td>- Nasal congestion with tadalafil</td>
</tr>
<tr>
<td>- Diarrhoea with risedronate</td>
</tr>
<tr>
<td>- Dizziness with rosuvastatin</td>
</tr>
<tr>
<td>- Stevens-Johnson syndrome with Zyban (bupropion)</td>
</tr>
<tr>
<td>- Alopecia with rosiglitazone</td>
</tr>
<tr>
<td>- Thrombocytopenia with penicillamine</td>
</tr>
</tbody>
</table>
Medication errors

“A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of a health professional, patient or consumer.”

Medication errors may be related to professional practice, products, procedures, environment or systems. They may involve prescribing and ordering; dispensing and distribution; preparation and administration; labelling, packaging and nomenclature; communications and education; or use and monitoring of treatment.

To improve patient safety both locally and nationally it is essential that all adverse drug events are reported. Both ADRs and medication errors can be reported using incident forms which can be obtained from the ward manager or by using the following link: Reports made to Pharmacy will be forwarded to the Risk Office.

Alerts are issued within the Trust to raise awareness of common errors and actions to be taken to reduce the risks.

All incidents reported to the Risk Office are forwarded to the National Patient Safety Agency’s National Reporting and Learning System (NRLS) where data from all trusts in England are assimilated and reviewed. Actions to be taken to reduce the risk of common errors recurring is then circulated to trusts.

The Trust is required to demonstrate that it has systems in place for reporting incidents and that all staff are aware of these systems.

Drug Interactions

A drug interaction occurs when the true effects of a drug that has been given to a patient are altered by the presence of another drug

- Interactions can occur between drugs and food, chemicals
- More than two drugs can be involved
- Drugs interact and so can their metabolites

What are the potential outcomes of a drug interaction?

- More of what you wanted to happen – synergistic
- Less of what you wanted to happen – antagonistic
- Something completely different - difficult to predict

Mechanisms of drug interactions

- Affect absorption
For example one drug decreases the absorption from the bowel of a second drug, the drug may alter GI pH, chelation may occur or the drug may affect motility
  e.g. antacids decrease the absorption of many drugs such as ciprofloxacin, iron, oxytetracycline.
Affect metabolism
For example one drug increases or decreases the metabolic inactivation of a second drug, the drugs are enzyme inducers or enzyme inhibitors e.g. rifampicin enhances the metabolic destruction of female sex hormones making the OCP unreliable.

Affect elimination
For example one drug increases or decreases the rate at which another drug is removed from the body, urinary pH is affected or active secretion occurs e.g. amiodarone reduces the elimination of digoxin by the kidney.

Affect protein binding
For example displacement from binding sites meaning that more active drug is available (warafrin for example is a drug that is highly protein bound).

Pharmacodynamic
For example two drugs have additive or opposing pharmacological effects. e.g. NSAIDs cause fluid retention, so a patient on diuretics may get less benefit if taking an NSAID, salbutamol and atenolol oppose each other’s effects.

Sources of information on drug interactions:
- BNF
- Manufacturer
- MI centre (x6908/6909)
- Ward pharmacist

Section covered:
F1 doctor signature.......................... GMC number.................
F2 doctor signature.......................... GMC number.................