Anticoagulant therapy and referral form

PE Rose on behalf of the Haemostasis and Thrombosis task force of the British Committee for Standards in Haematology

Many hospitals use the recommendations contained in the British Committee for Standards in Haematology anticoagulant guideline documents to develop local protocols for anticoagulant management. A combined anticoagulant treatment chart and referral form has been produced to help incorporate the recently updated recommendations for oral anticoagulation into day-to-day practice.

One of the main problems in anticoagulant management occurs when patients have been discharged from hospital with inadequate clinical information that relates to the reason and duration of anticoagulant therapy. It is therefore helpful to combine the treatment record and referral form (Rose, 1996).

The anticoagulant chart is for use at the patient's bedside and then at the commencement of outpatient monitoring of therapy. This approach should enable a seamless service for the management of anticoagulant care. It can be used within different hospital settings to ensure that the necessary clinical and treatment information is available to all clinicians involved in the management of the patient's anticoagulant treatment.

This chart consists of three treatment regimens: a heparin infusion schedule, a low molecular weight heparin regimen and warfarin dosage protocol for the initiation of treatment (Fennerty et al, 1988). Some hospitals may not wish to use all these modalities of treatment, or prefer to use unfractionated subcutaneous heparin in preference to an intravenous infusion (Hull et al, 1986).

Modification of the chart can be made according to local preference. The additional information contained should, however, be applicable to most hospitals involved in the management of adult anticoagulant care; it provides information for the rapid reversal of anticoagulation together with the recommended ranges and target international normalized ratios (INRs) for oral anticoagulant therapy.

It is important that follow-up arrangements for oral anticoagulant management are established before hospital discharge, with the section on discharge arrangements completed and the patient issued with a patient anticoagulant booklet. The referral information and discharge arrangements can easily be audited in the anticoagulant clinic. It is recommended that a copy of the combined request for continuation of anticoagulant management and treatment record should also be kept in the patient's hospital notes.

HEPARIN INFUSION SCHEDULE

Unfractionated heparin requires regular monitoring and the dosage adjusted according to the activated partial thromboplastin time (APTT) as per the chart. The usual therapeutic range quoted of an APTT of 1.5–2.5 should equate to a plasma heparin level of 0.2–0.4 iu/ml as measured by protamine sulphate titration (Chiu et al, 1987) or 0.35–0.7 iu/ml using the anti-Xa assay (Hirsh, 1991). Because of differences between APPT reagents and coagulometers in respect of heparin sensitivity, an APTT therapeutic range of 1.5–2.5 does not apply to all reagents and often needs local adjustment (Kitchen et al, 1996). Adherence to the infusion regimen can be easily monitored and audited to ensure that heparin therapy is not prescribed for more than a 24-hour period without an APTT measurement which is required on a daily basis.

LOW MOLECULAR WEIGHT HEPARIN SCHEDULE

Some low molecular weight heparins (LMWHs) are now licensed for the treatment of proximal venous thrombosis and more recently for pulmonary embolism (Hull et al, 1992; Simmonneau et al, 1997). The frequency of

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Anticoagulant chart and referral form — *Hospital*

Guidelines for anticoagulation of adult patients

Lower doses may be required for:
(i) the elderly, especially those with cardiac failure
(ii) patients with hepatic and/or severe renal failure

Patient ref no :
Name :
Address :
:
:
:
Telephone :
Date of birth :

Unfractionated heparin infusion schedule

iv bolus 5000 units (in severe pulmonary embolism, 10 000 units may be used)
iv infusion 15 000 units/12 hours
Check APTT ratio after 2–6 hours
- acceptable range 1.5–2.5

Monitor platelets after 4 days heparin treatment

Adjust heparin as follows:-

> 5.0	stop for 1 hour decrease by 6000 units/12 hours	- recheck APTT	in	2 - 6 hours
4.1 - 5.0	decrease by 3600 units/12 hours	- recheck APTT	in	2 - 6 hours
3.1 - 4.0	decrease by 1200 units/12 hours	- recheck APTT	in	2 - 6 hours
2.6 - 3.0	decrease by 600 units/12 hours	- recheck APTT	in	2 -12 hours
1.5 - 2.5	no change	- recheck APTT	within	24 hours
1.2 - 1.4	increase by 2400 units/12 hours	- recheck APTT	in	2 -12 hours
< 1.2	increase by 4800 units/12 hours	- recheck APTT	in	2 - 6 hours

Check APTT 2–6 hours after starting heparin
Do not represcribe heparin for more than 24 hours
Checking APTT on a daily basis is the mandatory minimum for all patients receiving intravenous heparin
See overleaf for guidance on correction of over anticoagulation
For further information please contact consultant haematologist

Continue heparin until oral anticoagulation is established and the international normalized ratio (INR) is stable in the appropriate therapeutic range

Subcutaneous low molecular weight heparin (LMWH) schedule

Name of LMWH=
Dose per kg body weight=

Treatment regimen for patients with confirmed DVT and/or PE (where licensed)

Frequency of sc injection based on body weight once/twice* per day (*delete as appropriate)

APTT monitoring is **not** routinely indicated

Treatment with LMWH should be for 5 days, and continued until the INR is stable within the appropriate therapeutic range 2.0–3.0 (target INR 2.5) or 3.0–4.0 (target INR 3.5) - see page 3

Monitor platelets after 4 days heparin treatment

Weight_____kg

Weight (kg)	dosage
130	
125	
120	
115	
110	
105	
100	
95	
90	
85	
80	
75	
70	
65	
60	
55	
50	
45	
40	

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Warfarin schedule

DVT start warfarin same day as heparin (includes LMWH)
PE, DVT and PE start warfarin same day as heparin or when diagnosis is confirmed

Warfarin dosing

Day	INR	Dose mg
1	< 1.4	10.0
2	< 1.8	10.0
	= 1.8	1.0
	> 1.8	0.5
3	< 2.1	10.0
	2.0 - 2.1	5.0
	2.2 - 2.3	4.5
	2.4 - 2.5	4.0
	2.6 - 2.7	3.5
	2.8 - 2.9	3.0
	3.0 - 3.1	2.5
	3.2 - 3.3	2.0
	= 3.4	1.5
	= 3.5	1.0
	3.6 - 4.0	0.5
	> 4.0	0.0

Warfarin dosing ...continued

Day	INR	Dose mg	
4	< 1.4		Refer to haematology department for advice
	= 1.4	8.0	
	= 1.5	7.5	
	1.6 - 1.7	7.0	
	= 1.8	6.5	
	= 1.9	6.0	
	2.0 - 2.1	5.5	
	2.2 - 2.3	5.0	
	2.4 - 2.6	4.5	
	2.7 - 3.0	4.0	
	3.1 - 3.5	3.5	
	3.6 - 4.0	3.0	
	4.1 - 4.5		Miss out one day's dose, then give 2.0 mg
	> 4.5		Miss out two day's dose, then give 1.0 mg
5 onward			Monitor INR daily until in range and stable (iv heparin can be stopped when two consecutive INR results in therapeutic range)

BLEEDING WHILE ANTICOAGULATED (UNFRACTIONATED HEPARIN)

As heparin has a short half-life it is usually sufficient to stop infusion
If bleeding is severe reverse anticoagulation with iv protamine sulphate as follows
→ 1mg protamine for every 100 units of heparin given over previous hour
→ Halve protamine dose if heparin infusion has been stopped for 1 hour, quarter dose if stopped for 2 hours
Give protamine slowly (5mg/min), not more than 40mg at one time
Note: a further dose may be required as protamine has a short half-life

BLEEDING WHILE ANTICOAGULATED (LMWH)

If bleeding is severe reverse anticoagulation with iv protamine sulphate as follows
→ 40mg protamine sulphate
Give protamine slowly (5mg/min)
As LMWH is continuously absorbed, repeat treatment may be necessary

BLEEDING WHILE ANTICOAGULATED (WARFARIN)

Life-threatening haemorrhage
→ Stop warfarin
→ 5mg vitamin K by slow iv injection
→ Factor II,IX,X and VII concentrates at 50 iu/kg
→ If no concentrate use fresh frozen plasma (FFP) approx 1L in an adult (15ml/kg)
Less severe haemorrhage
→ Withhold warfarin for 1 or more days. Restart at reduced dose when INR < 5.0
→ Consider vitamin K 0.5 - 2.0 mg iv
Unexpected bleeding at therapeutic levels
→ Investigate for underlying cause

If in doubt contact consultant haematologist

OVERANTICOAGULATION WITHOUT BLEEDING

INR>8.0 no bleeding
→ stop warfarin
→ give vitamin K 0.5mg iv or 5mg oral. Restart at reduced dose when INR<5.0
INR 5.0 - 8.0 without haemorrhage
→ Withhold warfarin for 1 or 2 days and review. Restart at reduced dose when INR<5.0

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Request for continuation of anticoagulant therapy as outpatient

An appointment for anticoagulant follow up *must* be made *before* the patient is discharged from hospital.

Telephone_____. This form *must* be completed and sent to _____.

Please tick one box	Venous thromboembolism	Target INR	range	Recommended duration
	Postoperative calf vein thrombosis without any risk factors	2.5	2 - 3	6 weeks
	Calf vein thrombosis in non-surgical patients without any risk factors	2.5	2 - 3	3 months
	Pulmonary embolus and proximal vein thrombosis	2.5	2 - 3	6 months
	DVT and/or PE with persistent risk factors	2.5	2 - 3	duration varies according to risk factor(s) - discuss with haematologist
	Recurrent DVT and/or PE	2.5	2 - 3	indefinite
	Recurrent DVT and/or PE while on warfarin (INR range 2–3)	3.5	3 - 4	indefinite
	Atrial fibrillation (AF)			
	Atrial fibrillation or other high risk arrhythmias	2.5	2 - 3	indefinite
	Heart valve prostheses and other cardiac indications			
	Mechanical prosthetic valves	3.5	3 - 4	indefinite
	Bioprosthetic heart valves (not aortic)	2.5	2 - 3	3 months*
	Cardiomyopathy, mural thrombus or akinetic segment	2.5	2 - 3	indefinite

* discontinue warfarin if there is no AF, intracardiac thrombus or history of systemic embolism
Patients not requiring warfarin should be considered for antiplatelet therapy, e.g. aspirin

Aspirin is first-line therapy for the following conditions:
If warfarin is considered appropriate:

	TIA / ischaemic stroke	3.5	3 - 4	indefinite
	Peripheral arterial thrombosis and grafts	3.5	3 - 4	indefinite
	Coronary artery thrombosis	3.5	3 - 4	indefinite
	Coronary artery graft thrombosis	3.5	3 - 4	indefinite
	Coronary angioplasty and coronary stents	3.5	3 - 4	indefinite
	Preferred treatment end date for anticoagulation			
	Other drug therapy:			
	If patient currently taking aspirin, should this continue?	YES / NO		
	Discharge home date/time			
	Date of follow-up as outpatient			
	Date of anticoagulant follow up			
	Yellow anticoagulant book issued to patient			
	Transport to anticoagulant clinic required	YES / NO		ambulance / car
	Signature of referring doctor / specialist nurse			

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Results and treatment record

Please us a SEPARATE LINE for heparin and warfarin

Date	Time of test	APTT ratio	IV Heparin dose per 12h	LMWH dose	INR	Warfarin dose per 24h	Doctor's signature	Time given	Administered by

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administration is either once or twice a day depending on the LMWH, and is given subcutaneously on a weight-adjusted basis. Laboratory monitoring is not routinely recommended; however, in severe renal failure and pregnancy monitoring with anti-Xa levels should be considered.

WARFARIN DOSAGE SCHEDULE

The warfarin dosage schedule is for patients requiring rapid anticoagulation. A recommended warfarin dosage is given for the first 4 days of treatment based on daily INR estimations. Thereafter dosage recommendations and recall are provided by the clinicians responsible for continuing anticoagulant management. This warfarin dosage schedule is not applicable for the commencement of treatment where the clinical condition is chronic as with most cases of atrial fibrillation. In these cases a loading dose regimen as shown is unnecessary.

CONCLUSION

By providing a template for the development of local anticoagulant treatment charts, it is hoped that recent changes in anticoagulant management can be rapidly incorporated into routine practice, and that the standard of information available to the clinicians involved in anticoagulant care can be improved. In particular, it should enable the commencement of anticoagulant therapy to be easily audited. Overall the aims of this treatment are to improve the information available to the clinician responsible for continuing anticoagulant care as well as the standards of hospital inpatient management for patients requiring anticoagulant treatment. HM

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KEY POINTS

- Combining the hospital anticoagulant therapy and referral form improves transfer of information to outpatient services.
- A daily activated partial thromboplastin time check is a mandatory minimum for all patients receiving intravenous heparin.
- Target international normalized ratio values provided on the anticoagulant chart help standardize clinical practice.