Clinical Practice Guidelines
Antithrombotic Therapy

Ischaemic Heart Disease

All patients with suspected acute myocardial infarction or unstable angina not already taking aspirin should be given aspirin (150-300 mg) as soon as possible (unless contraindicated)

☑ General practitioners should carry aspirin so that treatment can be initiated at diagnosis

Patients with acute myocardial infarction should also be considered for thrombolysis as quickly as possible after the onset of symptoms

Patients who are hospitalised with severe unstable angina should also be considered for full dose heparin or low molecular weight heparin

All patients with previous myocardial infarction, angina, or previous coronary artery surgery or angioplasty should (unless contraindicated) be considered for antiplatelet prophylaxis, usually with aspirin (75-300 mg/day)

In patients with contraindications to aspirin, clopidogrel (75 mg/day) should be considered for prophylaxis

Cerebrovascular Disease

Patients with acute stroke should have an early CT scan (preferably within 48 hours and no later than seven days)

Patients shown to have ischaemic stroke should receive aspirin as soon as the diagnosis is confirmed (150-300 mg) (unless contraindicated)

Anticoagulant therapy should be reserved for acute ischaemic stroke patients with a high risk of either venous thromboembolism or recurrent thromboembolic stroke

Patients with TIA should be investigated promptly

Patients with ischaemic stroke or TIA should (unless contraindicated) receive secondary

prevention with one of:

- aspirin (75-300 mg/day)
- dipyridamole (200 mg twice daily) for patients intolerant of aspirin and (in combination with aspirin) for those with recurrent events despite aspirin
- clopidogrel (75 mg/day) for patients intolerant of aspirin
- warfarin in suitable patients with atrial fibrillation or other suspected cause of cardioembolic stroke

Following carotid endarterectomy, patients should (unless contraindicated) receive aspirin (75-300 mg/day)

Peripheral arterial disease

Patients with intermittent claudication or a history of peripheral angioplasty or arterial grafts should receive aspirin (unless contraindicated) or clopidogrel (75 mg/day)

Atrial Fibrillation

(For other cardiac causes of systemic embolism, see full guideline)

Risk factors for systemic thromboembolism should be assessed routinely in all patients with atrial fibrillation

Risk factors for thromboembolism in AF are:

- previous ischaemic stroke or TIA
- age over 65 years
- hypertension
- diabetes mellitus
- cardiac failure
- echocardiography showing LV dysfunction or mitral valve calcification

Warfarin (target INR 2.5, range 2.0-3.0)
reduces stroke risk by 68%
Aspirin (75-300 mg/day) reduces stroke
risk by 20%

Patients with AF but without additional risk factors require no antithrombotic prophylaxis unless there are other indications for aspirin. Patients with one or more risk factors should be considered for warfarin therapy in preference to aspirin

Warfarin prophylaxis should also be considered in patients with atrial fibrillation and heart valve disease or prostheses, thyrotoxicosis, intracardiac thrombus, or non-cerebral thromboembolism

The decision to use warfarin or not should be based on discussion of the balance of risk and benefit with each individual, including assessment of compliance

☑ To minimise the risk of intracranial bleeding in patients on warfarin, hypertension should be controlled, compliance assessed and the risks and benefits of warfarin reviewed annually, especially in those aged over 75 years

Cardioversion to restore sinus rhythm should be considered in selected patients, because it may avoid the need for long term warfarin.

For recommended anticoagulant cover for cardioversion, see full guideline.

Annual Risk Of Stroke On No Treatment, Aspirin, Or Warfarin In High, Moderate And Low Risk Patients With Non-valvular Atrial Fibrillation

Risk group
Very high: - previous ischaemic stroke or TIA
High: - age over 65 and one other risk factor (hypertension, diabetes mellitus, heart failure, LV dysfunction)
Moderate: - age over 65, no other risk factors - age under 65, other risk factors
Low: - age under 65, no other risk factors

** Number needed to treat with warfarin instead of aspirin for one year to prevent one stroke*

Venous thromboembolism (deep vein thrombosis and/or pulmonary embolism)

DIAGNOSIS OF ACUTE VENOUS THROMBOEMBOLISM

Diagnostic imaging should be performed expeditiously (within 24 hours if possible) in patients with suspected DVT (venography, ultrasound) or PE (e.g. ventilation-perfusion lung scanning) to minimise exposure to the risks of inappropriate continued full-dose anticoagulation in those patients in whom venous thromboembolism is not confirmed

In all patients with clinically-suspected DVT, the diagnosis should be confirmed or excluded by diagnostic imaging, either:

- non-invasive testing by ultrasound (compression or Duplex scanning) followed by contrast venography if negative to detect calf DVT and non-occlusive proximal DVT; or
- contrast venography (detects both calf and proximal DVT); or
- serial (repeat after seven days) non-invasive testing by ultrasound to detect proximal extension of calf DVT

A single negative ultrasound may be sufficient to exclude DVT in patients with low clinical pre-test probability and/or a normal fibrin D-dimer assay

HEPARIN IN ACUTE TREATMENT OF DVT OR PE

Outpatients with clinically suspected DVT or PE should be referred to hospital for diagnosis and consideration of initial anticoagulation with heparin

A In clinically-suspected DVT or PE, heparin should be commenced (unless strongly contraindicated) until the diagnosis is excluded by objective testing

Monitoring of the APTT ratio should be performed expeditiously in patients receiving unfractionated heparin, and heparin doses adjusted according to a local protocol to achieve the therapeutic target range (usually 1.5-2.5) within 24 hours

Subcutaneous unfractionated heparin is an effective alternative to intravenous unfractionated heparin for the initial treatment of DVT. Low molecular weight heparins are effective alternative treatment to unfractionated heparin for DVT or PE

ORAL ANTICOAGULANTS IN ACUTE AND MAINTENANCE TREATMENT OF DVT OR PE

If therapeutic anticoagulation is contraindicated, inferior vena cava (IVC) filter insertion should be considered

Following initial heparinisation in patients with DVT or PE, maintenance of anticoagulation with oral anticoagulants is recommended in non-pregnant patients. Adjusted-dose subcutaneous heparin may be considered as an alternative therapy

☑ In intravenous drug users, the advisability of any continued anticoagulant therapy following hospital discharge should be assessed critically

Early institution of oral anticoagulants is recommended in most patients

A The optimal target INR during oral anticoagulant therapy for a first episode of venous thromboembolism is 2.5, range 2.0-3.0

The routine recommended duration of oral anticoagulant therapy following a first episode of DVT or PE is at least three

At three months, patients should be assessed for continuing risk factors (e.g. idiopathic, premature or familial presentation; thrombophilias; malignancy; chronic infection; inflammatory bowel disease; nephrotic syndrome; thromboembolic pulmonary hypertension)

The presence of continuing risk factors suggests consideration of anticoagulation long term, or until risk ractors resolve

Patients with thrombophilias should be referred to consultant haematologists or to centres with expertise in management of these patients

OTHER ANTITHROMBOTIC THERAPIES IN TREATMENT OF DVT OR PE

Graduated elastic compression stockings should be worn on the affected leg following proximal DVT for at least two years to reduce the incidence of severe post-thrombotic leg syndrome

Dosage, Monitoring, Reversal, And Contraindications To Antithrombotic Drugs

WARFARIN

Dose: usually 1-15 mg/day to maintain target INR
(range usually 2.0-3.0; patients with certain mechanical heart valves or recurrent thromboembolic events require higher target ranges)

☑ Monitoring of INR should be performed at 4-8 week intervals when stable, but more frequently when change in clinical state or medication

Patients and/or relatives or carers should be educated on advice in the DoH oral anticoagulant booklet

Clinicians providing anticoagulant care must have explicit systems for handling results promptly; making informed decisions on further treatment and testing; and communicating results to patients accurately

Surgeons, dentists and physicians intending to perform surgery or invasive procedures in patients receiving anticoagulant therapy should seek advice concerning management of such therapy from a haematologist

In patients with a high INR (>8.0) or other risk factors for bleeding, vitamin K1 (0.5 mg IV or 5 mg orally) should be considered

In patients with non-severe bleeding and a high INR, warfarin should be stopped for 1-2 days and vitamin K1 given (0.5-2 mg IV or 5-10 mg orally)

In patients with life threatening haemorrhage:

- factor IX complex concentrate should be given at a dose of 50 IU/kg body weight: such therapy is more efficacious than fresh frozen plasma
- if factor VII concentrate is available it should be given at a similar dose
- in addition, intravenous vitamin K1 should be given (5 mg, repeated as necessary)

Possible means to reduce the risk of excessive bleeding during and after surgery or other invasive procedures include:
- urgent reversal of oral anticoagulant therapy
- elective discontinuation of oral anticoagulant, or dose reduction, to achieve a lower INR
- substitution of heparin

The most common cause of fatal or disabling bleeding in patients receiving anticoagulant therapy is intracranial or intraspinal bleeding. Any such patients who have head injury, headache (recent, severe), confusion, impaired consciousness, or focal neurological symptoms and signs should have urgent CT scanning to detect such bleeding, followed by appropriate reversal of anticoagulant therapy

ASPIRIN

Dose: 75-300 mg/day is as effective as higher doses Although 75 mg/day suppresses platelet aggregation in most patients after several days, earlier effects are achieved with 150-300 mg in acute myocardial infarction or acute ischaemic stroke

The risk of major GI bleeding is 1:500 patient-years and is dose dependent above 300 mg/day

Gastric intolerance can be reduced by using the minimum effective dose (75 mg), using dispersible or enteric-coated preparations, or co-prescribing antacids, misoprostol, proton pump inhibitors or H2-receptor antagonists

Concomitant use of warfarin should be avoided, except in certain patients with prosthetic heart valves or recurrent thromboembolism with one or other drug alone

FULL DOSE UNFRACTIONATED HEPARIN

Monitor APTT ratio to achieve target range (usually 1.5-2.5)

Monitor platelet count after five days therapy; stop heparin if thombocytopenia detected

CONTRAINDICATIONS TO AND CAUTIONS WITH FULL-DOSE ANTICOAGULANT DRUGS

(Note: these depend on individual circumstances and are seldom absolute)

- Uncorrected major bleeding
- Uncorrected major bleeding disorder
  - e.g. thrombocytopenia, haemophilias, liver failure, renal failure
- Uncontrolled severe hypertension
  - e.g. systolic >200 mm Hg or diastolic >120 mm Hg
- Potential bleeding lesions
  - e.g. active peptic ulcer, oesophageal varices aneurysm, proliferative retinopathy recent organ biopsy recent trauma or surgery to head, orbit, spine recent stroke confirmed intracranial or intraspinal bleed
- Heparin
  history of heparin-induced thrombocytopenia or thrombosis
- Warfarin
  pregnancy (usually)
  homozygous protein C deficiency (risk of skin necrosis) history of warfarin-related skin necrosis
  uncooperative/unreliable patients (long term therapy)