**Stable angina**

**Clinical syndromes**

Stable angina is a clinical syndrome characterised by discomfort in the chest, jaw, shoulder, back, or arms, typically elicited by exertion or emotional stress and relieved by rest or

nitroglycerin. Characteristically, the discomfort (it is often not described by the patient as a pain) occurs after a predictable level of exertion, classically when climbing hills or stairs, and resolves within a few minutes on resting. Further investigations are needed to confirm the diagnosis and assess the need for intervention. The resting electrocardiogram (ECG) is normal in more than half of patients with angina. However, an abnormal ECG substantially increases the probability of coronary disease; Exercise testing is useful both in confirming the diagnosis and in giving a guide to prognosis. Alternatives such as myocardial scintigraphy (isotope scanning) and stress echocardiography (ultrasound) provide similar information. Coronary angiography is regarded as the gold standard for the assessment of CAD and involves the passage of a catheter through the arterial circulation and the injection of radio-opaque contrast media into the coronary arteries.

Non-invasive techniques, including magnetic resonance imaging (MRI) and multi-slice CT scanning, are being developed and tested as alternatives to angiography.

**Treatment of stable angina is based on two principles:**

•Improve prognosis by preventing myocardial infarction and death.

•Relieve or prevent symptoms.

Pharmacological therapy can be considered a viable alternative to invasive strategies, providing similar results without the complications associated with percutaneous coronary intervention (PCI).

**Anti thrombotic drugs**

**Aspirin** acts via irreversible inhibition of platelet COX-1 and thus thromboxane production, which is normally complete with chronic dosing of 75 mg/day. This antiplatelet action is apparent within an hour of taking a dose of 300 mg. The effect on platelets lasts for the lifetime of the platelet. The optimal maintenance dose seems to be 75–150 mg day

**Clopidogrel.** inhibits ADP activation of plate-lets and is useful as an alternative to aspirin in patients who are allergic or cannot tolerate aspirin. The usual dose is 300 mg once, then 75 mg daily. Although less likely to cause gastric erosion and ulceration, gastro-intestinal bleeding is still a major complication of clopidogrel therapy

**COX-2 inhibitors.** NSAIDs with high COX-2 specificity increase the risk of myocardial infarction and should be avoided where possible in patients with stable angina.

**ACE-inhibitors**  In addition to the vasodilation caused by inhibiting the production of angiotensin II, ACE inhibitors have anti-inflammatory, antithrombotic and anti-proliferative properties. Some of these effects are mediated by actions on vascular endothelium and might be expected to be of benefit in all patients with CAD. ACE inhibitors also reduce the production of ROS.

**Statins**

In addition to cholesterol-lowering properties, statins also have antithrombotic, anti-inflammatory and antiproliferative properties. They are also important in restoring normal endothelial function and inhibit the production of ROS in the vessel wall. There is some evidence that patients with elevated levels of CRP have better outcomes with statin therapy even if cholesterol levels are not raised. Most patients with stable angina will be on statins for their cholesterol-lowering effects.

**Symptom relief and prevention In stable angina**, much of the drug treatment is directed towards decreasing the workload of the heart and, to a lesser extent, improving coronary blood supply; this provides symptomatic relief and improves prognosis. Therapy to decrease workload is targeted at both decreasing afterload and controlling heart rate.

**β-Blockers**

Various studies have demonstrated the beneficial effect of β-blockers in angina and they are now considered first-line agents. β-Blockers reduce mortality both in patients who have suffered a previous myocardial infarction and in those with heart failure. They reduce myocardial oxygen demand by blocking β-adrenergic receptors, thereby decreasing the heart rate and force of left ventricular contraction and lowering blood pressure. The decreased heart rate not only reduces the energy demand on the heart but also permits better perfusion of the subendocardium by the coronary circulation. β-Blockers are particularly useful in exertional angina. Patients treated optimally should have a resting heart rate of around 60 beats/min. β-Blockers should be used with caution in patients with diabetes as the production of insulin is under adrenergic system control and thus their concomitant use may worsen glucose control. β-Blockers can also mask the symptoms of hypoglycaemia their tendency to cause bronchospasm and peripheral vascular spasm means that they are contraindicated in patients with asthma, and used with caution in chronic obstructive airways diseases and peripheral vascular disease as well as in acute heart failure and bradycardia. Cardioselective agents such as atenolol, bisoprolol and metoprolol are preferred because of their reduced tendency to cause bronchoconstriction, but no β-blocker is completely specific for the heart. Agents with low lipophilicity, for example, atenolol, penetrate the central nervous system (CNS) to a lesser extent than others, for example, propranolol, metoprolol, and do not so readily cause the nightmares, hallucinations and depres-sion that are sometimes found with lipophilic agents, which should not be used in patients with psychiatric disorders.

**Calcium channel blockers**

While short-acting dihydropyridine CCBs have been implicated in the exacerbation of angina due to the phenomenon of ‘coronary steal’, longer acting dihydropyridines, for example, amlodipine and felodipine or longer acting formulations, for example, nifedipine LA, have demonstrated symptom-relieving potential similar to β-blockers. Dihydropyridines have no effect on the conducting tissues and are effective arterial dilators, decreasing afterload and improving coronary perfusion but also causing flushing, headaches and reflex tachycardia. This may be overcome by combination with a β-blocker. The use of dihydropyridines in angina is based on efficacy in trials that have used surrogate markers such as exercise tolerance rather than mortality as the endpoint. CCBs with myocardial rate control as well as vasodilatory properties, for example, diltiazem, and those with predominantly rate-controlling effects, for example, verapamil, have also been shown to improve symptom control, reduce the frequency of anginal attacks and increase exercise tolerance. They should be avoided in patients with compromised left ventricular function and conduction abnormalities. Verapamil and diltiazem are suitable for rate control patients in whom β-blockers are contraindicated on grounds of respiratory or peripheral vascular disease.

**Nitrates**

Organic nitrates are valuable in angina because they dilate veins and thereby decrease preload, dilate arteries to a lesser extent thereby decreasing afterload, and promote flow in collateral coronary vessels, diverting blood from the epicardium to the endocardium. They are available in many forms but all relax vascular smooth muscle by releasing nitric oxide, which was formerly known as endothelium-derived relaxing factor, which acts via cyclic GMP

Tolerance is one of the main limitations to the use of nitrates. This develops rapidly, and a ‘nitrate-free’ period of a few hours in each 24-h period is beneficial in maintaining the effectiveness of treatment. The nitrate-free period should coincide with the period of lowest risk, and this is usually night time, but not early morning, which is a high-risk period for infarction. Many patients receiving short-acting nitrates two or three times a day would do well to have their doses between 7 a.m. and 6 p.m. There are many nitrate preparations available, including intravenous infusions, conventional or slow-release tablets and capsules, transdermal patches, sublingual tablets and sprays and adhesive buccal tablets. Slow-release preparations and transdermal patches are expensive, do not generally offer such flexible dosing regimens as short-acting tablets.

**Nicorandil** is a compound that exhibits the properties of a nitrate but which also activates ATP-dependent potassium channels. The main benefit for patients in the nicorandil group was a reduction in unplanned admission to hospital with chest pain.

**Ivabradine** represents a class of antianginal agents which block the If current. If is a mixed Na+–K+ inward current activated by hyperpolarisation and modulated by the autonomic nervous system. This regulates pacemaker activity in the sinoatrial node and controls heart rate. Inhibition, there-fore, reduces heart rate without affecting the force of contrac-tion. Ivabridine is similar in efficacy to atenolol and CCBs and may be of particular use in patients in whom β-blockers are contraindicated. The most frequent adverse drug reactions are dose-dependent transient visual symptoms

**Ranolazine**, a selective inhibitor of late sodium influx, attenuates the abnormalities of ventricular repolarisation and contractility associated with ischaemia. It has been shown to increase exercise tolerance, reduce anginal episodes and reduce the use of GTN. Side effects include dizziness, constipation , nausea, and the potential for prolongation of the QTc interval.