The goals of therapy in chronic ischemic heart disease are to decrease the frequency of anginal attacks, to prevent acute coronary syndromes such as myocardial infarction, and to prolong survival.In addition, atherosclerosis–associated endothelial cell dysfunction causes inappropriate vasoconstriction of the coronary resistance vessels.New surgical techniques (increased use of various arterial grafts, less invasive operations); novel adjuncts to stenting (potent antithrombotic drugs, advanced approaches to prevent in–stent restenosis); and progress in pharmacologic management (e.g., aggressive use of statins and antithrombotic drugs) will likely further improve outcomes and better define the best therapeutic approaches for specific subsets of patients with chronic CAD.They relieve myocardial ischemia by (1) decreasing oxygen demand (vasodilatation reduces ventricular filling and size, arterial dilatation reduces the resistance against which the left ventricle contracts, and both actions reduce wall stress); and (2) increasing myocardial oxygen supply via coronary dilatation.However, care should be taken in combining a ?–blocker with a nondihydropyridine calcium channel blocker (verapamil or diltiazem) because the additive negative chronotropic effect can cause excessive bradycardia, and the combined negative inotropic effect could precipitate heart failure in patients with LV contractile dysfunction.That late phase tends to be abnormally enhanced in ischemic myocardium, and the associated increased sodium influx results in higher–than–normal intracellular Ca++ (mediated by the transsarcolemmal Na+–Ca++ exchanger; see Fig.Organic nitrates (e.g., nitroglycerin, isosorbide dinitrate, isosorbide mononitrate), as previously mentioned, relieve ischemia primarily through vasodilatation (i.e., lower Ischemic Heart Disease 161 wall stress results from a smaller ventricular radius) and possibly through coronary vasodilatation.The benefits of statin therapy are believed to extend beyond their lipid–altering effects, because there is evidence that they decrease vascular inflammation and improve endothelial cell dysfunction and thus may help stabilize atherosclerotic plaques.Longer–acting anginal prevention can be achieved through a variety of nitrate preparations, including oral tablets of isosorbide dinitrate (or mononitrate) or a transdermal nitroglycerin patch, which is applied once a day.This medication has been shown to decrease the frequency of anginal episodes and improve exercise ca162 Chapter Six 10090–06_CH06.qxd 8/31/06 5:22 PM Page 162 Ischemic Heart Disease 163 pacity in patients with chronic CAD but differs from other anti–ischemic drugs in that it does not affect the heart rate or blood pressure.Aspirin has antithrombotic actions through inhibition of platelet aggregation (and therefore reduces the release of platelet–derived procoagulants and vasoconstrictors) as well as anti–inflammatory properties that may be important in stabilizing atheromatous plaque.Platelet aggregation o Gastrointestinal irritation or bleeding BP, blood pressure; D, diltiazem; LV, left ventricular; N, nifedipine and other dihydropyridine calcium++ channel antagonists; V, verapamil.The following sections describe medical and surgical strategies to (1) reduce ischemia and its symptoms by restoring the balance between myocardial oxygen supply and demand, and (2) prevent acute coronary syndromes and death in patients with chronic CAD.(However, as described in Chapter 9, ?–blockers actually improve outcomes in patients with stable heart failure conditions.) ?– Blockers are also relatively contraindicated in patients with marked bradycardia or certain types of heart block to avoid additional impairment of electrical conduction.Moreover, although ?–blockers have demonstrated mortality benefits in patients after MI, none of has been shown to improve longevity in patients with chronic stable angina

and preserved LV function.However, the combination of aspirin and cladogram is superior to aspirin alone in reducing death and ischemic complications in patients with acute coronary syndromes and in those undergoing elective percutaneous coronary stenting. All patients with CAD should have their LDL cholesterol maintained at 50%) stenosis of the left main coronary artery and patients with multivessel disease who also have reduced LV contractile function or diabetes.Improvements in other risk factors for CAD, including obesity and physical inactivity, are also likely to reduce the risk of adverse outcomes, although the benefits of these interventions are less well documented.Consequently, ?–adrenergic antagonists decrease the force of ventricular contraction and heart rate, thereby relieving ischemia by reducing myocardial oxygen demand.In addition to suppressing angina, several studies have shown that ?–blockers decrease the rates of recurrent infarction and mortality following an acute MI (see Chapter 7).Although ?1–selective blockers are theoretically less likely to exacerbate bronchospasm in such patients, drug selectivity for the ?1– receptor is not complete, and in general, all ?–blockers should be avoided in patients with significant obstructive airway disease.However, these agents have additional beneficial antianginal effects stemming from their more potent cardiac depressant actions: they reduce the force of ventricular contraction (inotropy) and slow the heart rate.In particular, HMG–CoA reductase inhibitors (statins; see Chapter 17) lower MI and death rates in patients with established coronary disease and in those at high risk of developing CAD.They are directed against ?–receptors, of which there are two classes: ?1–adrenergic receptors are restricted to the myocardium, whereas ?2–adrenergic receptors are located throughout blood vessels and the bronchial tree.One might also expect that ?–blockers would decrease myocardial blood perfusion by blocking the vasodilating ?2–adrenergic receptors on the coronary arteries.Medical Treatment to Prevent Acute Cardiac Events Platelet aggregation and thrombosis are key elements in the pathophysiology of acute MI and unstable angina (see Chapter 7).As described in Chapter 17, they irreversibly bind to the platelet ADP receptor P2Y12, thereby preventing platelet activation and aggregation.Data convincingly demonstrate the benefit of smoking cessation, cholesterol reduction, blood pressure control, and serum glucose control in lowering the risk of coronary disease events (see Chapter 5).In addition, when taken immediately before a person engages in activities known to provoke angina, these rapidly acting nitrates are useful as prophylaxis against anginal attacks.A limitation to chronic nitrate therapy is the development of drug tolerance (i.e., decreased effectiveness of the drug during continued administration), which occurs to some degree in most patients.?–Blockers are also generally not used in patients with acutely decompensated LV dysfunction because they could intensify heart failure symptoms by further reducing inotropy.No dihydropyridine calcium channel blockers (verapamil and diltiazem) also act as vasodilators but are not as potent in this regard as the dihydropyridines.In meta–analyses of randomized trials, these drugs have been associated with an increased incidence of MI and mortality.Pending further studies and experience, ranolazine is currently approved only for patients who have not responded adequately to the standard antianginal drugs described earlier.Preload (vasodilatation) o Hypotension o Reflex tachycardia ?1.10).2.