Antiplatelet drugs

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ABSTRACT

- Antiplatelet drugs protect against myocardial infarction, stroke, cardiovascular death and other serious vascular events in patients with a history of previous vascular events or known risk factors for cardiovascular disease.
- Aspirin reduces the risk of serious vascular events in patients at high risk of such an event by about a quarter and is recommended as the first-line antiplatelet drug.
- Clopidogrel reduces the risk of serious vascular events among high-risk patients by about 10% compared with aspirin. It is as safe as aspirin, but much more expensive. It is an appropriate alternative to aspirin for long-term secondary prevention in patients who cannot tolerate aspirin, have experienced a recurrent vascular event while taking aspirin, or are at very high risk of a vascular event (⩾ 20% per year).
- Addition of clopidogrel to aspirin reduces the risk of serious vascular events among patients with non-ST-segment elevation acute coronary syndromes by 20%, and patients undergoing percutaneous coronary intervention by 30%, compared with aspirin alone.
- Addition of a glycoprotein IIb/IIIa receptor antagonist to aspirin reduces the risk of vascular events among patients with non-ST-segment elevation acute coronary syndromes by 10% and among patients undergoing percutaneous coronary intervention by 30%, compared with aspirin alone; it appears to provide incremental benefit in patients also treated with clopidogrel.
- Addition of dipyridamole to aspirin seems to be more effective than aspirin alone for preventing recurrent stroke, but its overall effect in preventing serious vascular events in patients with ischaemic stroke and transient ischaemic attack has not been determined.

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THE MAJOR ROLE of antiplatelet drugs in clinical practice is to prevent the adverse clinical sequelae of thrombosis in atherosclerotic arteries to the heart (acute coronary syndromes [ACS]), brain (ischaemic stroke), and limbs (intermittent claudication and rest pain); and thrombosis of stagnant blood in veins (venous thromboembolism) and heart chambers (atrial fibrillation, heart failure).

The pivotal role of platelets in thrombosis is illustrated in Box 1.[1]

Antiplatelet drugs

Aspirin, clopidogrel, dipyridamole and the glycoprotein IIb/IIIa receptor antagonists (abciximab and tirofiban) are antiplatelet drugs approved for use in Australia (see Box 2).

Aspirin

Mechanism of action: Aspirin (acetylsalicylic acid) irreversibly inhibits prostaglandin H synthase (cyclooxygenase-1) in platelets and megakaryocytes, and thereby blocks the formation of thromboxane A_2 (TXA_2; a potent vasoconstrictor and platelet aggregant).[3] It is only the parent form, acetylsalicylic acid, which has any significant effect on platelet function. Because platelets are unable to regenerate cyclooxygenase, the immediate antithrombotic effect of aspirin remains for the lifespan of the platelet (8–10 days). As, after stopping aspirin therapy, normal haemostasis may be regained when about 20% of platelets have normal cyclooxygenase activity, daily aspirin intake is recommended.

Dose and administration: Formulations of aspirin currently available in Australia include a 100 mg enteric-coated form as well as 300 mg and 324 mg soluble tablets.

Aspirin is rapidly absorbed from the gastrointestinal (GI) tract, with peak concentrations achieved in 30–40 minutes.

When given as a single oral dose, at least 160 mg of soluble aspirin is required to maximally inhibit platelet function within 30 minutes. Thus, this dose (half 324 mg tablet) should be given as a loading dose if a rapid antiplatelet effect is required.

Soluble aspirin (40–80 mg daily) and enteric-coated aspirin (80–100 mg daily) have a cumulative effect, so that platelet TXA_2 formation is maximally inhibited (by more than 95%) after 4–5 days.[3,4]

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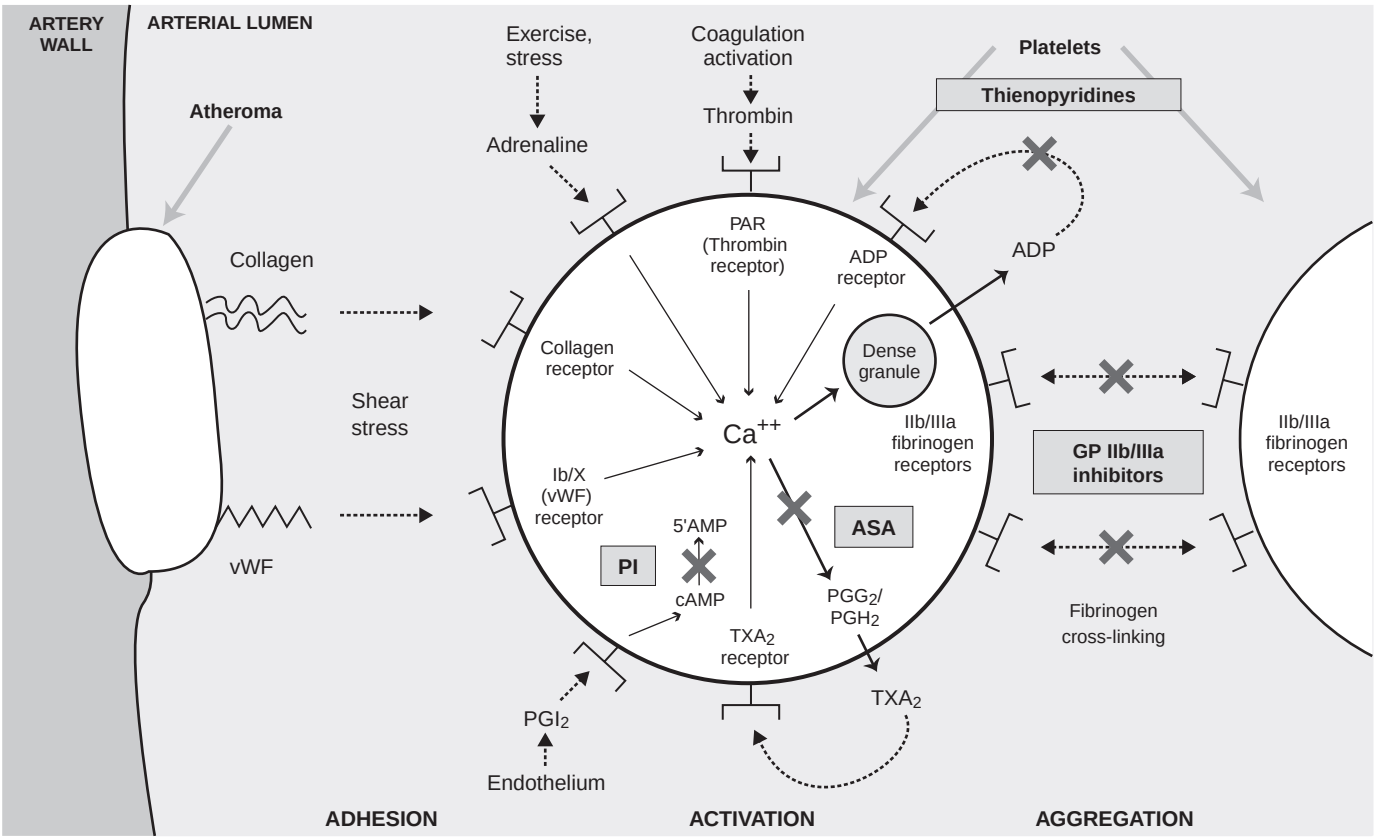
The evidence from randomised controlled trials (RCTs) supports daily doses of aspirin in the range 75–150 mg for the long-term prevention of serious vascular events in high risk patients (E1; Box 3).[5] Higher doses of 500–1500 mg aspirin daily are no more effective (E1)[5] (for an explanation of level-of-evidence codes, see Box 4).

Adverse effects: Aspirin use is associated with dose-related symptoms of upper-GI toxicity (nausea, heartburn, epigastric pain). High doses of aspirin (500–1500 mg daily) compared with medium (75–325 mg daily) or low (30 mg) doses, significantly increase the risk of upper-GI symptoms (E1).[12-15] Enteric-coated aspirin may cause less gastric irritation than soluble aspirin.[4]

1: Pivotal role of platelets in thrombosis and the sites of action of currently approved antiplatelet drugs



Adhesion of platelets to proteins (collagen, von Willebrand factor), particularly under conditions of high shear stress, and the action of platelet agonists (adrenaline, thrombin, ADP, thromboxane A_2) leads to the mobilisation of calcium ion (Ca^{++}), which functions as a mediator of platelet activation. Aspirin inhibits thromboxane A_2 synthesis by irreversibly acetylating cyclooxygenase-1; the thienopyridines (clopidogrel, ticlopidine) irreversibly block the ADP receptor; and glycoprotein IIb/IIIa inhibitors block the final common pathway of platelet activation leading to fibrinogen cross-linking of platelets and platelet aggregation. Phosphodiesterase inhibitors (dipyridamole, cilostazol) elevate intracellular cyclic AMP levels and thereby inhibit platelet function.
ADP = adenosine diphosphate; ASA = aspirin; cAMP = cyclic adenosine monophosphate; GP = glycoprotein; PGG_2 = prostaglandin G_2; PAR = Protease activated receptor; PGH_2 = prostaglandin H_2; PGI_2 = prostacyclin; PI = phosphodiesterase inhibitor; TXA_2 = thromboxane A_2; vWF = von Willebrand factor.

Aspirin is associated with about a 60%–70% excess of non-fatal extracranial haemorrhage (mostly from the GI tract), which corresponds to an absolute excess risk of about one or two per 1000 patients treated per year (E1).[5,16] The risk of bleeding is not significantly different with different daily aspirin doses or different aspirin formulations (plain, enteric-coated and buffered aspirin).[12,16] Aspirin is associated with an increased risk of intracranial haemorrhage of about one per 1000 patients treated for 3 years (E1).[17] Again, there is no clear variation in risk with the dose of aspirin used (E1).[17]

Clopidogrel and ticlopidine

Mechanism of action: The thienopyridine derivatives (clopidogrel and ticlopidine) are metabolised in the liver to active compounds which covalently bind to the adenosine phosphate (ADP) receptor on platelets and dramatically reduce platelet activation (see Box 1).

Dose and administration: An oral loading dose of 300–600 mg clopidogrel produces detectable inhibition of ADP-induced platelet aggregation after 2 hours, which becomes maximal after 6 hours.[18,19] If a loading dose of clopidogrel is not used, repeated daily oral doses of 75 mg clopidogrel are required to achieve a steady-state maximal platelet inhibition, which is comparable with that produced by 250 mg ticlopidine orally, twice daily.[20]

Adverse effects: Compared with aspirin, the thienopyridines are associated with a lower risk of GI haemorrhage (odds ratio [OR], 0.71; 95% CI, 0.6–0.9) and upper-GI symptoms (OR, 0.84; 95% CI, 0.8–0.9), and an increased risk of diarrhoea and of skin rash (E1).[21] Ticlopidine doubles the risk of skin rash (OR, 2.23; 95% CI, 1.7–2.9) and diarrhoea (OR, 2.27; 95% CI, 1.9–2.8) compared with aspirin (E1), whereas clopidogrel increases skin rash (OR, 1.32; 95% CI, 1.2–1.5) and diarrhoea by about a third (OR, 1.34; 95% CI, 1.2–1.6), compared with aspirin (E2).[21] Clopidogrel has superseded ticlopidine because the latter is associated with an

2: Profile of antiplatelet drugs approved for use in Australia

Class and agents	Dose	Route	$t_{½}$*	Contraindications	Adverse effects	Cost ($)[2]
Cyclooxygenase inhibitors						
Aspirin	Load: ⩾ 160 mg Maintenance: 75–150 mg once daily	Oral Sublingual Rectal	20 min	NSAID hypersensitivity Active peptic ulcer Severe hepatic/renal disease	GI bleed (1–2/1000 per year) Intracranial bleed (1/1000 per 3 years) GI toxicity Hypersensitivity Alopecia (rare)	$6.09 for 112 x 100 mg tabs ($19.85 per year)
Thienopyridines						
Clopidogrel	Load: 300 mg Maintenance: 75 mg once daily	Oral	8 h	Severe hepatic disease Pregnancy Lactation	Diarrhoea Skin rash	$84.00 for 28 x 75 mg tabs ($1095.00 per year)
Ticlopidine	250 mg twice daily	Oral	24–36 h	Severe hepatic disease Pregnancy Lactation	Thrombocytopenia Neutropenia Diarrhoea Skin rash Raised lipid levels Liver dysfunction	$155.33 for 60 x 250 mg tabs ($1889.85 per year)
Phosphodiesterase inhibitors						
Dipyridamole†	200 mg SR twice daily	Oral	10–12 h	Severe CAD Subvalvular aortic stenosis Haemodynamic instability	Headache GI upset Dizziness	$33.85 for 60 capsules ($411.84 per year)
Glycoprotein IIb/IIIa receptor antagonists‡						
Abciximab	Bolus: 250 μg/kg Infusion: 0.125 μg/kg/min	Intravenous infusion 24–72 h	30 min	Active bleeding Concurrent warfarin History of intracranial bleed Previous thrombocytopenia with glycoprotein IIb/IIIa antagonists Within 30 days of bleeding, stroke, major surgery, or severe trauma	Thrombocytopenia Bleeding Nausea Fever Headache Rash	$1531.23 for 3 x 10 mg ampoules ($1930.24 per 72 h infusion§)
Tirofiban	Bolus: 0.4–0.6 μg/kg Infusion: 0.10–0.15 μg/kg/min	Intravenous infusion 24–72 h	1.2–1.6 h			$372.62 for 12.5 mg in 50 mL ($376.64 per 72 h infusion§)

* Half-life of the active metabolite (the antiplatelet effect may last as long as the life of the platelet). † Also available as a combination with 25 mg aspirin. ‡ The glycoprotein IIb/IIIa receptor antagonist eptifibatide is not marketed in Australia. § For a 70 kg patient receiving the (median) recommended dose
CAD = coronary artery disease; GI = gastrointestinal; NSAID = non-steroidal anti-inflammatory drug; SR = sustained release.

excess of neutropenia compared with aspirin (OR, 2.72; 95% CI, 1.5–4.8) (E1), particularly in the early months of therapy, whereas clopidogrel is not (OR, 0.63; 95% CI, 0.3–1.4) (E2).[21] Furthermore, ticlopidine is associated with a significant excess of thrombocytopenia and of thrombotic thrombocytopenic purpura (TTP) (E32),[22,23] whereas clopidogrel is not (E2).[6,21] Although TTP has been reported in 20 patients taking clopidogrel,[24,25] the association between clopidogrel and TTP is likely to be coincidental (E32).[26] Therefore, if ticlopidine is to be used, haematological monitoring should be undertaken at commencement and every 2 weeks in the first 4 months of therapy.

Dipyridamole

Dipyridamole inhibits phosphodiesterase, which inactivates cyclic AMP (Box 1). Increased intraplatelet concentrations of cyclic AMP reduce the activation of cytoplasmic second messengers. Dipyridamole also stimulates prostacyclin release and inhibits thromboxane A_2 formation. Because the effect is short-lasting, repeated dosing or slow-release preparations are required to inhibit platelet function for 24 hours.

Glycoprotein IIb/IIIa receptor blockers

Mechanism of action: Glycoprotein IIb/IIIa receptor antagonists block the final common pathway for platelet aggregation (Box 1). Abciximab is a humanised mouse antibody fragment with a high binding affinity for the glycoprotein IIb/IIIa receptor. Tirofiban (a non-peptide derivative of tyrosine) and eptifibatide (a synthetic heptapeptide) mimic part of the structure of fibrinogen that interacts with the glycoprotein IIb/IIIa receptor and thus compete with ligand binding of fibrinogen to the glycoprotein IIb/IIIa receptor. Eptifibatide is not currently approved for use in Australia.

Dose and administration: Glycoprotein IIb/IIIa receptor antagonists are given intravenously as a bolus injection, followed by a continuous infusion for up to 72 hours. At 24 hours after cessation of an infusion of abciximab, there is persistent blockade of more than 50% of platelet glycopro-

3: Evidence of benefits and risk of antiplatelet therapy (E1)[5]

Antiplatelet therapy and indication	Mean treatment duration	Stroke, myocardial infarction or vascular death: Relative risk reduction* (SE)	Stroke, myocardial infarction or vascular death: Number of events (SE) avoided per 1000 patients treated	Extracranial bleeds: Number of events caused per 1000 patients treated
Antiplatelet therapy versus placebo[5†]				
Acute myocardial infarction	1 month	30% (4)	38 (5)	0
Acute ischaemic stroke	0.7 months	11% (3)	9 (3)	4
Previous myocardial infarction	27 months	25% (4)	36 (5)	0
Previous ischaemic stroke or TIA	29 months	22% (4)	36 (6)	5
Other high risk patients	22 months	26% (3)	22 (3)	9
Overall	24 months	22% (2)	25 (2)	4‡
Aspirin versus placebo (all high risk)	24 months	23% (2)	31 (3)	4‡
Clopidogrel versus aspirin				
Previous myocardial infarction, stroke, or PVD[6]	23 months	10% (4)	10	0
Clopidogrel plus aspirin versus aspirin				
Non-ST-segment elevation ACS[7]	9 months	20%	21	10
Percutaneous coronary intervention[8]	12 months	27%	30	21
Dipyridamole versus aspirin (all high risk patients)[6]	24 months	6% (6)	6	0
Glycoprotein IIb/IIIa receptor plus aspirin versus aspirin[5]	24–72 hours§	19% (4)	20 (4)	23
Non-ST-segment elevation ACS[9]	24–72 hours§	12% (5)	15	10
Percutaneous coronary intervention[10]	24–72 hours‡§	32% (6)	37§	12

* Data from the Antithrombotic Trialists' Collaboration[5] were reported as % odds reduction. However, in most cases relative risk reduction is a reasonable approximation of odds reduction when absolute event rates are low (eg, 5%–10% per year). † Most trials represented by these data were performed with aspirin. ‡ This estimate includes patients treated during the acute phase, in whom the risk of bleeding is higher than during long-term treatment (1–2 events per 1000 patients treated). § Outcome measured at 30 days.
SE = standard error; ACS = acute coronary syndromes; PVD = peripheral vascular disease; TIA = transient ischaemic attack.

tein IIb/IIIa receptors, but platelet function recovers after 2 days. By contrast, the antiplatelet effects of tirofiban rapidly dissipate after cessation of the infusion.

Adverse effects: Thrombocytopenia is relatively common (1.6% compared with 0.7% for placebo), and can be delayed for up to 5 days (E2). Acute severe thrombocytopenia ($< 20 \times 10^9$/L in 24 hours) occurs in 0.6% of patients, and needs to be differentiated from other causes such as immune heparin-induced thrombocytopenia (E2). The risk of recurrent thrombocytopenia is increased with re-exposure to abciximab.[27]

Therapeutic uses of antiplatelet drugs

A summary of indications for antiplatelet drugs and appropriate regimens is given in Box 5, and new messages about antiplatelet therapy are summarised in Box 6. Messages for patients are outlined in Box 7.

Patients at high vascular risk ("secondary" prevention)

Aspirin

In the absence of contraindications, immediate treatment with 160 mg aspirin is appropriate for all patients with suspected acute ischaemic syndromes of the brain, heart and limbs, including those undergoing percutaneous interventions (E1).[5] Long-term treatment (with 75–150 mg aspirin daily) is indicated thereafter (E1).[5] Treating 1000 patients at high risk of vascular events with aspirin for about 2 years, at a cost of about $20 per patient per year (ie, $40 000 total), prevents about 31 serious vascular events, compared with no aspirin (Box 3) (E1). This equates to spending less than $1250 over 2 years to save one serious vascular event.

4: Level-of-evidence codes

Evidence for the statements made in this article is graded according to the NHMRC system[11] for assessing the level of evidence.

- E1 Level I: Evidence obtained from a systematic review of all relevant randomised controlled trials.
- E2 Level II: Evidence obtained from at least one properly designed randomised controlled trial.
- $E3_1$ Level III-1: Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
- $E3_2$ Level III-2: Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case–control studies, or interrupted time series with a parallel control group.
- $E3_3$ Level III-3: Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.
- E4 Level IV: Evidence obtained from case-series, either post-test, or pre-test and post-test.

5: Clinical indications for antiplatelet drugs

Indication	Antiplatelet regimen
Acute ischaemic event	
ST-segment elevation ACS	Aspirin ⩾ 160 mg load, 75–150 mg once daily thereafter for years
Non-ST-segment elevation ACS	Aspirin ⩾ 160 mg load, 75–150 mg once daily thereafter for years
	Clopidogrel 300 mg load, 75 mg once daily thereafter for at least 9–12 months
Percutaneous coronary intervention (coronary angioplasty and stent)	
Before procedure	Aspirin 160–325 mg once daily > 2 hours before
	Clopidogrel 300 mg load at least 72 hours before (or ticlopidine*)
	Glycoprotein IIb/IIIa receptor antagonist (eg, abciximab) if high risk†
During procedure	Glycoprotein IIb/IIIa receptor antagonist (eg, abciximab) if high risk†
After procedure	Aspirin 75–150 mg once daily for years
	Clopidogrel 75 mg once daily for at least 12 months (or ticlopidine*)
	Glycoprotein IIb/IIIa receptor antagonist (eg, abciximab) for 12 hours if high risk†
Acute ischaemic stroke	Aspirin ⩾160 mg load, 75–150 mg once daily thereafter for years
High risk of serious vascular events (> 3% per year)	
Previous myocardial infarction	Aspirin 75–150 mg or clopidogrel 75 mg once daily
Stable angina/coronary artery disease	Aspirin 75–150 mg or clopidogrel 75 mg once daily
Previous ischaemic stroke or TIA	Aspirin 75–150 mg or clopidogrel 75 mg once daily or aspirin 50 mg once daily plus dipyridamole 200 mg sustained-release capsules twice daily
Peripheral arterial disease	Aspirin 75–150 mg or clopidogrel 75 mg once daily
Revascularisation procedures	
Lower limb arterial graft	Aspirin 75–150 mg or clopidogrel 75 mg once daily
Carotid endarterectomy	Aspirin 75–150 mg or clopidogrel 75 mg once daily
Coronary artery bypass surgery	Aspirin 75–150 mg once daily within 48 hours after revascularisation and 75–150 mg once daily thereafter
Atrial fibrillation	Aspirin 75–300 mg daily if low risk (< 1% per year)‡
Prosthetic heart valves	
Bioprosthesis in sinus rhythm	Aspirin 75–150 mg once daily (oral anticoagulation for the first 3 months after the operation)
High risk mechanical valves§	Aspirin 75–150 mg once daily plus oral anticoagulation
Diabetes	Aspirin 75–150 mg once daily
Haemodialysis	Aspirin 75–150 mg once daily
Medium risk of serious vascular events (⩾ 0.6% per year)	
Vascular risk factors¶	Aspirin 75–150 mg once daily

* Ticlopidine 250 mg twice daily is an effective alternative, but is not generally recommended because of its adverse side effects profile and higher cost in Australia. † High-risk percutaneous coronary intervention includes: recurrent or persistent chest pains with associated electrocardiographic changes (ST-segment depression or transient ST elevation) despite anti-ischaemia treatment; elevated troponin concentrations (troponin T > 0.1 μg/L or troponin I equivalent); age > 65 years; comorbidity, particularly diabetes; development of pulmonary oedema or haemodynamic instability within observation period; development of major arrhythmia (repetitive ventricular tachycardia or ventricular fibrillation); early postinfarction unstable angina. ‡ Low risk includes patients aged under 65 years with no history of systemic embolism, hypertension, or diabetes, or structural heart disease.[28] § High-risk mechanical valves includes: tilting disk valves, bileaflet mechanical valves in the mitral position or in the aortic position in patients also in atrial fibrillation, previous systemic embolism despite adequate oral anticoagulation. ¶ Risk stratification should incorporate specific information about multiple risk factors (see text)
ACS = acute coronary syndromes; TIA = transient ischaemic attack.

Clopidogrel

Immediate treatment with a 300 mg loading dose of clopidogrel is appropriate for all patients with a suspected non-ST-segment elevation acute coronary syndrome, and for long-term treatment (with 75 mg daily) for at least 9–12 months, in combination with aspirin (E2).[7] Clopidogrel is also used, in combination with aspirin in patients undergoing percutaneous coronary intervention and placement of a stent (E2).[8,29-31] Clopidogrel is given to patients with ACS scheduled for angiography, unless there is a likelihood that the patients will proceed to surgery within 5 days.

The benefits of clopidogrel, compared with aspirin, in the long-term prevention of serious vascular events in high-risk patients are modest, but significant (odds reduction, 10%; 95% CI, 2%–18%). Treating 1000 patients at high risk of vascular events with clopidogrel for about 2 years, at a cost of about $1095 per patient per year (ie, $2 190 000 in total), prevents about 10 serious vascular events, compared with treatment with aspirin. This equates to spending about $219 000 over 2 years to save one serious vascular event. As the cost to the community of managing a serious vascular event, such as a stroke, is about $50 000, it is not cost-

6: New messages about antiplatelet therapy

Primary prevention

- Aspirin therapy is indicated for primary prevention in patients for whom the risk of future vascular events is ⩾ 0.6% per year and who are not at increased risk of gastrointestinal bleeding (⩾ 0.1% per year).

Prevention of venous thromboembolism

- Antiplatelet therapy (aspirin) prevents venous thromboembolism in patients undergoing hip replacement or hip fracture surgery, but is not as effective as anticoagulants (eg, low-molecular-weight heparin), which remain first-line therapy.

Non-ST-segment elevation acute coronary syndromes

- Clopidogrel should be used in combination with aspirin for immediate and long-term management (at least 9 months).

Percutaneous coronary intervention

- Clopidogrel should be used in combination with aspirin for the immediate and long-term management (at least 12 months) of patients undergoing percutaneous coronary intervention and stent insertion.
- Short-term addition of an intravenous infusion of a glycoprotein IIb/IIIa antagonist to aspirin prevents vascular events in high-risk patients having a percutaneous coronary intervention, and those with non-ST-segment elevation acute coronary syndrome, but causes increased bleeding.

Secondary prevention of vascular events

- Antiplatelet therapy protects against vascular events in patients with stable angina, intermittent claudication and, if oral anticoagulation is unsuitable, atrial fibrillation.
- Antiplatelet therapy can be started immediately after acute presumed ischaemic stroke and continued long term.
- Daily aspirin doses of 75–150 mg per day appear to be as effective, and less gastrotoxic, than higher doses for long-term secondary vascular prevention.
- Clopidogrel is an appropriate alternative for patients with a contraindication to aspirin, those who have a recurrent vascular event while taking aspirin, or those at high risk of recurrent vascular events (> 20% per year).
- Oral glycoprotein IIb/IIIa antagonists combined with aspirin are less effective and less safe than aspirin alone.

effective to treat all high-risk patients with long-term clopidogrel.[32] Clopidogrel should be reserved for patients who are allergic to aspirin, cannot tolerate aspirin, have experienced a recurrent *atherothrombotic* vascular event while *taking* aspirin (ie, compliant), or who have an absolute risk of a serious vascular event in excess of 20% per year. In the latter group a 10% relative risk reduction of clopidogrel over aspirin would reduce their risk to 18% per year, which means that treating 100 (or fewer) such high-risk (> 20% per year) patients for 1 year, at a cost of about $100 000 (or less) would prevent two serious vascular events per year (at a cost of about $50 000 each).

Dipyridamole

The addition of dipyridamole to aspirin for all high-risk patients has not been shown to produce significant additional reductions in serious vascular events (E1).[5] However, one large trial in patients with transient ischaemic attack and ischaemic stroke showed substantial reductions in recurrent stroke, but not in myocardial infarction or vascular death.[33] Reasons for part or all of the favourable effect on stroke in that study include the possibility that the newer (and more bioavailable) formulation of dipyridamole was more effective than the older preparation used in earlier trials, that dipyridamole reduced stroke by lowering blood pressure rather than an antiplatelet effect, that the comparative dose of aspirin (25 mg twice daily) was insufficient (ie, a placebo), and random error (chance). The combination of dipyridamole and aspirin is being tested further in the European and Australian Stroke Prevention In Reversible Ischaemia Trial (ESPRIT).[34]

7: Important messages for patients

- Individuals who are about to undergo a medical procedure to clean out their arteries, or who are at medium or high long-term risk (⩾ 0.6% per year) of a serious vascular event should be considered by their doctors for antiplatelet drug therapy
- Most antiplatelet drugs are taken orally, once or twice daily, and have roughly similar (favourable and unfavourable) effects
- Effective antiplatelet drugs reduce, by about one quarter to one third, the chances of blood clots forming in blood vessels (arteries and veins) and the heart, and causing serious vascular events
- Antiplatelet drugs can cause minor bleeding (eg, easy bruising), gastrointestinal symptoms (dyspepsia, diarrhoea), rash, headache, or allergic reactions; serious bleeding is uncommon
- The prices of antiplatelet drugs vary widely

Glycoprotein IIb/IIIa receptor inhibitors

Treatment with a glycoprotein IIb/IIIa receptor inhibitor (together with aspirin and heparin) is recommended in all patients with ACS who undergo percutaneous coronary intervention (E1).[9,10] The infusion should be commenced about 24 hours before the procedure and continued for 12 hours (abciximab) or 24 hours (tirofiban, eptifibatide) after the procedure. The benefits are greatest in patients with elevated concentrations of troponin T or I, of whom 11 need to be treated to prevent one death or acute myocardial infarction at 30 days (E1). Patients with ACS who have diabetes also derive particular benefit from glycoprotein IIb/IIIa receptor inhibitors.

Treatment with a glycoprotein IIb/IIIa receptor inhibitor reduces the risk of death or myocardial infarction in patients with non-ST-segment elevation ACS not routinely scheduled for early percutaneous coronary intervention (E1). The event reduction is greatest in patients at high risk of thrombotic complications.[9,10]

Ongoing trials are examining the safety and effectiveness of abciximab in acute ischaemic stroke (E2).[35]

Patients at low to medium vascular risk ("primary prevention")

Aspirin (75–150 mg/day) decreases the incidence of coronary heart disease in adults who are at increased risk (> 0.6% per year) of heart disease, but it increases the incidence of gastrointestinal bleeding (E1).[36-39] For every 1000 patients with a 3% risk of a coronary event over 5 years, long-term aspirin therapy prevents 4–12 coronary events and causes 0–2 haemorrhagic strokes and 2–4 major gastrointestinal bleeding events (E1). This is a benefit-to-harm ratio of about 2.0.

Individuals at increased cardiovascular risk who may wish to consider long-term aspirin therapy (with 75–150 mg/day) are men older than 40 years of age, postmenopausal women, and younger people with risk factors for cardiovascular disease.[36-39] Risk factors for cardiovascular disease include increasing age, male sex, cigarette smoking, increasing blood pressure, increasing blood total cholesterol concentration, decreasing high-density lipoprotein cholesterol concentration, raised fasting blood glucose concentration (ie, diabetes mellitus), and a positive family history of cardiovascular disease (in younger adults).[36-39]

Risk factors for haemorrhagic complications of aspirin include increasing age, any bleeding diathesis, uncontrolled hypertension, and concomitant use of other non-steroidal anti-inflammatory agents or anticoagulants. Enteric-coated or buffered preparations of aspirin do not clearly reduce adverse haemorrhagic effects.

Prevention of venous thromboembolism

Antiplatelet therapy for high-risk patients reduces the odds of deep-vein thrombosis by 37% (95% CI, 29%–44%) and fatal or non-fatal pulmonary embolism by 53% (95% CI, 41%–63%) among surgical and medical patients.[40,41] However, anticoagulants such as heparin or low-molecular-weight heparin are still the preferred method of thromboprophylaxis in most patients, because they are likely to be more effective than aspirin.

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