from 47% to 95%^{12 13}; it may be developed as an immuno-chromatographic strip test for use with unboiled urine. Another potential test detects erythrocyte sialic acid, which is positive in patients with active disease but becomes negative after cure.¹⁴ The test warrants further clinical evaluation.

The World Health Organization could help in ensuring that these tests remain available for the people who need them. Two manufacturers have already stopped producing dipsticks (Arista Biological and Amrad). Academic studies are needed for evaluation, and public health action is needed to incorporate good tests into national policies while recognising the commercial needs of manufacturers. Progress in neglected diseases like leishmaniasis is often hampered by lack of commitment from industry, and diagnostics and drugs are abandoned when profits are insufficient.

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Combining aspirin with antithrombotic agents

Risk of bleeding is increased but can be minimised

The use of aspirin and other antiplatelet agents has sky rocketed in the past decade as the indications have widened to include primary and secondary prevention of myocardial and cerebrovascular ischaemia. In the United States, an estimated 34.8% of men and 26.2% of women over 40 years use aspirin every day or on alternate days.¹ Half of these patients are classified as at high risk of cardiovascular disease. With the development of safer antiplatelet agents such as thienopyridines and the publication of major randomised studies, the combination of aspirin and clopidogrel has become a class I recommendation (that is, it is considered to be beneficial, useful, and effective) after percutaneous coronary interventions with stenting in the US and in Europe.^{2 3} Combined antithrombotic therapy is recommended for up to 12 months "in patients who are not at high risk of bleeding."² The problem for clinicians is to balance the benefits of combined antiplatelet therapy with the potentially increased risk of gastrointestinal bleeding. In this week's *BMJ* a case control study by Hallas and colleagues goes some way to measuring this risk.⁴

Aspirin is widely known to cause mucosal ulceration that can lead to upper gastrointestinal bleeding. Lower doses and slow release formulations of aspirin have been used in the hope that they carry a reduced risk of bleeding. In a meta-analysis of almost 66 000 people, Derry and colleagues found no relation

between gastrointestinal bleeding and aspirin dose or formulation.⁵ They also showed that risk of bleeding was not lower with prolonged use of aspirin, so the notion of mucosal tolerance to aspirin remains a myth. These findings were confirmed in a later study from Spain, which focused on patients taking low dose aspirin to prevent cardiovascular diseases.⁶

Clopidogrel has been recommended as the treatment of choice for patients with coronary heart disease who cannot tolerate aspirin.⁷ This is based primarily on the CAPRIE study, which compared the efficacy of clopidogrel with aspirin in preventing myocardial ischaemia.⁸ Gastrointestinal bleeding was reported in 1.99% of patients taking clopidogrel and 2.66% of those taking aspirin ($p=0.05$). It has been shown repeatedly that combining aspirin with clopidogrel increases the risk of gastrointestinal bleeding compared with using aspirin⁹ or clopidogrel alone.¹⁰

Hallas and colleagues found that upper gastrointestinal bleeding was associated with the use of low dose aspirin, dipyridamole, and vitamin K antagonists but not with clopidogrel.⁴ The finding that clopidogrel did not increase bleeding risk contradicts other reports.¹¹ This discrepancy could be related to the relatively small sample size of the current study (only 1443 participants, with 30 cases of bleeding). Importantly, the authors found that combining aspirin with any of the antithrombotic agents (clopidogrel, dipyridamole,

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Recommended strategy to prevent upper gastrointestinal bleeding in patients who need aspirin alone or aspirin combined with another antiplatelet agent

Treatment	Risk of gastrointestinal bleeding		
	Low	Moderate	High
Aspirin alone	No gastrointestinal prophylaxis	<i>H pylori</i> eradication	<i>H pylori</i> eradication plus proton pump inhibitor
Aspirin and another antiplatelet agent	Proton pump inhibitor	<i>H pylori</i> eradication plus proton pump inhibitor	<i>H pylori</i> eradication plus proton pump inhibitor plus short term combined treatment

Risk factors for gastrointestinal bleeding include age over 65 years, history of peptic ulcer, *Helicobacter pylori* infection, concurrent use of non-steroidal anti-inflammatory drugs, and concurrent use of cyclo-oxygenase-2 inhibitors. Low risk is defined as no risk factors for bleeding and no history of ulcer; moderate risk is one or two risk factors for bleeding and no history of ulcer complications; high risk is multiple risk factors for bleeding or history of ulcer.

or vitamin K antagonist) greatly increased the risk of bleeding. The highest risk of bleeding came from combining aspirin with clopidogrel (odds ratio 7.4, 95% confidence interval 3.5 to 15). Thus, should we or should we not use combined antiplatelet agents in patients with high risk of cardiovascular or cerebrovascular disease?

The risk of gastrointestinal bleeding varies among users of antiplatelet agents. Older people, those with a history of gastrointestinal bleeding or peptic ulcer, and those who use non-steroidal anti-inflammatory drugs or cyclo-oxygenase-2 inhibitors are more likely to develop aspirin induced bleeding.¹² Aspirin users who are infected by *Helicobacter pylori* are also more prone to bleeding, but the risk is greatly reduced when the infection is cleared.¹³ These variations provide some guidance for assessing and balancing the risk of cardiovascular or cerebrovascular events against the risk of gastrointestinal bleeding.

The table shows the recommended strategy to prevent upper gastrointestinal bleeding in patients who need aspirin alone or aspirin combined with another antiplatelet agent. No randomised trials or observational studies are available to inform recommendations for patients who need combined antithrombotic therapy (such as aspirin and clopidogrel). The recommendations are therefore based on logical deductions and are open for debate.

In addition to these strategies, combined antithrombotic therapy should be given for the shortest duration possible to minimise the risk of bleeding. As

the number of people needing combined antithrombotic therapy is increasing every day, carefully designed clinical trials are needed to devise the best ways to protect patients at high risk of cardiovascular and gastrointestinal events.

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Morbidity and mortality after emergency surgery

Quality measures and performance indicators may reduce this toll

Patients who have emergency surgery, especially those with comorbidities, have a high risk of adverse outcomes. Of 20 000 reported surgical deaths, most occurred within days of emergency or major surgery.¹ Pneumonia was the most common cause of death (www.ncepod.org.uk/pdf/200304DeathData.pdf), and suggests that organ (lung) failure can progress rapidly in susceptible people.

Recent initiatives, such as the National Confidential Enquiry into Patient Outcomes and Deaths (under the auspices of the Patients Safety Agency), aim to reduce morbidity and mortality after emergency surgery. The multidisciplinary Improving Surgical Outcomes Group has also released a document with the same aims.² It describes system changes (such as better preoperative assessment) and interventions (such as