Limitations of the study included its cross-sectional design, use of a single set of inflammatory marker measurements and incomplete data on lifetime doses of medications. As chronic inflammation is likely to have a role in the early onset of atherosclerosis in patients with RA, the authors emphasize the need for prospective management of cardiac risk factors in addition to aggressive RA therapy.

Claire Braybrook

Original article Roman MJ *et al.* (2006) Preclinical carotid atherosclerosis in patients with rheumatoid arthritis. *Ann Intern Med* 144: 249–256

Optimum duration of clopidogrel pretreatment before PCI

Thienopyridines are commonly administered before percutaneous coronary intervention (PCI) to prevent thrombotic complications, but no consensus has been reached regarding the optimum treatment duration. Steinhubl and co-workers report on the relationship between duration of pretreatment with clopidogrel—a thienopyridine derivative—and the occurrence of ischemic complications.

In this post hoc analysis of the Clopidogrel for the Reduction of Events During Observation (CREDO) trial, patients were randomized to receive a loading dose of 300 mg clopidogrel ($n=847$) or placebo ($n=915$) initiated 3–24 h before PCI. All patients were given 75 mg clopidogrel and 325 mg aspirin daily for 28 days after the procedure. When compared with placebo, clopidogrel pretreatment reduced the 28-day combined endpoint of death, myocardial infarction, or urgent target vessel revascularization only when administration began at least 10–12 h before intervention. Clopidogrel pretreatment of at least 15 h was necessary to significantly reduce the occurrence of the primary endpoint (relative risk reduction 58.8%; $P=0.028$); the effect was greatest when pretreatment was initiated 24 h before PCI.

Pretreatment with a 300 mg loading dose of clopidogrel therefore seems to be effective only if administration begins at least 15–24 h before PCI. Because other trials report that a much more rapid effect is achieved with a higher 600 mg loading dose of clopidogrel, however, the authors recommend administration of this higher dose when feasible.

Pippa Murdie

Original article Steinhubl SR *et al.* (2006) Optimal timing for the initiation of pre-treatment with 300 mg clopidogrel before percutaneous coronary intervention. *J Am Coll Cardiol* 47: 939–943

Safety of clopidogrel in children with arterial ischemic stroke

Antiplatelet therapy with aspirin is widely used for the secondary prevention of stroke in patients who have experienced an arterial ischemic stroke (AIS). Long-term use of aspirin, however, can cause gastric and respiratory adverse effects, and resistance to therapy often occurs. Researchers in Canada have investigated the safety and tolerability of clopidogrel, an alternative antiplatelet treatment, in children with AIS.

This study included 17 children (mean age 8.8 years) recruited at time of initial AIS diagnosis. Children in whom aspirin intolerance or failure occurred began clopidogrel therapy; eight children received clopidogrel alone and seven received clopidogrel in conjunction with aspirin.

No major side effects were reported during clopidogrel treatment alone. Complications were reported in four patients, but two of these—hand numbness and headaches—were unlikely to be clopidogrel-related, as they started before clopidogrel treatment commenced, and persisted when clopidogrel was discontinued. Two patients on clopidogrel plus aspirin suffered intracranial hemorrhage. Both of these patients had potential risk factors for hemorrhage—one patient had undergone surgery recently and the other had hypertension, and both had cerebral atrophy.

The authors conclude that clopidogrel seems to be well tolerated in children resistant to aspirin, but that the combination of aspirin plus clopidogrel should be used with caution in children who have risk factors for hemorrhage. AIS did not recur in any patient in the study, but no conclusions can be drawn from this as the sample size was small and the study was not designed to assess effectiveness of clopidogrel in stroke prevention.

Rebecca Ireland

Original article Soman T *et al.* (2006) The risks and safety of clopidogrel in pediatric arterial ischemic stroke. *Stroke* 37: 1120–1122