GLOSSARY

PROVE IT–TIMI 22
Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22

C-reactive protein levels and cardiovascular risk after statin therapy

In patients with known cardiovascular disease, lowering LDL cholesterol to target levels is the main focus of statin therapy. Ridker *et al.* hypothesized that patients whose C-reactive protein (CRP) levels were lowered using statin therapy would have better outcomes than those whose CRP levels remained high.

The study included 3,745 patients from the PROVE IT–TIMI 22 trial. All had recent myocardial infarction or high-risk unstable angina and were randomized in a 1:1 ratio to intensive therapy with atorvastatin (80 mg daily) or moderate therapy with pravastatin (40 mg daily). LDL-cholesterol and CRP levels were measured in plasma samples taken at the 30-day follow-up visit; there was very little correlation between the 'achieved' levels of LDL and CRP.

During the mean follow-up of 2 years, the risk of recurrent myocardial infarction or cardiovascular death was significantly lower in patients with achieved LDL-cholesterol levels below 1.8 mM/l (70 mg/dl) than in those with higher levels. An almost identical reduction in risk was seen in patients with achieved CRP levels below 2 mg/l compared with those with higher levels, irrespective of the achieved LDL-cholesterol level. The best outcomes by far were seen among those who lowered both LDL and CRP to <1.8 mM/l (70/dl) and <2 mg/l respectively, suggesting that physicians need to consider this dual goal to best manage their patients.

The study indicates that treating inflammation is an important aspect of cardiovascular risk reduction in patients with acute coronary syndromes, and the authors propose that CRP levels should be monitored in patients receiving statins. An ongoing study known as JUPITER is investigating whether this approach is also appropriate for primary prevention.

Original article Ridker PM *et al.* (2005) C-reactive protein levels and outcomes after statin therapy. *N Engl J Med* **352:** 20–28

C-reactive protein and LDL cholesterol in atherosclerosis

Intensive statin therapy has been shown to be more effective than moderate therapy in reducing the progression of atherosclerosis and improving clinical outcomes in patients with coronary artery disease. Nissen and colleagues have investigated whether and how these effects are related to accompanying reductions in atherogenic lipoproteins and C-reactive protein (CRP).

By use of intravascular ultrasonography, the investigators measured the degree of atherosclerosis in 502 patients with coronary artery disease, at baseline and after 18 months of either moderate treatment (40 mg pravastatin daily) or intensive treatment (80 mg atorvastatin daily). As expected, progression of atherosclerosis—indicated by changes in percent atheroma volume and total atheroma volume—was slower in the intensive treatment group than in those receiving moderate therapy. Reductions in LDL cholesterol, non-HDL cholesterol, apolipoprotein B-100 and CRP were significantly related to the rate of progression, and most of these associations remained significant in a multivariate analysis. Although the closest correlation was between percent atheroma volume and LDL cholesterol, CRP levels showed a similarly close relationship to atherosclerosis progression. Regression of atheroma was observed in patients with the greatest reductions in CRP.

The study provides more evidence of the role of CRP in the development of atherosclerosis, and Nissen *et al*. conclude that reductions in the levels of this inflammatory biomarker, along with LDL cholesterol and other atherogenic proteins, are significantly associated with the slower rate of disease progression observed in patients receiving intensive statin treatment.

Original article Nissen SE *et al.* (2005) Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. *N Engl J Med* **352:** 29–38

Retinopathy predicts congestive heart failure

Microvascular disease has been implicated in the pathogenesis of congestive heart failure (CHF). By the use of retinopathy as a marker of systemic microvascular disease, Wong *et al.* have examined its relationship with the risk of CHF in a large, population-based cohort study.