lipid concentration in the serum. The rareness of this entity is corroborated by one of us (I.R.) who has been examining synovial fluid for crystals for over 15 years and has never seen this form of crystal before.

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Coxibs and cardiovascular risk

Jill Cotter and Eric Wooltorton¹ highlight the importance of differences in cyclooxygenase 2 (COX-2) selectivity as a potential explanation for the prothrombotic effects of coxibs. However, they neglect important evidence that celecoxib might not share the same cardiovascular (CV) risk as rofecoxib.

An increased thrombotic risk with celecoxib has been demonstrated only in the APC (Adenoma Prevention with Celecoxib) study.² On the other hand, data from the CLASS trial³ and a meta-analysis of multiple controlled trials⁴ have not uncovered any prothrombotic effect of celecoxib compared with either conventional NSAIDs or placebo. This is consistent with many observational studies that found increased CV risk with both high and low doses of rofecoxib but not with celecoxib.⁵⁻⁷

It is noteworthy that the APC trial demonstrated a trend toward increased

CV risk of celecoxib among ASA users. Celecoxib might have caused this effect by interference with ASA-induced inactivation of platelet COX-1, which can occur at significantly lower concentrations of celecoxib than are necessary for inhibition of platelet COX-1 activity.⁸ This notion does not contradict our previously stated view that ASA might mitigate CV risk associated with coxibs.⁹ However, a recent case-control study showed that the risk-modifying effects of ASA were seen only at a low dose but not at a high dose of rofecoxib.⁷ We have, therefore, suggested that higher doses of coxibs could also interfere with the anti-inflammatory effects of ASA mediated by COX-2.¹⁰

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Jill Cotter and Eric Wooltorton¹ indicated that COX-2 inhibitors appear to increase the risk of cardiovascular adverse events in a dose-related fashion. The CLASS and VIGOR clinical trials of COX-2 inhibitor(s) suggested that both celecoxib and rofecoxib can increase the risk of cardiovascular events.² The VIGOR trial compared rofecoxib with the NSAID naproxen in patients with rheumatoid arthritis³ and indicated a 5-fold increase in the relative risk of developing serious cardiovascular events between the rofecoxib group and the naproxen group.

Clinical data have shown that expression of COX-2 is upregulated by inducible nitric oxide synthase (iNOS) that might play a protective role in the