show that a simple give away is not the entire answer. For this population at least it may be necessary for public health officials to use more passive detectors, install and maintain them, or to require sprinklers in all new housing for people with low incomes. Disappointing as the results must be for this team, encouraging byproducts of their work are new directives from the local housing authority in the United Kingdom urging some such actions.[6]

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Treating acute gouty arthritis with selective COX 2 inhibitors

Preliminary evidence supports their relative efficacy and safety

Few arthritides are as painful, incapacitating, and stressful as a severe attack of acute gout, pseudogout, or calcific periarthritis. Successful treatment of these acute microcrystalline events depends on early use of an effective and safe anti-inflammatory drug in full dosage. The sooner such treatment is started the more rapid and complete the response. Treatment options include colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), and corticosteroids including adrenocorticotrophic hormone.[1] Although colchicine is traditionally rooted in the treatment of acute gout, in recent years its use has declined steadily.[1] Its drawbacks include slow onset of action, narrow ratio of benefit to toxicity, and reduced efficacy when used more than 24 hours after the an attack begins. Colchicine (0.6 mg orally every 2 hours, up to 4-6 mg/day) is now reserved for patients without renal, hepatic, or bone marrow disease, in whom the more effective NSAIDs are contraindicated or poorly tolerated. Intravenous colchicine is best avoided given its potential for serious toxicity, which potentially can result in myelosuppression, hepatic necrosis, renal failure, hypotension, seizures, and death.

Intra-articular corticosteroids (for example, methylprednisolone acetate 5-25 mg per joint), systemic corticosteroids (oral prednisone 20 mg/day tapered off over 4-10 days, or intramuscular triamcinolone hexacetonide 60 mg/day, repeated in 1-4 days), and corticotrophin (40-80 IU every 6-24 hours) are valuable, highly effective, and relatively safe alternatives in patients with acute microcrystalline synovitis in whom neither NSAIDs nor colchicine are recommended. Such patients include elderly people and those with renal insufficiency, hepatic dysfunction, cardiac failure, peptic ulcer disease, and hypersensitivity to NSAIDs.[1] The duration of treatment is usually short, and side effects due to steroids are rare.[1]

Non-salicylate NSAIDs are the drugs of choice in the treatment of acute crystal induced arthritis.[1] Although no comparative studies have been conducted, NSAIDs are generally better tolerated and have more predictable therapeutic effects than colchicine. The patient is usually supplied with the appropriate NSAIDs (preferably carried with the person, for all too often gout strikes when the patient is far from home) and instructions to how to self treat the acute episode at the first "twinge" of an attack. No clear advantage is known of any one NSAID over another, but large initial doses are recommended: indomethacin 150-200 mg/day, naproxen 1000 mg/day, or diclofenac sodium 150 mg/day.[1] Although adverse reactions may occur, the duration of treatment with NSAIDs is generally short (4-8 days), and serious toxicity leading to drug withdrawal (such as gastrointestinal bleeding) is rare.

Conventional NSAIDs exert their anti-inflammatory effects mainly through inhibition of the enzyme cyclo-oxygenase, which catalyses the conversion of arachidonic acid to proinflammatory prostaglandins, particularly prostaglandin E_2. These play a major part in both experimental and clinical crystal induced inflammation, and act synergistically with other mediators (for example, bradykinin, leukotriene B4) to enhance capillary dilatation, pain sensitivity, and neutrophil chemotaxis.[2] Cyclo-oxygenase exists in two isoforms: cyclo-oxygenase-1 and cyclo-oxygenase-2.[3 4] Cyclo-oxygenase-1 is constitutively expressed in most tissues and is relatively unaffected by inflammatory mediators. It supports biosynthesis of prostanoids required for normal homeostatic "housekeeping" functions such as renal blood flow and maintaining the integrity of gastric mucosa. By contrast, cyclo-oxygenase-2 is constitutively expressed in a few tissues but is highly inducible in response to cytokines, endotoxin, mitogens, and growth factors, which implies a role in inflammation, infection, and cellular proliferation. In crystal and other inflammatory arthritides, cytokines—for example, interleukins, IL-1, IL-6, and IL-8—increase production of prostaglandin via induction of cyclo-oxygenase-2 expression in synoviocytes, and macrophages.[3 4] Although both cyclo-oxygenase-1 and cyclo-oxygenase-2 isoenzymes are expressed in mononuclear cells from gout and pseudogout synovial effusions, the exact role of cyclo-oxygenase-1 in inflammation is poorly understood.[5] Urate crystals

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(gout), but not calcium pyrophosphate dihydrate crystals (pseudogout), induce in vitro expression of cyclo-oxygenase-2 and production of prostaglandin E_2 by human blood monocytes.[6]

Conventional NSAIDs inhibit both cyclo-oxygenase-1 and cyclo-oxygenase-2. Their anti-inflammatory effects are largely due to suppression of cyclo-oxygenase-2, and most adverse effects, particularly gastrointestinal toxicity, result from inhibition of cyclo-oxygenase-1.[3 4] The newer NSAIDs, such as celecoxib, rofecoxib, valdecoxib, and etoricoxib, are highly cyclooxygenase-2 selective.[7] Although both selective and standard NSAIDs inhibit cyclo-oxygenase-2 equally, the real advantage of selective cyclo-oxygenase-2 inhibitors, as suggested by Vane and Warner, is that they are highly cyclo-oxygenase-1 sparing drugs, accounting for reduction in gastrointestinal toxicity by about 50%.[3 4 7 8] These drugs are generally well tolerated, and their clinical efficacy in patients with osteoarthritis or rheumatoid arthritis is comparable to that of non-selective NSAIDs.[4 7 8]

A recent randomised, double blind, eight day trial comparing etoricoxib 120 mg once daily with indomethacin 50 mg thrice daily in acute gout showed the two drugs to be equally efficacious, with etoricoxib showing an improved safety profile.[9] The findings support a potential role for cyclo-oxygenase-2 inhibitors in managing acute gout, and raise important questions. Firstly, are other selective cyclo-oxygenase-2 inhibitors also effective in treating acute gout and other microcrystalline events? This is probably true given the central role of cyclo-oxygenase-2 and prostaglandin E_2 in inflammation. Secondly, do the same contraindications and precautions for the use of dual cyclo-oxygenase-1 and cyclo-oxygenase-2 inhibitors (non-selective NSAIDs) also apply to selective cyclo-oxygenase-2 inhibitors? Yes—COX 2 inhibitors should be used with caution in patients with cardiac failure, renal insufficiency, hypertension, hepatic dysfunction, peptic ulcer, or on anticoagulants, or with hypersensitivity to NSAIDs. Thirdly, is potential gastrointestinal toxicity a concern? Yes—until further clinical data show a low risk of gastroduodenal ulceration associated with short term use of cyclo-oxygenase-2 inhibitors for acute gout.

Whether the treatment of acute gout with selective cyclo-oxygenase-2 inhibitors, in place of the well established NSAIDs, will prove to be more advantageous in terms of efficacy, gastrointestinal safety, and cost effectiveness remains to be shown by additional controlled studies. These promising drugs may, however, be of particular benefit in patients who are intolerant to non-selective NSAIDs, and in those presenting with an acute gouty attack of several days' duration since a longer course of treatment is likely to be required.

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Mattresses, microenvironments, and multivariate analyses

No reason to change current practices for reducing risk of sudden infant death

Papers p 1007

Despite the success of "Back to Sleep" campaigns in many countries, sudden infant death syndrome remains responsible for the largest group of deaths in infants between one month and one year of age.[1] The importance of sleeping in the prone position as a contributory factor has led to studies of the pathophysiological effects of the prone position on the infant and to studies of microenvironmental factors that might contribute to this risk.[2 3] The carefully conducted study by Tappin and colleagues in this issue (p 1007) is set in Scotland and emphasises the potential importance of the infant's microenvironment during sleep as a contributory factor to the risk of sudden infant death syndrome, but as emphasised by the authors, caution must be exercised in the interpretation of these results.[4]

Tappin and colleagues have shown an apparently increased risk of sudden infant death syndrome for infants sleeping on a mattress previously used by another infant (54% cases, 28% controls), confirming the observation by the same group in an earlier study.[5] The previous Scottish study was criticised because infants sharing beds with adults were included with infants sleeping on mattresses used by another infant.[6] In the present study this criticism has been addressed. The earlier study was, however, also criticised for a lack of adjustment of potential confounders related to the use of mattresses, in particular the socioeconomic

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