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Comment on: Efficacy of acupuncture in fibromyalgia syndrome—a systematic review with a meta-analysis of controlled clinical trials: reply

SIR, We appreciate the comment of Prof. Ernst [1]. Mayhew and Ernst [2] summarized the results of a qualitative analysis of five controlled trials with acupuncture in fibromyalgia syndrome (FMS) as follows: ‘Their methodological quality was mixed and frequently low. Three RCTs suggested positive but mostly short-lived effects and two yielded negative results. There was no significant difference between the quality of the negative and the positive RCTs’ (p. 1). ‘The existing evidence is mixed’ (p. 4). Therefore, we think that we summarized the results of their work correctly. We share the conclusion of Mayhew and Ernst that acupuncture cannot be recommended for the management of FMS [3].

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Comment on: Gout: an independent risk factor for all-cause and cardiovascular mortality

SIR, Kuo *et al.* [1] found that gout, but not hyperuricaemia, was an independent risk factor for all-cause and cardiovascular mortality independent of age, gender, metabolic syndrome and proteinuria. However, the mechanisms underlying this association were not clearly defined. A plausible pathophysiological mechanism might be related to inflammation, which represents the characteristic difference between gout and hyperuricaemia. Indeed, it is well known that hyperuricaemia and/or crystal deposition are not sufficient to cause gouty attacks. We propose that iron may represent a factor that triggers inflammation and heightens cardiovascular risk in gouty patients.

Accumulating evidence suggests that gout is a disease of iron overload. Uric acid accumulation, as both an antioxidant and an iron chelator [2], has been found in response to iron overload [3, 4]. In fact, human tophi and the SM contain iron [5]. Furthermore, it has been shown that some portion of the gouty inflammation after urate crystal deposition could result from the incomplete complexation of iron with subsequent catalytic generation of reactive oxygen species [3]. On the other hand, mounting evidence suggests a link between abnormal iron storage and the development of coronary artery disease [6].

Interestingly, it was found that iron depletion prevented the relapse of the acute arthritis of primary gout in 58% of gouty patients and markedly reduced its frequency and severity in the remaining 42% [7]. Although a study of iron depletion in the primary prevention of cardiovascular disease has not been performed so far, it is highly plausible that the protection against ischaemic cardiovascular disease in individuals with severely impaired haemostasis might be related to the decrease in stored tissue iron caused by recurrent bleeding [8].

Iron depletion may prevent cardiovascular disease and gouty arthritis through multiple cooperating mechanisms [7, 9]. A general mechanism with multiple consequences is an effect of stored iron on the availability of redox-active iron. In fact, the amount of free iron available at sites of oxidative or inflammatory injury appears to be a function of the stored iron level [7, 10]. Therefore, iron may represent an important biological link between gout and cardiovascular disease.

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Comment on: Gout: an independent risk factor for all-cause and cardiovascular mortality: reply

SIR, We acknowledge the comments of Mascitelli *et al.* [1] regarding our recent publication [2]. As an epidemiological study, our recent study cannot provide the underlying mechanism resulting in different mortality impact between gout and hyperuricaemia. We concur that inflammation is the underlying distinction between gout and

hyperuricaemia. As low-grade inflammation has been demonstrated to be of importance in the development of atherosclerosis and subsequent cardiovascular events [3, 4], higher mortality risk of gout in contrast to pure hyperuricaemia is conceivable. The recent finding that monosodium urate crystal is a trigger of inflammasome [5], which is the pivotal molecular complex in the maturation of IL-1, can also explain the presence of inflammation in gout, but not pure hyperuricaemia. Whether iron overload is related to the difference is subject to further investigation.

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