Response to: 'Knee osteoarthritis and bisphosphonates: Could BCP crystals be the missing link?' by Murphy *et al*

I read with great interest the letter from Murphy and McCarthy[1]: 'knee osteoarthritis and bisphosphonates: could BCP crystals be the missing link?'.[1]

I recently gave comments on two case-control studies,[2] in which the need for a total knee prosthesis was around 25% lower in bisphosphonate (BP) users than in controls.[3 4] What could be the explanation? It could be related to epidemiology: BP-users have a healthier lifestyle than non-users, by doing more exercise therapy, preventing overweight and so on. The other option is a biological effect, for example, an effect of BPs on the underlying subchondral bone in patients with osteoarthritis (OA).[5]

Murphy and McCarthy bring in that BPs have a strong affinity for basic crystal phosphates (BCPs) and that this might inhibit inflammatory reactions in the synovial fluid.[1] They argued that BCPs have been found in the cartilage of 100% of patients with OA at the time of joint replacement and that BCPs might contribute to inflammation in OA.

Although this is certainly a valuable suggestion, the incidence of clinically manifest knee-osteoarthritis based on BCP-crystals is low in patients with OA. Since knee-OA is a whole joint disease, cartilage, bone, synovial inflammation and muscular weakness all play a role,[6] it is very likely that other factors are among the mean determinants of inflammation and pain in patients with knee-OA. So, BCP-crystals are probably not 'the' missing link, but might be a' missing link.

Nevertheless, since the pathogenesis of OA is not fully elucidated and therapeutic options are scarce, further research in the direction of BCPs and BPs in patients with knee-OA is very welcome.

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