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 McCarthy¹: '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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