1. In 2016, an IIAC member highlighted a research letter about rheumatoid arthritis (RA) and steel working (Murphy et al, 2016). A more than six-fold higher risk of the disease had been reported in male Italian furnace workers (Cappelletti et al, 2016) and the letter speculated that this could be due to occupational inhalation of cadmium dust or fume. This note concerns the case for prescribing RA in respect of occupational exposures to cadmium under the Industrial Injuries Disablement Benefit (IIDB) Scheme.

2. RA is a relatively common chronic multisystem inflammatory disease affecting some 0.8%-1.5% of the population. The target tissue for inflammation is the synovium, which lines the synovial joints and bursae, ligaments and tendon sheaths. Untreated, the disease causes destruction and deformity of the joints in a symmetrical distribution. It is also associated with non-articular manifestations affecting other organ systems including the cardiac, respiratory and nervous systems and the eyes. It is associated with high levels of disability and increased mortality, notably because of ischaemic heart disease.

3. RA was first described in 1804. Extensive studies of skeletal remains prior to this have not found evidence of the disease. When allied with the very low concordance of disease in monozygotic (identical) twins, a view has developed that disease occurrence is importantly influenced by factors in the environment.

4. Among suspected candidates is the heavy metal cadmium, industrial emissions of which have grown substantially since the 19th century.

5. The evidence on cadmium and RA has several strands that are outlined in a commentary by Hutchinson (2015). Firstly, cigarette smoking, which is an
established risk factor for RA (Stolt et al, 2003), is also a source of cadmium exposure, with serum levels raised three-fold in current smokers (Elinder et al, 1983); secondly, in a few (but not all) reports, higher concentrations of cadmium have been found in the blood, urine and scalp hair of patients with RA than in people without the disease (independent of smoking habits) (Afridi et al, 2012); thirdly, reported increases in risk of RA among people living adjacent to major highways (De Roos et al, 2014) could possibly have their origins in higher exposure to cadmium dust; fourthly, nanoparticles of cadmium in dust and cigarette smoke are believed capable of inducing a lung process which could play a part in the initiation of RA; further, in a commonly used animal model of RA (collagen-induced arthritis), cadmium chloride in drinking water can potentially exacerbate some of the biological features that may occur during the disease’s induction phase (Ansari et al, 2015).

6. Regarding occupational causes of RA, Hutchinson highlighted three published reports (Sverdrup et al, 2005; Olsson et al, 2000; Olsson et al, 2004) and one research abstract (Ilar et al, 2016) in which elevated risks of the disease (raised 1.4- to 14-fold) were found in rubber and plastic workers, smelters and metal foundry workers, bricklayers and concrete workers, electrical and electronics workers, workers exposed to mineral oil or hydraulic oil, asphalts, printmakers and process engravers, and conductors, freight and transport workers. It was suggested that these occupations shared an increased exposure to cadmium in common and that “appreciable cadmium contents can be inhaled in the workplace as dust or fumes” arising from cement, mineral and hydraulic oils, plasterboard, asphalt, plastics, dyes, wood and diesel emissions. In citing Hutchinson’s commentary, Murphy et al hypothesised that the elevated risk in steelworkers could be explained in this fashion.

7. It should be noted that Hutchinson wrote his commentary under the heading of ‘novel hypothesis’, and that his article and that by Murphy et al were both speculative discussion pieces. Further, Murphy et al noted that foundry dust potentially comprises a wide range of other environmental contaminants (iron, aluminium, zinc, manganese, lead, chromium, nickel, cadmium, mercury,
arsenic, polycyclic aromatic hydrocarbons, polychlorinated biphenyls and
dioxins), to which may be added silica, which others suspect to be a risk
factor for RA and autoimmune disease (IIAC, 2014). Also, no evidence on
actual exposures to cadmium existed in any of the reviewed studies and
cadmium was not mentioned as a possible cause of RA in any of them.

8. Rather, Hutchinson adduced indirect evidence of exposures from a large
survey of US workers participating in the Third National Health and Nutrition
Examination Survey (NHANES III, 1988-1994) who underwent urinary
measurements of cadmium (Yassin et al, 2004). Geometric mean (GM) levels
of cadmium in urine were 0.32 (95%CI 0.29-0.33) µg/L in men overall and
0.29 (95%CI 0.27-0.31) µg/L in women overall, but higher in workers from the
metal industry (0.48, 95%CI 0.36-0.60 µg/L) and transportation (0.39, 95%CI
0.33-0.45 µg/L), while among labourers they varied from a GM of 0.27 to 0.36
µg/L. However, levels comparable to those in construction and transportation
were seen among health service workers (GM 0.36, 95%CI 0.30-0.42 µg/L)
and exposure estimates were not available for individual occupational titles
such as smelter, bricklayer, asphalter or printer. Separately, Murphy et al
identified a small survey in which significantly higher levels of cadmium were
found in the urine, blood, and scalp hair of steel mill production workers from
Pakistan than in quality control workers and other workers (Afridi et al, 2006),
illustrating the potential for cadmium exposures to arise.

9. In January 2017, the Council undertook a review of the literature on cadmium
and autoimmune diseases, including RA. No references additional to those
mentioned above were discovered.

10. The Council has concluded that the evidence base on this putative hazard is
still at a preliminary stage. It is possible, but not yet established, that cadmium
can cause RA in at least some circumstances. As such, it is not yet a well-
established hazard for the disease. Nor are the circumstances in which a
doubling or more of risk (the usual threshold for prescription within the IIDB
Scheme) might arise at all defined: what risk cadmium poses of RA, to whom,
and to what degree require further elaboration. More evidence is needed
therefore before the Council can contemplate recommending prescription. It will continue to keep this emerging literature under review.

Prevention

11. Although it is currently not clear whether cadmium can cause RA, there is evidence that exposure to this metal and its compounds can cause both short-term adverse health effects (such as eye and respiratory irritation, headache, dizziness, fever, digestive and muscle problems) and serious longer-term effects including kidney damage and lung cancer.

12. The Control of Substances Hazardous to Health Regulations 2002 (COSHH) aim to protect workers from hazardous substances in the workplace and apply to a wide range of substances – including cadmium and its compounds – that have the potential to cause harm if inhaled, ingested or absorbed through the skin. COSHH requires the employer to carry out a risk assessment, to establish the hazards associated with the substances being used, and to put processes in place to control those risks.

13. Under the COSHH regulations, employers are required to prevent exposure to carcinogens such as cadmium by substituting them with a safer substance or by totally enclosing the process. Where this is not possible, COSHH requires exposure to be controlled to as low a level as reasonably practicable and for it to be adequately controlled by the use of appropriate work processes, systems, engineering controls and measures including local exhaust ventilation systems to control exposure at source. Suitable respiratory protective equipment may be used where adequate control cannot otherwise be achieved.
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