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POSITION PAPER 14

Silica – related Renal and Connective Tissue Diseases

SUMMARY

1. A growing body of evidence links exposure to respirable crystalline silica with renal disease and certain connective tissue diseases. This report considers whether there are grounds for prescription.
2. The question was prompted by representations from Members of Parliament and a consultant renal physician, following a local excess of renal disease in an area where fluorspar (localised to silica-rich seams) was mined. In response, a literature review was conducted and expert evidence was assembled.
3. The Council found a significant body of research evidence suggesting an association between silica and renal disease, including kidney failure. However, observations that enable the qualifying exposure to be defined for prescription purposes are limited, mainly to one high-quality survey in the United States (US) sand industry and one corroborating data set from the US gold mining industry.
4. The Council also considered the possibility of prescribing for renal disease in workers with silicosis, or industries where silicosis is already a prescribed risk, but found insufficient evidence to support this approach.
5. The review encompassed several other immunologically-mediated diseases linked to occupational silica exposure – specifically, systemic lupus erythematosus (SLE) or lupus, scleroderma and rheumatoid arthritis. As with renal disease some positive associations were found in the research literature, but the evidence base was weaker and a similar problem arose in defining the qualifying exposure.
6. On balance the Council regards the evidence base as insufficient to recommend prescription of renal disease or connective tissue diseases in silica-exposed workers. However, this is an active area of research and the Council will continue to monitor emerging evidence.

INTRODUCTION

The Industrial Injuries Disablement Benefit scheme

1. The Industrial Injuries Advisory Council (IIAC) is an independent statutory body established in 1946 to advise the Secretary of State for Social Security on matters relating to the Industrial Injuries Disablement Benefit (IIDB) scheme. The major part of the Council's time is spent considering whether the list of prescribed diseases for which benefit may be paid should be enlarged or amended.
2. The IIDB scheme provides a benefit that can be paid to an employed earner because of an industrial accident or Prescribed Disease (PD).

The legal requirements for prescription

3. The Social Security Contributions and Benefits Act 1992 states that the Secretary of State may prescribe a disease where he is satisfied that the disease:
 - a) ought to be treated, having regard to its causes and incidence and any other relevant considerations, as a risk of the occupation and not as a risk common to all persons; and
 - b) is such that, in the absence of special circumstances, the attribution of particular cases to the nature of the employment can be established or presumed with reasonable certainty.
4. In other words, a disease may only be prescribed if there is a recognised risk to workers in an occupation and the link between disease and occupation can be established or reasonably presumed in individual cases.
5. In seeking to address the question of prescription for any particular condition, the Council first looks for a workable definition of the disease. Then it searches for a practical way to demonstrate in the individual case that the disease can be attributed to occupational exposure with reasonable confidence. For this purpose reasonable confidence is interpreted as being based on the balance of probabilities according to available scientific evidence. If the condition might result from occupational exposure in the absence of an identifiable accident the Council must consider whether it should be included in the list of diseases that are prescribed for benefit purposes. In these circumstances it may be possible to ascribe a disease to a particular occupational exposure in two ways – from specific clinical features of the disease or from epidemiological evidence that the risk of disease is at least doubled by the relevant occupational exposure.

Clinical features

6. For some diseases attribution to occupation may be possible from specific clinical features of the individual case. For example, the proof that an individual's dermatitis is caused by his occupation may lie in its improvement when he is on holiday and regression when he returns to work and in the demonstration that he is allergic to a specific substance with which he comes into contact only at work. It can be that the disease only occurs as a result of an occupational hazard (e.g. coal workers' pneumoconiosis).

Doubling of risk

7. Other diseases are not uniquely occupational and when caused by occupation are indistinguishable from the same disease occurring in someone who has not been exposed to a hazard at work. In these circumstances attribution to occupation on the balance of probabilities depends on epidemiological evidence that work in the prescribed job, or with the prescribed occupational exposure, increases the risk of developing the disease by a factor of two or more. The requirement for, at least, a doubling of risk is not arbitrary. It follows from the fact that if a hazardous exposure doubles risk, for every 50 cases that would normally occur in an unexposed population, an additional 50 would be expected if the population were exposed to the hazard. Thus, out of every 100 cases that occurred in an exposed population 50 would do so only as a consequence of their exposure, while the other 50 would have been expected to develop the disease, even in the absence of the exposure. Therefore, for any individual case occurring in the exposed population, there would be a 50% chance that the disease resulted from exposure to the hazard and a 50% chance that it would have occurred even without the exposure. Below the threshold of a doubling of risk only a minority of cases in an exposed population would be caused by the hazard; and individual cases therefore could not be attributed to exposure on the balance of probabilities. The epidemiological evidence required should ideally be drawn from several independent studies and be sufficiently robust that further research at a later date would be unlikely to overturn it.

BACKGROUND TO THE REVIEW

8. Crystalline silica¹, otherwise known as silicon dioxide (SiO₂), is the basic constituent of sand, quartz and granite. It is a common substance found in sand, mortar, concrete and stone, but also in the air and soil. Exposure to crystalline silica has historically been linked with a range of diseases such as silicosis, tuberculosis and lung cancer. Primary carcinoma of the lung with accompanying silicosis is covered under the IIDB Scheme as Prescribed Disease (PD) D11, for exposure to silica dust in a variety of industries.
9. The Council received representations from Members of Parliament and a consultant nephrologist to consider adding renal disease due to silica exposure to the list of prescribed diseases. Further investigation was considered appropriate, especially as members of the Council were aware of a growing research literature on the topic.

Method of investigation

10. The Council undertook a literature review and received evidence from experts in the field of nephrology, toxicology and epidemiology. (A list of those who gave evidence is presented in Appendix 1). A call for evidence was also advertised in the medical press and on the Council's website.
11. During the inquiry the literature review was extended to consider the association of silica with several rheumatic diseases (rheumatoid arthritis, scleroderma, systemic lupus erythematosus (SLE) and systemic sclerosis). Some evidence existed that these diseases might be triggered by silica according to a mechanism similar to that purported to cause kidney disease: the Council decided to assess the strength of this evidence in parallel with the main inquiry.

¹Silicon (Si) is the chemical element which constitutes part of silica. This report refers to the crystalline form of silica which has been identified as a health hazard, as compared with the amorphous type, which has not.

Preliminary remarks on renal disease

The kidney's functions

12. A healthy kidney is essentially a filtering system. As blood passes through the kidneys the body's waste products and excess fluid are removed, while any necessary products (water, salts etc.) are retained. Each kidney is made up of about 1 million units called nephrons. Within each, the filtering function is performed by the glomerulus - a twisted mass of tiny tubes through which the blood passes. Kidney function is usefully expressed numerically by the amount of filtration performed - the glomerular filtration rate (GFR). The glomerulus is semipermeable allowing water and soluble wastes to pass through to be eliminated as urine; the filtered blood passes out of the glomerulus and returns into circulation. The kidney also balances the blood's chemistry and produces hormones that control blood pressure and maintain healthy blood cells and bones.

Kidney failure

13. Kidney failure occurs in two forms - acute (sudden reversible failure of kidney function) or chronic (gradual loss of kidney function). Acute renal failure has occurred after very high exposures to silica (e.g. when blasting silica) but such an event is too rare to be expected under current circumstances of work in the UK. This report considers chronic renal failure arising through a gradual, progressive and irreversible loss of the ability of the kidneys to excrete wastes, concentrate urine and conserve body salts (electrolytes).
14. The phrase chronic renal failure, although widely used, is imprecise as renal function declines from normal (GFR = 120ml/min) through increasing severities of chronic kidney disease until eventually reaching end stage renal disease (ESRD), when symptoms are increasingly severe and health can only be maintained by the introduction of renal replacement therapy (RRT) by dialysis or transplantation. The steady loss of GFR is due to continuing nephron death. The rate at which this proceeds is highly variable and depends on the underlying disease and response to treatment. From disease onset to ESRD can take from weeks to decades as nephrons gradually die due to the underlying disease process.
15. Chronic renal failure results in accumulation of fluid and waste products in the body. Uraemia is the state of ill-health resulting from renal failure. Most body systems become affected with many potential complications and untimely death.
16. Common symptoms in advanced renal failure include weight loss, nausea, vomiting, malaise, fatigue, headaches and itching. Other consequences are cramps, easy bruising and bleeding, confusion, drowsiness and, in extremis, coma. Poor renal function can lead to hypertension, which in turn may further damage the kidneys. Without careful clinical management bone disease may ensue, while fluid overload can aggravate or precipitate heart failure.

17. The annual incidence of patients commencing RRT for ESRD in the UK exceeds 100 per million of the adult population. This is an underestimate of the incidence of ESRD as some patients do not commence RRT, because of co-morbidity and under-provision of facilities for RRT in the UK. The true incidence is probably around 200 per million per annum. The two commonest causes, diabetes and hypertension, account for most cases. Other important causes include glomerulonephritis (immune-mediated kidney damage); renal infection; renal stones; obstructions and developmental abnormalities of the renal tract (obstructive nephropathy, reflux nephropathy and polycystic kidney disease) and certain analgesics consumed in large amounts (analgesic nephropathy).

Glomerulonephritis

18. Glomerulonephritis (GN), which accounts for about a third of ESRD in the UK, is a particular focus of this report. Much of the research evidence points to a particular link with this outcome.
19. The glomerulonephritides are a complex family of renal diseases that can exist in acute and chronically progressive forms. They all seem to be due to abnormalities in various components of the immune system. The glomeruli are the principal targets of injury because the circulating components of the immune system tend to lodge in the glomeruli as they pass through the filtration mechanism, and then set off damaging inflammatory responses. Disorders caused by abnormal immune responses directly against the patient's own tissues are called 'autoimmune' diseases. This mechanism is suggested in GN by the discovery of antibodies or other components of the immune system within the glomeruli. These diseases can be confined to the kidneys (primary GN) or part of a multisystem autoimmune disease. Most common among the latter are ANCA (anti-neutrophil cytoplasmic antibodies) associated systemic vasculitis (AASV) and systemic lupus erythematosus (SLE). The most common primary GN is IgA nephropathy, characterised by the deposition of IgA within the glomeruli.

Diagnosis

20. GN is suspected in the presence of proteinuria, with or without progressive renal failure. Characteristic involvement of other systems and serological evidence of immune abnormalities may be highly suggestive, but renal biopsy and histological examination are usually necessary for precise diagnosis. The diagnostic criteria for immune-mediated GN include a combination of specific histopathology in renal biopsy specimens and sometimes characteristic serological evidence of auto-immunity e.g. pANCA-positivity in systemic vasculitis. In advanced renal impairment it can be difficult to identify specific types of GN. IgA nephritis has a specific biopsy appearance and blood or protein in the urine.
21. The underlying cause of renal failure is not always diagnosable with certainty. It is likely, however, that a substantial proportion of ESRD of undiagnosed cause arises from undetected GN.

Illness due to renal disease

22. The level of disability arising from kidney disease will depend on whether it is progressive or non-progressive and on the level of residual renal function.
23. Symptomatic kidney failure starts when about 75% of function is lost, and causes some or all of the problems outlined in paragraph 15. By the time that 90% of total kidney function is lost (ESRD), dialysis or renal transplantation is required.
24. There is no correlation between a single blood test and the likelihood of progression to ESRD but change in serum creatinine over time is a good indicator. It is similarly a fair but not a perfect indicator of clinical status.

Evidence received

25. At the outset of inquiry the Council's attention was drawn to an excess of renal disease that had been observed among patients from a small village in Upper Weardale, County Durham. The patients were all current or former fluorspar workers (fluorspar seams are surrounded by quartz, a rich source of silica). A comparison was made of the prevalence of known renal disease from the area of Upper Weardale most associated with fluorspar mining with the surrounding non-mining area. Overall, the prevalence of renal disease was greater in patients from the mining area (4.9 per 1000 population) than in those from the non-mining area (0.36 per 1000 population). A subset of patients in the mining area had GN which was particularly over-represented in this location (4.25 per 1000 cases) relative to the non-mining area (0.18 per 1000 cases). The prevalence of renal replacement therapy was 1216 per million in the mining area, versus 357 per million in the comparison area.
26. Of the 8 cases of renal disease from the mining area, 6 had been exposed to silica for 11–35 years and reportedly breathed in dust for several hours a day. Cases from the non-mining area had no history of exposure to silica. No patient had silicosis, the fibrotic lung disease caused by inhalation of silica.
27. This evidence suggests a possible link between exposure to crystalline silica and autoimmune disease affecting the kidney. One caveat however, is that actual incidence rates of renal disease were not available for a well-defined cohort of fluorspar miners and a suitable cohort of non-miners. The main comparisons were ecological and so may have been confounded by other factors.
28. Wider inquiry was undertaken to place the observations in context relative to other research observations.

Biological plausibility of silica-related renal disease

29. Several studies lend weight to the plausibility of silica as a cause of renal disease, including immunologically-mediated GN. Evidence exists as to silica's toxicity, its potential to redistribute in the body and its capacity to induce chronic inflammation and autoimmune responses.
30. Knowledge of the mechanisms is not exact. However, silica particles in aqueous media such as found in biological systems can produce reactive oxygen species, such as hydroxyl free radicals. These disrupt and destroy molecules and tissues in a process known as oxidative stress: the hydroxyl free radical is particularly injurious. Free radicals can cause inflammation via chemicals called cytokines and chemokines, which have been implicated in experimental animal models and patients with silica-induced lung fibrosis.
31. Chronic inflammation may lead to autoimmunity. The surface of the silica molecule may become coated with denatured host proteins which are antigenic to the immune system, stimulating the production of antibodies and immune complexes which recognise and attack the host's own tissues. Again experimental evidence exists in susceptible mice that silica exposure can induce this effect. Silica has been shown to potentiate the immune response, to activate key inflammatory cells and to encourage release of mediators from immune cells.
32. Silica has been implicated in several other autoimmune diseases – including AASV (cANCA as well as pANCA), SLE, rheumatoid arthritis and scleroderma (discussed below). This strengthens belief in its capacity to cause widespread immunological injury.

Variability in risk from silica exposure due to molecular surface modifications

33. The injurious effects of silica vary considerably, even at apparently similar levels of exposure. In silicosis, epidemiological studies point to some heterogeneity of risk and this has prompted the idea that modifications to the surface of the particle (which vary industry by industry) modify silica's toxicity. The surface is the part that interacts with the body's cells to induce a biological response. The surface area of the silica particle therefore correlates to the "effective" dose. Differences in surface area may account for some of the difference in observed risk in epidemiological studies of silicosis - smaller particles, having greater surface areas, may have a larger biological effect.
34. In animal experiments, silica's capacity to cause lung inflammation can be reduced by coating the particle surface with aluminium – present in nature, as a common component of the same geological strata as quartz. Similarly, dust from coalmines may modify the reactive surface. Thus, quartz in certain industrial settings may be more active biologically than in other settings.
35. This variability is relevant to the current review insofar as it raises a question about the appropriateness of extrapolating data on risks of renal disease from silica exposure between settings.

Literature review: Silica exposure and renal kidney disease

Case reports

36. There have been many case reports linking silica exposure to renal disease. For example, Chevailler et al. (1994) reported 8 slate workers with varying types of GN, all of which were positive for the pANCA antibody marker of microscopic polyarteritis. Three cases of pANCA-positive nephritis have been reported in dental technicians. Case reports provide only limited evidence on causation, however. A better level of evidence comes from formal epidemiological studies with a comparator (control) group.

Case-control studies

37. Several case-control studies have been published. Most have been set in renal care facilities and so are based upon cases that hold a broad range of occupations. Typically in this design, renal patients and controls are interviewed about the work they have done, and some expert judgement is made on their likely exposure to respirable crystalline silica.
38. An important strength of this design is that by taking the starting point as a specialist service, reasonable numbers of cases of rare diseases can be assembled and carefully investigated and classified. A major weakness however, is that the actual levels of exposure to silica tend to be poorly characterised. Such studies provide useful information on the existence and nature of the hazard, but not on the amount of exposure needed to cause harm.
39. A typical example is the study by Gregorini et al., which compared cases of ANCA-positive rapidly progressive GN admitted to a renal department during 1987-1992 with patients admitted with other renal diseases around the same time. Diagnosis was generally confirmed by kidney biopsy. An occupational hygienist interviewed subjects about jobs held for more than six months. Seven of 16 cases and 1 of 32 controls were considered to have a history of silica exposure, with p-ANCA antibodies in 6 of the 7 exposed cases. The odds of having renal failure were estimated (with substantial statistical uncertainty) to be 14 times greater in those who held a job with silica exposure for more than six months than in those who did not.
40. Another example is provided by the case-control study of Steenland et al. (1990). Three hundred and twenty five men aged 30-69 years with ESRD diagnosed in 1976-84 in Michigan were selected from its state kidney registry (excluding diabetes, congenital disorders and obstructive nephropathies). Community controls were recruited by random digit dialling and matched by age, race, sex and area of residence. Interviews were completed with 69% of cases and 79% of controls. Questions were asked about jobs held for more than 6 months since age 18 years. Higher risks were found for brick and foundry workers (odds ratio 1.9), sandblasters (odds ratio 3.8) and workers in jobs thought to have any silica exposure (odds ratio 1.7).
41. The Council identified several other case-control studies. These generally suggested an elevated risk of ESRD in workers occupationally exposed to silica, with even higher risks for immunologically-related forms of ESRD; none helped the Council to define the precise level of exposure likely to double the risk of renal failure.

Cohort studies

42. Cohort studies, set within highly exposed occupations, have the important extra potential to quantify levels of exposure (although such data were seldom discovered).
43. Set against this has been the problem of accumulating enough cases of a rare outcome to be confident of the findings. Cohort studies that focussed on deaths from renal disease had a further potential limitation – that those with renal disease might die of competing causes or be treated successfully, leading to a possible underestimation of the strength of association with serious but not fatal renal disease.
44. In spite of these difficulties, most of the cohort studies identified by the Council suggested a higher risk of ESRD in workers exposed to silica.
45. In general, higher risks were found for studies of morbidity than for studies of mortality (in line with paragraph 43 above), and higher risks were observed for immunologically-mediated GN than for other causes of ESRD.
46. A good example of the cohort study type is provided by Calvert et al. (1997), who followed 3,332 gold miners from South Dakota, USA during 1977-1992 and checked the occurrence of names on a major database for ESRD. The incidence rate in miners was estimated in comparison with age, sex and race-matched national reference data. The risk of ESRD was increased 1.37-fold overall, but the risk of GN was elevated 4.27-fold. The rate of development of new cases of 'non-systemic' ESRD (mostly GN) was 7.7 times more frequent for miners who had spend more than 10 years underground.
47. Higher risks of GN were also found in an industrial cohort of Italian ceramic workers (raised 3.2-fold), but with less information on likely exposure levels.
48. Another US study, by Steenland et al. on a cohort of 4,626 industrial sand workers, provides a rare estimate of the exposure-response relationship. As for the South Dakota study, names from the cohort were sought on a major database for ESRD (the ESRD Programme) and incidence rates calculated relative to national figures. In this study more than 4,000 industrial hygiene specimens were taken over an extended period to assess exposures to silica. A matrix was constructed of likely exposures in different jobs at different times and used to estimate workers' cumulative exposures.
49. The estimated absolute risk of ESRD was 4.3 per 100,000 per mg/m³/yr of exposure. Assuming a background rate of 7.4/100,000 in the literature, a doubling of risk was estimated to occur at a cumulative level of about 2 mg/m³/yr.
50. The shape of the relationship, however, was based on only a few cases of disease at each level. Moreover, this well-conducted and detailed study represents the only clear attempt so far to estimate this dose-response relationship and is confined to a single industry.
51. The published data from the US sand workers' cohort do not readily permit the separate effects of intensity and duration (and so, peak vs. cumulative exposure) to be disentangled. Peak exposure may be a more relevant exposure metric if the mechanism of injury is immunological.

Studies relating to patients with silicosis

52. Renal disease (including GN) has also been found in autopsy specimens taken from patients dying of silicosis – both in case reports and in a few epidemiological studies. These observations tend to confirm an association between renal disease and silica exposure, although the relation is inconsistent.
53. The Council considered whether to prescribe for GN in workers with silicosis or more generally in occupations and exposure circumstances currently sufficient to enable prescription of silicosis.
54. However, the first of these possibilities was discounted after failing to discover a clear doubling of risk of GN in the few surveys of silicotics so far published; and the second because the Council received written evidence suggesting that the dose-response relationship is likely to be steeper for silicosis than for ESRD.

The Council's interpretation of the evidence

55. A significant body of evidence links silica with renal disease. The clearest association is with immune-related GN, for which biologically plausible mechanisms can be postulated.
56. Despite this literature, observations that enable the dose of silica that leads to harm (specifically, the dose that doubles the risk of ESRD from causes plausibly linked to silica) are limited mainly to one high-quality survey in the US sand industry.
57. One important issue the Council considered was whether or not such data could be extrapolated to other circumstances of exposure. There are theoretical reasons why risk of renal disease might vary by the circumstances, as well as the level of exposure (paragraphs 33-35), but no direct evidence of heterogeneity. Set against this are observations that the hazard is widely distributed, with reports across a broad range of occupations and industries.
58. On balance the Council considered it reasonable to extrapolate the dose-response relationship, as defined in the sand industry, to other industries and settings in order to identify hazardous levels of exposure.
59. Of more concern was the limited data on which to define a qualifying exposure and occupational coverage. Generally, in framing its recommendations, the Council seeks compelling and consistent evidence from several high quality surveys in the expectation that new research will not quickly invalidate its advice. For renal disease and silica exposure there is compelling consistent evidence of a hazard, but limited evidence on which to decide the terms of prescription.
60. On balance the Council feels that the evidence base is insufficient at present to define a schedule of exposure. However, this is an active area of research and the Council intends periodically to check the currency of this position.

Silica and other rheumatic diseases

61. Exposure to respirable crystalline silica has also been linked with several autoimmune diseases, often considered rheumatic in nature. A literature review, conducted in parallel with the main inquiry, identified more than a hundred abstracts and over twenty relevant epidemiological reports.

Nature of these disorders

62. Systemic lupus erythematosus (SLE or lupus) is an autoimmune disease, linked in some research reports with exposure to silica. This disease can affect almost all of the body's organs. It has many manifestations, including fatigue, flu-like illness, skin rashes (especially a 'butterfly' rash on the cheeks and nose), hair loss, eye problems, mouth ulcers and importantly, internal organ involvement. Pleurisy, kidney disease and brain inflammation can arise and sometimes a clotting tendency that may lead to thrombosis in veins or arteries. Although comparatively rare, over 30,000 people have the disease in the UK (90% are female). Aggressive treatment may be needed using steroids, immunosuppressive and other drugs to control the disease.
63. Scleroderma (literally 'hard skin') is really a group of diseases that involve the abnormal growth of connective tissue (the tissue that supports the skin and internal organs). In some forms of localised scleroderma, hard, tight skin is the entire extent of the disease, or just the skin and the muscle below. But, in other forms (systemic sclerosis) connective tissue is affected more widely, in blood vessels and internal organs such as the heart, lungs and kidneys. Calcium deposits may be formed in the connective tissues. The muscles of the oesophagus (the tube connecting the throat and the stomach) may lose normal movement, affecting swallowing, and people with diffuse disease often suffer from fatigue, weight loss and swollen, painful joints. When the skin is affected it may appear swollen, shiny and tight and may impair the function of the hand. Sometimes, severe kidney, lung, digestive or heart problems occur.
64. In scleroderma the immune system is thought to stimulate certain cells (fibroblasts) to produce too much collagen. It is this build up that affects the skin, blood vessels and other organs. Women of late childbearing years are at highest risk suggesting that female hormones may play some part in the disease; another trigger is thought to be exposure to viral infections in those who are genetically predisposed, but the exact causes are not well understood.
65. Rheumatoid arthritis is an inflammatory disease that causes pain, swelling, tenderness and stiffness in the joints. The wrist and finger joints are most commonly involved, but many other sites (shoulder, knee, hip, elbow, feet etc) can be involved, often in a symmetrical pattern. The disease may cause destructive changes in affected joints, with deformity and loss of function. It can also affect other bodily organs and cause general symptoms of fatigue, fever and malaise, anaemia, dry eyes and mouth, inflammation of the blood vessels, pleurisy and pericarditis (inflammation of a sac that encloses the heart). The disease can be relapsing and remitting, with flare-ups and periods of improvement, or can be severe and relentless through a lifetime, with serious joint damage and disability. Specific specialist treatments can improve the outlook.

Evidence linking each disorder with exposure to silica

66. The literature on connective tissues and silica has some similarities with that on renal disease and it raises similar issues. Numerous case reports preceded several epidemiological studies, mostly of the population-based case-control design (with the strengths and limitations highlighted in paragraph 38). Scleroderma and systemic sclerosis have been most frequently studied, but a few reports were also found on SLE and rheumatoid arthritis.
67. Most reports suggested a positive association. However, the Council was unable to define from them a clear the level of exposure required to at least double the risk of any of these diseases.
68. A few studies considered the concurrence of silicosis and connective tissue diseases. For example, Calvert et al. (2003) found that on death certificates the diagnoses of systemic sclerosis and silicosis appeared together more often than expected; Roseman et al. (1999) collected a case series of patients with silicosis and found mention of scleroderma, SLE and rheumatoid arthritis in their medical records more often than expected; and Brown et al. (1997) found that on comparison with other male admissions, Swedish men hospitalised for silicosis during 1965-1983 were 8 times more likely to have an admission for rheumatoid arthritis and 37 times more likely to be admitted with SLE. But owing to the rarity of connective tissue disease, only the observations on rheumatoid arthritis were based on reasonable numbers of cases. Moreover, the Council was concerned that selection bias might influence the findings of Brown et al.

The Council's interpretation of the evidence

69. As with ESRD there is suggestive evidence that silica may cause scleroderma, SLE and rheumatoid arthritis. However the evidence base on which to prescribe is limited and falls short of that normally sought by the Council. As with ESRD, an important obstacle lies in defining the qualifying level of exposure.
70. The Council was encouraged by the studies in paragraph 68 to consider prescription for those with silicosis. However, the studies that raise this possibility are few in number and potentially beset with biases. Further corroboration is needed before recommending prescription.

Preventative measures

71. Silica-related diseases can be prevented by ensuring that workers who come into contact with silica-containing materials are not exposed to the respirable dust released when working with such materials. The Control of Substances Hazardous to Health Regulations 2002 (COSHH) requires employers to assess the risks to their employees from being exposed to respirable crystalline silica (RCS). Where there is a significant health risk from exposure to an agent, the employer must introduce appropriate measures to prevent exposure, or if this is not possible, to control the risk.
72. Prevention or substitution are the best options. Control measures are based on good working practices and depending on the circumstances, may include: better design of the work process; control of exposure e.g. by dust suppression or extraction; administrative and behavioural controls and where adequate control of exposure cannot be achieved otherwise, the provision of appropriate respiratory protective equipment.
73. Under COSHH, RCS is subject to a workplace exposure level (WEL) of 0.3mg/m³ measured over an 8-hour time weighted average. However, current scientific evidence suggests that a more stringent limit is needed – long-term exposure at 0.3mg/m³ is associated with a 20% risk of developing silicosis. A reduction in the WEL to 0.1mg/m³ would reduce the risk considerably. HSE will shortly be consulting on proposals to reduce the WEL from 0.3mg/m³ to 0.1mg/m³.
74. If the proposal is agreed, HSE would bring the new WEL into force in 2006. A WEL set at 0.1mg/m³ would be accompanied by advice on good practice. This would be freely available in the form of "Silica Essentials", a series of COSHH Essentials-style control advice sheets, covering a wide range of tasks and processes in which RCS is produced. It includes advice on air sampling and health surveillance.

Recommendations

75. The Council has concluded that there is insufficient evidence at present to recommend prescription of renal disease, or any of the autoimmune rheumatic disorders in relation to occupational exposure to silica. However, in view of the growing body of research evidence in this area, the Council intends keeping this topic under review.

APPENDIX 1

Annex of consultation with experts

Professor Ken Donaldson University of Edinburgh, Edinburgh

Dr John Main James Cook University Hospital, Middlesbrough

Professor Corbett McDonald Royal Brompton Hospital, London

Professor Kyle Steenland Emory University, Atlanta, US

Details of the scientific references that are referred to in this report are available from the IIAC Secretariat on request.