



Department for Work and Pensions

Social Security Administration Act 1992

Extrinsic Allergic Alveolitis

Report by the Industrial Injuries Advisory Council in accordance with Section 171 of the Social Security Administration Act 1992 reviewing the prescription of extrinsic allergic alveolitis for work involving exposure to mists from metalworking fluids.



Department for Work and Pensions

Social Security Administration Act 1992

Extrinsic Allergic Alveolitis

Report by the Industrial Injuries Advisory Council in accordance with Section 171 of the Social Security Administration Act 1992 reviewing the prescription of extrinsic allergic alveolitis for work involving exposure to mists from metalworking fluids.

*Presented to Parliament by the Secretary of State for Work and Pensions
by Command of Her Majesty
July 2006*

© Crown Copyright 2006

The text in this document (excluding the Royal Arms and departmental logos) may be reproduced free of charge in any format or medium providing that it is reproduced accurately and not used in a misleading context. The material must be acknowledged as Crown copyright and the title of the document specified.

Any enquiries relating to the copyright in this document should be addressed to The Licensing Division, HMSO, St Clements House, 2-16 Colegate, Norwich, NR3 1BQ.

Fax: 01603 723000 or e-mail: licensing@cabinet-office.x.gsi.gov.uk

Industrial Injuries Advisory Council

Current members:

Professor A J NEWMAN TAYLOR, CBE, FRCP, FFOM, FMedSci (Chairman)

Dr J ASHERSON, BSc, D Phil, MBA, MIOSH

Professor M AYLWARD, CB, MD, FRCP, FFPM, FFOM, DDAM

Dr M G BRITTON, MD, MSc, FRCP, Dip(Ind. Health)

Dr A COCKCROFT, MD, FRCP, FFOM, MB, BS

Mrs D KLOSS, LLB, LLM

Dr I J LAWSON, MB, BS, DRCOG, MIOSH, FFOM

Mr S LEVENE, MA

Dr K T PALMER, MA, MSc, DM, FFOM, FRCP, MRCP

Mr J PRESTON-HOOD, MBA, DipHS, MIOSH, RSP

Mr H ROBERTSON

Dr A SPURGEON, BSc, PhD, CPsychol

Ms C SULLIVAN, MA, GradDipPhys, MCSF

Mr A TURNER, TechSP

Mr F WHITTY, BA

Dr L WRIGHT, BMedSci, BM, BS, FFOM

Previous members:

Mr M PLATT, BA(Hons), MSc

Health and Safety Executive Observer: Dr J OSMAN

IIAC Secretariat

Medical & Scientific Secretary:

Dr P STIDOLPH

Scientific Advisor:

Dr M SHELTON and Dr S BUNN

Administrative Secretary:

Mr P CULLEN-VOSS

INDUSTRIAL INJURIES ADVISORY COUNCIL

Letter to Secretary of State

Dear Secretary of State,

This report details a review in which we consider extending prescription of extrinsic allergic alveolitis to cover work involving exposure to mists from metalworking fluids.

The matter was brought to our attention in September 2005. We have reviewed written and oral evidence and compiled our report, with its recommendations, in eight months. This is illustrative, I believe, of our effectiveness as an advisory council.

Three outbreaks of extrinsic allergic alveolitis have occurred in workers from three different factories in the UK exposed to mists generated from work with metalworking fluids. There is a body of research evidence supporting an association between extrinsic allergic alveolitis and exposure to mists from metalworking fluid. Whilst the specific causal agent within the metalworking fluid mist responsible for the outbreaks has not been identified, evidence strongly implicates microbial contaminants. The disease is uncommon, and diagnosis is relatively straightforward, with a strong presumption of work causation in individually affected workers.

We recommend that occupational coverage for extrinsic allergic alveolitis be extended to include work involving exposure to mists from metalworking fluid.

Yours sincerely,

Professor A J Newman Taylor
Chairman

Date: July 2006

Summary

1. Extrinsic allergic alveolitis (EAA) is a potentially serious respiratory disease caused by exposure to a variety of sensitizing agents, often encountered in occupational settings. EAA is already a prescribed disease in relation to several occupational exposures (Prescribed Disease [PD] B6). Recently, three outbreaks of EAA have been reported in Birmingham, South Yorkshire and Nottinghamshire at factories where workers were exposed to mists of metalworking fluids (MWF). This review considers extending occupational coverage for PD B6 (EAA) to work involving exposure to mists generated during metalworking.
2. A Health and Safety Executive (HSE) investigation concluded that exposure to metalworking fluid mists was responsible for the Birmingham outbreak. Investigations are current at the other outbreak sites but exposure to mists from MWF was common to all affected workers. Several studies of different research designs reported in the scientific literature provide evidence to support the association of exposure to aerosolized MWF with the development of EAA.
3. It seems likely that EAA is the outcome of microbial contamination of MWF, which becomes aerosolised as an airborne respirable mist. However, the specific aetiological agent in EAA associated with MWF has been hard to pinpoint and may vary between individuals and between outbreaks.
4. Analysis of the MWF from the three UK outbreaks showed the presence of microbial contaminants to which a minority of the affected workers demonstrated a serological response.

5. EAA is an uncommon disease, which is often occupational in causation. The disease is relatively straightforward to diagnose by non-invasive techniques. In cases that arise in workers exposed to mists from MWF, the presumption of occupational attribution is strong, even in the absence of confirmatory serological investigation.

6. On this basis IIAC recommends that the prescription for EAA (PD B6) be extended to include work involving exposure to mists from metalworking fluids.

Scope of the current review

7. In September 2005, trade union representatives brought to the attention of the Industrial Injuries Advisory Council (IIAC) an outbreak of EAA associated with MWF. Subsequently we learnt of two further outbreaks of EAA which had occurred in similar circumstances. The cases occurred in automotive parts manufacturers located throughout the United Kingdom - in Birmingham, Nottinghamshire and South Yorkshire. At the time of writing these outbreaks are still the focus of HSE investigations.

8. EAA was last reviewed by the Council as part of the review of the prescribed biological diseases (“B diseases”). This review was published in November 2003 in the Command Paper ‘Conditions due to Biological Agents’ Cm 5997. This current review focuses specifically on whether there is sufficient evidence to extend the prescription of prescribed disease (PD) B6 (EAA) to include exposure to mists from MWF.

Method of investigation

9. IIAC referred the question of EAA and exposure to MWF to the Council’s Research Working Group (RWG). A literature search was carried out using the PubMed database and relevant research papers were obtained and evaluated. The Council consulted those involved in the investigation of the outbreaks, including HSE officials and clinicians who had identified and researched the EAA cases from the UK outbreaks.

Extrinsic allergic alveolitis – the disease

10. EAA, also known as hypersensitivity pneumonitis, is an allergic reaction (usually mediated by T lymphocytes) in the gas exchanging parts of the lung (alveoli) to inhaled antigens, often poorly degradable particulate antigen, such as microbial fragments. The level of exposure to the antigen needed to induce an allergic reaction is unclear, but in an allergic individual exposure to the causal agent can provoke a systemic and pulmonary reaction within hours of the inhalation. EAA can present in an acute or a chronic form. Acute EAA is caused by exposure to high concentrations of the antigen, typically provoking breathlessness and flu-like symptoms. These symptoms usually develop within 6 to 8 hours of exposure and resolve without further exposure in 48 hours, although lung function can take weeks to improve and months to recover. Chronic EAA can be the outcome of repeated episodes of acute disease or of long term exposure to lower levels of exposure to the sensitising antigen, by themselves insufficient to cause acute EAA but sufficient to cause progressive lung damage. Chronic EAA is characterised by the development of irreversible pulmonary fibrosis (scarring), which causes breathlessness on exertion. Symptoms do not resolve with avoidance of further antigen exposure. Early diagnosis with avoidance of exposure can prevent progression to chronic EAA.

11. EAA has a low incidence and prevalence. It was first described in dairy farmers exposed to mouldy hay. Since then, many antigens, the majority of fungal origin, have been associated with the development of EAA. These have common features, such as small easily respirable size (1-5 μ), presence in high levels during exposure, and poor degradability. Many of the antigens associated with EAA are encountered in an occupational setting (see table below).

Disease	Source
Farmer's lung	Mouldy hay, straw, grain
Bird fancier's lung	Avian excreta and bloom
Bagassosis	Mouldy bagasse
Maltworker's lung	Mouldy maltings
Mushroom worker's lung	Spores released during spawning
Ventilation pneumonitis	Contamination of air conditioning units

EAA – the prescribed disease

12. EAA has been a prescribed disease since 1964 for farmer's lung due to "exposure to the dust of mouldy hay or other mouldy vegetable produce". The terms of prescription were extended in 1983. The current terms of prescription are given in the table below.

Prescribed disease	Occupation
B6 Extrinsic allergic alveolitis	Exposure to moulds or fungal spores or heterologous proteins by reason of employment in a) agriculture, horticulture, forestry, cultivation of edible fungi or maltworking; or b) loading or unloading or handling in storage of mouldy vegetable matter or edible fungi; or c) caring for or handling birds; or d) handling bagasse.

13. These terms were last reviewed in November 2003. At this time a literature search was undertaken, experts in the field were consulted and a call for evidence was made to the public; but no evidence was found to suggest the terms of prescription for PD B6 should be amended. The recent UK outbreaks of EAA among autoworkers have prompted a reassessment of the case.

Metalworking fluid – the basics

14. Metalworking fluid (MWF) is commonly used wherever metal is cut, drilled, milled or shaped with cutting tools and acts to dissipate heat, lubricate, remove debris (or 'swarf') and protect tools from corrosion.

There are three types of MWF:

- a. Straight oils – pure petroleum oils.
- b. Semisynthetic fluids – emulsions of petroleum in a water base.
- c. Synthetic fluids – emulsions of synthetic oils in a water base.

15. The fluid is generally applied to the material being worked on as a jet or spray. The drained fluid is recycled into a sump where it is filtered before being pumped back to the work area. Aerosols are formed by three main processes:

- a. impaction – small droplets are formed as the MWF is pumped at high velocity onto the work area and become aerosolised upon hitting a moving or rotating surface.
- b. centrifugal force – aerosols are generated by rotating work pieces.
- c. evaporation/condensation – hot surfaces cause evaporation of MWF; as the vapour moves away to cooler areas it condenses to form small droplets.

16. MWF is able to sustain growth of various bacterial and fungal species.

Microbial contamination renders MWF less effective. Thus, biocides (such as bromopol, morpholine and triazine compounds) are added to the fluid to inhibit bacterial and fungal growth. However, the fluid is never 'sterile' and *Pseudomonas* species, *Proteus mirabilis*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae* *Mycobacterium* species and various fungal species such as *Fusarium*, *Cephalosporium*, *Candida* and *Acinetobacter* have been identified as

contaminants. The 'Monday morning' or 'rotten egg' smell produced when workers start up machines after a weekend is due to heavy bacterial growth depleting oxygen and releasing hydrogen sulphide.

17. MWF also contain corrosion inhibitors, such as borates and phosphates and surfactants for lubrication properties. Thus, in-use MWF represents a complex mixture of constituents, some of which can be biologically active.

18. Exposure to the mist of MWF has been associated with various respiratory symptoms such as work-related asthma, chronic bronchitis and, in recent years, EAA.

EAA and metalworking fluids - analysis of the literature

19. The association between EAA and exposure to MWF was initially described by Bernstein *et al.* (1995) in an outbreak in 6 American auto-parts manufacturing workers. The phrase 'machine operator's lung' was coined to describe the disease in line with other occupational causes of EAA. Since this first report, there have been a number of documented outbreaks of EAA associated with exposure to MWF within auto-parts manufacturing settings, mostly in America.

20. The cases of EAA described in the literature as occurring in association with MWF shared similar clinical features. They had abnormal lung function tests, abnormal chest radiographs and symptoms of lung disease such as breathlessness, cough, wheeze, fatigue and fever. In certain cases, lung biopsy (the most definitive investigation) confirmed the characteristic pathological changes of EAA. Symptoms deteriorated if the worker was not removed from exposure to MWF and sometimes led to permanent decrements in lung function. Conversely, when affected workers were removed from the source of exposure their symptoms stabilized or improved.

21. An exposure-response relationship has been demonstrated between the level in air of MWF aerosols and the risk of development of EAA. In one outbreak reported in the literature cases were categorised in low, medium and high exposure, as judged by the levels of MWF aerosols generated at different locations. The greater the exposure, the greater the proportion of individuals with EAA.
22. Most evidence points to microbiological contamination of the fluid in-use as the cause of adverse health effects. Several bacterial and fungal species have been isolated from MWF, some of which could be causal. In America, evidence suggests that the nontuberculous mycobacterial species, *Mycobacteria immunogenum* or *Mycobacteria chelonae* in contaminated MWF are involved in the toxic pulmonary changes associated with EAA. Inhalation of aerosols of mycobacterial species are also implicated in another form of EAA – ‘hot tub lung’. EAA-like pneumonitis has been induced in mice with heat-killed and lysed *Mycobacterium immunogenum*. The pathologic changes induced were indistinguishable from those caused by *M. immunogenum*-contaminated MWF, suggesting that this nontuberculous mycobacterium could be involved in the EAA outbreaks at the automotive parts plants.
23. Mycobacterial species have been less commonly isolated from contaminated MWF in European EAA outbreaks. This may reflect a difference in microbial flora or could be due to different culturing techniques. Microbial analyses of European MWF have yielded primarily pseudomonads, rather than mycobacteria.

24. It has been suggested that the use of biocides in suppressing microbial growth may alter the natural diversity of the microbial flora of MWF. The biocides used predominantly target Gram negative bacteria, allowing other species such as mycobacteria to flourish. As mycobacteria have been implicated as a causal agent the use of biocides might indirectly influence the development of EAA in workers exposed to treated MWF. Biocides themselves have also been linked with the ability of MWF to cause pulmonary irritation in animal studies.
25. Several studies have suggested that the endotoxin present in microbially contaminated MWF could elicit EAA-like inflammatory responses. Endotoxin is a lipopolysaccharide released from the cell walls of Gram negative bacteria when the microbes are killed or lysed. In-use MWF has been shown to elicit an inflammatory response in inbred endotoxin sensitive CH3 mice whereas endotoxin resistant CH3 mice showed no response. It has been proposed that the toxicity of biocides in used MWF could be due to the release of endotoxin following the death of contaminating bacteria.
26. However, confirming the exact cause of symptoms is not straightforward. In particular, the relation between contaminants, serological response, and health complaints is complex. Contaminants of MWF can be found in the absence of EAA, asymptomatic individuals can show a serological response, and in confirmed cases a serological response is often absent. The biocides and other agents added to discourage microbial contamination may hamper detection of the causal agent (the antigenicity of a microbe can outlive its capacity to survive and grow in culture). Thus, none of the previously published studies has clearly identified the aetiological agent in MWF involved in any of the reported EAA outbreaks. The findings in the UK outbreak are described below.

27. There is also no simple relationship between the concentration of microbes in contaminated MWF sumps and the degree of airborne exposure. Instead, this is a function of the ability to form aerosols.
28. Maintaining the cleanliness of MWF can be difficult, where highly adaptable, rapidly growing microbes are involved. Studies have shown that after system cleaning, microbial recontamination is common and fairly rapid.

The UK outbreak

29. There have been three outbreaks of respiratory disease in engineering works in the UK – in Birmingham, Barnsley in South Yorkshire and Pinxton in Nottinghamshire. Work involving exposure to mists from MWF was common to all of the cases arising in the outbreaks.
30. Information from the lead HSE investigators in May 2006 indicates that in the Nottinghamshire outbreak, there have so far been some confirmed diagnoses of occupational asthma and EAA with an estimated forecast, after clinical investigations are completed, of about 13 cases in total. Some workers are thought to be suffering from both diseases.
31. In South Yorkshire there has so far been 1 confirmed diagnosis of EAA, with another possible case under consideration; in addition, after clinical investigations are completed, there may be 2 -3 cases of occupational asthma, although extensive health surveillance has only just started.

32. The outbreak in Birmingham was the subject of clinical investigation, and an HSE report outlining the emerging lessons was published in April 2006. Outbreak cases shared similar clinical features between the different sites, which were typical of EAA, such as improvement of respiratory symptoms after time away from the exposure (e.g. at the weekend) and worsening of symptoms upon return to work (e.g. at the start or during the working week); decreased lung function measurements and characteristic radiological and histological changes of EAA. Several affected workers (11 of the 24 cases) were also diagnosed as having asthma.

33. Microbiological analyses of the MWF sumps in the Birmingham outbreak revealed *Acinetobacter* and *Ochrobacter* species. The levels of fungal contamination were not elevated above background environmental levels and no mycobacterial contamination was found. Endotoxin did not appear to be a significant factor in the outbreaks. Despite a decrease in cases of respiratory disease following the clean-up, the concentrations of endotoxin remained similar before and after the clean-up operation.

34. A summary of the serological investigation undertaken for the Birmingham outbreak is available at <http://www.hse.gov.uk/>. In brief:

- three workers (out of 12 workers) diagnosed with EAA and two (out of 72 workers) with occupational asthma had a serological response to crude MWF extract, taken from a large sump (the Mayfram sump) in April 2004;
- three workers diagnosed with EAA had a serological response to *Ochrobacter anthropi* and seven workers with EAA had a serological response to *Acinetobacter species*, both bacteria present as DNA fragments in samples from the Mayfram sump taken in April 2004;

- in November 2005 one worker diagnosed with EAA and another with occupational asthma showed reactions in the lungs when challenged with samples of used MWF taken from the Mayfram sump in September 2004, but no reaction when challenged with samples of unused MWF of the type used in the same sump;
- serological evidence of a response to bacterial contaminants of used MWF was observed in a minority of those diagnosed with EAA.

The case for prescription

35. When considering a disease, and an accompanying occupational exposure, for prescription, IAC must adhere to the legal requirements for prescription (see Appendix, paragraph 43). In brief, 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. Attribution is usually based on epidemiological evidence, but can be on the basis of the clinical features of individual cases.

36. EAA is an uncommon disease reported infrequently to national surveillance schemes. Cases which occur in an occupational setting do so in response to airborne antigens in the workplace.

37. The particulars of the three UK outbreaks, and findings on EAA from the wider published literature, indicate that mists of MWF are a potential cause of EAA. Where EAA occurs in a worker exposed to mists of MWF there is a strong presumption of occupational attribution in the individual case.

38. The diagnosis of EAA is reasonably straightforward and usually possible by non-invasive means. Its differential diagnoses (e.g. cryptogenic fibrosing alveolitis and sarcoidosis) are sufficiently uncommon that a compatible clinical appearance in a worker exposed to the mist of MWF is very likely to be work-related EAA.

39. In the majority of EAA cases caused by agents already prescribed, prescription has been supported by the demonstration in individual cases of specific serological response to the antigens in question. However, its absence in many cases of MWF-associated EAA, and the uncertainty about the exact constituents of MWF responsible for symptoms, do not preclude prescription. There can be little doubt that exposure to aerosolised mists of MWF has been the cause of occupational occurrences of EAA.

Recommendations

40. IIAC recommends that the terms of prescription for PD B6 be extended to include work involving exposure to metalworking fluid mists as shown in the table below.

Prescribed disease	Occupation
B6 Extrinsic allergic alveolitis	Exposure to moulds or fungal spores or heterologous proteins by reason of employment in a) agriculture, horticulture, forestry, cultivation of edible fungi or maltworking; or b) loading or unloading or handling in storage of mouldy vegetable matter or edible fungi; or c) caring for or handling birds; or d) handling bagasse; or e) work involving exposure to metalworking fluid mists.

Appendix

The Industrial Injuries Disablement Benefit Scheme

41. The Industrial Injuries Disablement Benefit (IIDB) scheme provides a benefit that can be paid to an employed earner because of an industrial accident or PD. The benefit is non-contributory and 'no-fault', and is paid in addition to other incapacity and disability benefits. It is tax-free and administered by the Department for Work and Pensions (DWP).

The Industrial Injuries Advisory Council

42. IIAC is an independent statutory body set up in 1946 to advise the Secretary of State for Social Security on matters relating to the 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.

The legal requirements for prescription

43. 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.

44. 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.

45. In seeking to address the question of prescription for any particular condition, the Council first looks for a workable definition of the disease. The Council then 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 the available evidence in the scientific literature. 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

46. 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

47. 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.
48. The evidence on MWF-associated EAA is such that attribution can be made, or reasonably presumed, in the individual case on the basis of the clinical features.

Prevention

49. MWF is covered under the Control of Substances Hazardous to Health (COSHH) 2002 Regulations. There are no exposure limits given for exposure to MWF in the UK but the HSE has published guidance about what the law requires by way of preventive measures. Prevention requires the completion of risk assessments, the minimization of fluid contamination, including bacterial contamination, the prevention or control of mists and health surveillance where there is exposure to mist. Detailed guidance on how to do this can be found at hse.gov.uk/metalworking.



Published by TSO (The Stationery Office) and available from:

Online

www.tsoshop.co.uk

Mail, Telephone, Fax & E-mail

TSO

PO Box 29, Norwich NR3 1GN

Telephone orders/General enquiries 0870 600 5522

Order through the Parliamentary Hotline *Lo-call* 0845 702 3474

Fax orders 0870 600 5533

Email book.orders@tso.co.uk

Textphone 0870 240 3701

TSO Shops

123 Kingsway, London WC2B 6PQ

020 7242 6393 Fax 020 7242 6394

68-69 Bull Street, Birmingham B4 6AD

0121 236 9696 Fax 0121 236 9699

9-21 Princess Street, Manchester M60 8AS

0161 834 7201 Fax 0161 833 0634

16 Arthur Street, Belfast BT1 4GD

028 9023 8451 Fax 028 9023 5401

18-19 High Street, Cardiff CF10 1PT

029 2039 5548 Fax 029 2038 4347

71 Lothian Road, Edinburgh EH3 9AZ

0870 606 5566 Fax 0870 606 5588

TSO Accredited Agents

(See Yellow Pages)

and through good booksellers

ISBN 0-10-168672-2



9 780101 686723