Institution: University of Southampton

Unit of Assessment: 01 Clinical Medicine

Title of case study: 01-25 Metal fume and infectious pneumonia

1. Summary of the impact

In 2011, largely on the strength of evidence assembled by Southampton based researchers, the Department of Health (DH) recommended that employers offer welders vaccination against pneumococcus, a decision with potential to benefit some 80,000 workers, and to prevent an estimated 130 cases of invasive pneumococcal disease over 10 years, a significant proportion of which would be fatal. The advice has received extensive media attention, and more recently has been extended to other workers exposed to metal fume, offering scope for even greater benefits. It has influenced research and safety practice internationally.

2. Underpinning research

National analyses of occupational mortality are carried out or commissioned every ten years by the Office for National Statistics (ONS) (previously, the Office of Population Census and Surveys), sometimes jointly with the Health and Safety Executive (HSE). In 1992 the Southampton-based MRC team, led by David Coggon, Professor of Occupational and Environmental Medicine, was asked to undertake an analysis covering 1979-80 and 1981-90, published subsequently in 1995 **[3.1]**. Keith Palmer, Professor of Occupational Medicine, joined the team at that time (1995-date).

The team's findings indicated a marked excess of deaths from pneumococcal and other lobar pneumonia in welders and other workers exposed to metal fume. Among welders of working age 55 deaths from lobar pneumonia were observed, 2.55 times more than the 21.6 expected **[3.2]**. Furthermore, there was no excess of deaths after normal retirement age. This implied that the elevated risk could not be attributed to aspects of lifestyle, such as smoking, and suggested a hazard that disappeared after exposure ceased.

The same team highlighted that this hazard had existed for many decades. On reviewing earlier national analyses of occupational mortality, they found consistently elevated death rates from pneumonia among occupations exposed to metal fume in successive analyses dating back as far as 1930 **[3.3]**. However, this had not attracted attention when those analyses had originally been conducted.

Possible mechanisms were examined in Coggon and Palmer's 1997 paper, which set out evidence linking iron (a nutrient for bacteria) with susceptibility to infection, as well has considering the toxicity of metal fume **[3.3]**.

Building on the findings from death certificates, the MRC Southampton team undertook Britain's largest study of hospitalised community-acquired pneumonia (CAP). This compared 525 men with CAP admitted to 11 hospitals in the West Midlands during 1996-1999, and 1,122 controls, admitted to the same wards with other disorders **[3.4]**. Pneumonia was associated with occupational exposure to metal fume in the previous 12 months (odds ratio (OR) 1.8) but not in earlier periods (OR 1.1). The risk was highest for lobar pneumonia and recent exposure to ferrous fume (OR 2.3). For bacteriologically proven cases of pneumococcal infection, the OR for exposure to ferrous fume was 3.1. The data confirmed a risk of pneumococcal and lobar pneumonia from recent exposure to metal fume and showed an effect on disease incidence as well as on fatality **[3.4]**.

Further analysis of occupational mortality for the period 1991-2000, commissioned by ONS, showed that the excess of deaths attributable to metal fume exposure continued unabated. The 45.3 excess deaths were compared to 62.6 deaths in the same period from occupational asthma, a condition attracting far more attention to prevention **[3.5]**.

Work is ongoing, but preliminary in vitro evidence suggests ultrafine particulates in metal fume help pneumococci to adhere to bronchial epithelium **[3.6]**. The goal is to develop a biomarker for the

effect that would allow safe exposure levels to be defined. Meanwhile, it is proposed that workers be protected through vaccination. The team has now been asked by ONS to analyse occupational mortality for 2000-2010.

3. References to the research

References

3.1. **Coggon D, Inskip H**, Winter P, Pannett B. Occupational mortality of men. In Drever F (ed). Occupational Health Decennial Supplement. London: HMSO, 1995. 23-43.

3.2. **Coggon D, Inskip H**, Winter P, Pannett B. Lobar pneumonia - an occupational disease in welders. Lancet 1994; 344:41-43.

3.3. **Palmer K, Coggon D**. Does occupational exposure to iron promote infection? Occup Environ Med 1997; 54:529-34.

3.4. **Palmer KT**, Poole J, Ayres JG, Mann J, Sherwood Burge P, **Coggon D**. Exposure to metal fume and infectious pneumonia. Am J Epidemiol 2003; 157:227-233.

3.5. **Palmer KT**, Cullinan P, Rice S, Brown T, **Coggon D**. Mortality from infectious pneumonia in metal workers: a comparison with deaths from asthma in occupations exposed to respiratory sensitizers. Thorax 2009; 64:983-986.

3.6. Suri R, **Palmer K**, Ross JAS, **Coggon D**, Grigg J. Exposure to welding fume and adhesion of Streptococcus pneumoniae to A549 alveolar cells. Thorax 2012; 67:A51

Grants

A. Analysis of occupational mortality for Decennial Supplement. £5,000 from Health and Safety Executive. One off payment awarded 1992 (Coggon D).

B. Case-control study of community-acquired pneumonia (CAP) £194,970 funding from Health and Safety Executive. 1996-2002 (Palmer KT, Coggon D).

C. Mechanistic studies supported by The Worshipful Company of Blacksmiths. £5,000. One off payment awarded 2000 (millennium award) (Palmer KT, Coggon D, Frew A, Holgate S).

D. Mechanistic studies supported by Colt Foundation. £141,015. 2006-2009 (Palmer KT, Ayres J, Ross J).

E. Coggon, D, Palmer KT. MRC core funding. £2 million. 2010-15 (five years).

4. Details of the impact

A sustained programme of research, carried out by the University of Southampton at relatively low cost, accumulated sufficient evidence for the Department of Health, on the advice of the Joint Committee on Vaccination and Immunisation (JCVI), to recommend in 2011 that welders and, from 2012, other workers with exposure to metal fume, be offered immunisation against pneumococcal infection **[5.1]**.

An excerpt from the October 2012 revision of the Green Book, DH's official guidance on immunisation for health professionals, states: "There is an association between exposure to metal fume and pneumonia and infectious pneumonia, particularly lobar pneumonia (Palmer *et al*., 2003; Palmer *et al*., 2009; Industrial Injuries Advisory Council, 2010; Toren *et al*., 2011) and between welding and invasive pneumococcal disease (Wong *et al*., 2010)… [Pneumococcal polysaccharide vaccine] should be considered for those at risk of frequent or continuous occupational exposure to metal fume (e.g. welders) taking into account the exposure control measures in place" **[3.4, 3.5, 5.1b, 5.1c]**.

The chair of the JCVI, Professor Andy Hall, corresponded and spoke with the Southampton MRC team in deciding to proceed with the Green Book recommendation and in framing its terms. The

main evidence cited in favour of vaccination in the Green Book comprised reports from Southampton. Evidence generated by the MRC team has also been reviewed by the Industrial Injuries Advisory Council (the statutory body advising government on compensation for occupationally-related disease), and the evidence for a hazard was accepted.

While the DH recommendation has been made, as yet it is too early to judge the overall uptake of the vaccine and its preventive impact. However, there are almost 80,000 full-time welders in the UK who could benefit, and many workers in other jobs entailing exposure to metal fume.

During 1991-2000 – the latest period for which there is information – there were an estimated 45 excess deaths nationally from infectious pneumonia (principally pneumococcal) in welders and other occupations exposed to metal fume **[5.2]**. In addition, there will have been many more excess cases of pneumonia that were non-fatal, but nevertheless caused substantial illness. The introduction of immunisation therefore has the potential to prevent significant numbers of deaths and serious infections occurring at relatively young ages. The Southampton team has estimated that 588 welders would need to be vaccinated every ten years to prevent one case of invasive pneumococcal disease **[5.3]**. This is not unreasonable when viewed in comparison with other well-respected public health policies.

Keith Palmer produced a review about the vaccination policy, to alert occupational physicians in the UK to the recommendations **[5.3]**. The review won the Esso Prize for 2013. It was distributed to key stakeholder organisations and featured in the Institution of Occupational Safety and Health (IOSH) newsletter; the Association of Local Authority Medical Advisors (ALAMA) website; and a press release from the Society of Occupational Medicine (SOM) in July 2012 **[5.4]**.

The story was taken up widely by the British trade press in 2012, especially in the construction, engineering, and safety industries. Print and online titles referring to the research included *Welding Design and Fabrication* **[5.5]**, *Personnel Today* **[5.6]**, *Construction Enquirer* **[5.7]** and *Medical News Today* **[5.8]**. The research also reached a consumer audience when it was referenced in *Men's Health* magazine. Articles typically picked up on a quote from Dr Richard Heron, President of the Society of Occupational Medicine, "A £30 jab may save a life." In the wake of such extensive coverage, the Southampton team received a flood of enquiries from employers seeking more information about the risks and their obligations.

The main body of evidence internationally on this occupational hazard comes from the Southampton team, and the UK is ahead of other parts of the world in developing a vaccination policy. However, encouraged by the work undertaken at Southampton, Toren et al (2011) have since shown that Swedish welders have a five- to six-fold greater risk of hospital admission with lobar pneumonia, and Wong et al (2010) have reported a three-fold increased risk of invasive pneumococcal disease in Canadian welders. Shortly after the team's initial report, the Norwegian Labor Inspectorate issued a health alert on the hazard to physicians in Norway. To increase awareness of the research findings overseas, the team wrote a research letter for publication in the international journal, *Occupational and Environmental Medicine* **[5.9]**. A paper was also published in the international respiratory medicine journal, *Thorax* (Palmer et al **[5.2]**) and a letter to general physicians in the UK in the RCP's journal *Clinical Medicine* **[5.10]**.

If other countries follow the UK in adopting vaccination for workers exposed to metal fume, many more lives may be saved and substantially more serious morbidity prevented. Meanwhile, the MRC team have been asked to contribute to the development of HSE guidance on vaccination for metal workers.

5. Sources to corroborate the impact

5.1 Department of Health. Immunisation against infectious disease. October 2012, https://www.wp.dh.gov.uk/immunisation/files/2012/10/Green-Book-updated-251012.pdf, p306.

b) Toren K, et al. Increased mortality from infectious pneumonia after occupational exposure to

inorganic dust, metal fumes and chemicals. *Thorax* 2011; 66:992-6.

c) Wong A, et al. Welders are at increased risk for invasive pneumococcal disease. *Int. J.Infect. Dis* 2010; e796-9.

5.2 Palmer KT, Cullinan P, Rice S, Brown T, Coggon D. Mortality from infectious pneumonia in metal workers: a comparison with deaths from asthma in occupations exposed to respiratory sensitizers. *Thorax* 2009; 64:983-986.

5.3 Palmer KT, Cosgrove M. Vaccinating welders against pneumonia. *Occup Med* 2012; 62:325–330.

5.4 https://www.som.org.uk/news/media-releases/single-media/article/welders-told-to-get-vaccination-29

5.5 http://weldingdesign.com/news/WeldersPneumonia/index.html

5.6 http://www.personneltoday.com/articles/31/07/2012/58701/pneumonia-vaccine-should-be-given-to-welders-says-research.htm#.UNBL6I5LrzI

5.7 http://www.constructionenquirer.com/2012/07/05/30-vaccine-can-save-welders-lives/

5.8 http://www.medicalnewstoday.com/releases/247490.php

5.9 Palmer KT, Cosgrove M. Vaccinating welders against pneumonia. *Occup Environ Med* 2012;0:1 doi: 10.1136/oemed-2012-101057

5.10 Palmer, KT, Cosgrove, M. Community-acquired pneumonia and welding. *Clin Med* 2013; 13:214-215.