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IN-DEPTH REVIEW

# Vaccinating welders against pneumonia

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| **Background** | In 2011, the Department of Health in England recommended that welders should each receive a single dose of the 23-valent pneumococcal polysaccharide vaccine (PPV23). |
| **Aims** | To assess the evidence behind the advice and its practical implications. |
| **Methods** | The review was informed by a systematic search in Medline, which related pneumonia to welding and/or exposure to metal fume, and was supplemented using the personal libraries of the authors. |
| **Results** | There is consistent evidence that welders die more often of pneumonia, especially lobar pneumonia, are hospitalized more often for lobar and pneumococcal pneumonia, and more often develop invasive pneumococcal disease (IPD). It is estimated that one case of IPD may be prevented over a 10-year period by vaccinating 588 welders against pneumococcal infection. |
| **Conclusions** | A good case exists that employers should offer PPV23 vaccination to welders and other employees exposed to metal fume. Additionally, reasonable measures must be taken to minimize exposure to welding fume, and welders should be encouraged not to smoke. |
| **Key words** | Infective risk; metal fume; occupation; pneumococcal. |

## Introduction

The bacterium *Streptococcus pneumoniae*, otherwise known as the pneumococcus, is commonly found in the upper respiratory tract in healthy humans. Frequently, the microorganism is carried as a commensal in the nose or throat (by up to 70% of people), but among the more than 90 different serotypes that exist, some may give rise to serious infective illnesses, including pneumonia, septicaemia and meningitis. The term 'invasive pneumococcal disease' (IPD) covers clinical conditions where a pneumococcus is isolated from a normally sterile body fluid such as blood or cerebrospinal fluid, and this complication carries an appreciable case fatality rate, estimated at perhaps 5–12% in adults of working age [1,2].

In November 2011, the Department of Health's 'Green Book', 'Immunisation against Infectious Disease', advised that welders should be added to the list of patient groups for whom pneumococcal vaccination was recommended [3]. In this review, we summarize the evidential background to this recommendation and discuss the implications of the advice for occupational physicians who include welders among the client populations they serve.

## Methods

To inform the review, we conducted a search in Medline covering the period 1950 to January 2012, in which we combined terms for the exposure of interest, welding, with the outcome of pneumonia. For the former, we used a Medical Subject Heading (MESH) term for welding, as well as text words for weld$, metal work$, metal fume or welding fume; and for the latter, MESH terms for pneumonia, bacterial pneumonia, pneumococcal pneumonia were used as well as pneumonia as a text word. This search yielded 58 titles for screening, from which we excluded irrelevant hits, reports on animal experiments and studies focussed solely on metal fume fever or metal pneumonitis. The bibliographies of retrieved papers were checked for further information. Also, as a significant proportion of the relevant research has been undertaken by one of us (K.T.P.), and the other (M.P.C.) has maintained an ongoing record of reports to advise

TWI (formerly The Welding Institute), for completeness, a check was made of the personal libraries available to us.

## Scientific background

A report in 1980 by Beaumont and Weiss [4], on the mortality experience of 8679 male members of a metal trades union employed in shipyards, metal fabrication shops and small boat yards, recorded a significant excess of deaths from pneumonia in welders relative to that expected from rates in all US men. Five years later, Newhouse *et al.* [5] also found a significant excess death rate from pneumonia among welders employed at a shipyard in north-east England compared with platers and electricians from the same site.

Most information on the mortality of welders has accrued, however, from the Decennial Supplements on occupational mortality for England and Wales. Successive analyses have demonstrated increased death rates from pneumonia among welders in a pattern that can be followed back for more than five decades. During 1949–53, 70 deaths were observed compared with 31 expected [6]; in 1959–63, 101 deaths with 54.9 expected [7]; and in 1970–72, 66 deaths versus 42.0 expected [8].

In 1994, an analysis covering the extended period 1979–80 and 1982–90 (disrupted by a year of industrial action among the registrars of births and deaths) offered greater statistical power to explore potential determinants [9]. This confirmed the association with welding but went further in clarifying that the excess was attributable largely to deaths from pneumonias other than bronchopneumonia (principally lobar pneumonia) and was, moreover, limited to men below the normal retirement age of 65 years (55 observed deaths from lobar pneumonia versus 21.6 expected). Thus, excess risk existed for welders still in the occupation but not in men who had retired from it, making confounding by smoking and other non-occupational factors an unlikely explanation. Finally, the heightened risk was found to apply to several other occupations entailing exposure to metal fume, such as moulders and coremakers and furnacemen in foundries [9]. When taken together, these findings suggested that inhalation of metal fume increases susceptibility to infectious pneumonia, and the effect was reversible following cessation of exposure.

A subsequent mortality report extended observations with the addition of data from the Registrar General's Supplements for 1910–12, 1930–32 and 1949–53 [10]. As in previous analyses, occupations with potential exposure to metal fume, particularly welders, moulders, coremakers and furnacemen, had significantly elevated mortality from pneumonia. Excesses were also apparent for metal grinders and polishers, although these were less marked. Also, the excess mortality from pneumonia in fume-exposed occupations was confined to men of working age, while the at-risk occupations were found not to have comparable excesses of lung cancer or of mortality from non-respiratory infections, adding to the evidence against confounding as an explanation.

In the years 1930–32 and 1949–53, unlike in later reports, workers in ferrous foundries were distinguished from foundrymen working other metals, and iron ore miners from miners of tin, copper and other metalliferous ores. When disaggregated in this way, it was found that the elevation of mortality from pneumonia was generally more marked in those working with ferrous metal, with no consistent differences in mortality from bronchitis. Similarly, during 1910–12, the risk of death from pneumonia in iron founders was twice that in brass founders, and that in iron miners and quarriers was 50% greater than in lead miners, but there was no corresponding excess mortality risk from bronchitis [10].

Generally, the pattern was considered compatible with a specific hazard from iron, and multiple strands of evidence indicate that free iron can promote infections in biological systems, acting either as a growth nutrient for microorganisms or as a cause of free radical injury (for a full review see Palmer and Coggon [10]). Iron is seldom 'free' at body surfaces; instead, most of the body's stores are intracellular, in ferritin, haemosiderin and haem, and the extracellular fraction is bound to high-affinity iron binding proteins (transferrin in serum and lactoferrin in external secretions) that keep the concentration of free iron in equilibrium as low as $10^{-18}$ M (moles per litre). However, a battle for free iron exists between host and microorganisms, the normal flora of the respiratory tract reflecting in part the nutrient-limited balance finally achieved. In situations where the balance is disturbed, for example when exogenous supplies of iron exceed the capacity of the iron binding protein system, overgrowth of organisms may be encouraged or free radical injury of host defences against infection could ensue. Thus, an 'iron hypothesis' has been mooted to explain the consistently higher risk of pneumonia in metal fume-exposed workers [10].

Analysis of death certificates can only take matters so far, being limited, for example, in its capacity to explore the iron hypothesis, and whether risks are specific to certain metal(s) or general to many metals, or to assess whether the excess risk applies to all categories of pneumonia or only to those caused by certain microorganisms. Another uncertainty is whether the effect of metal fume is on the incidence of disease (the risk of acquiring pneumonia) or on the case fatality rate (the risk of dying once the disease has occurred).

To garner further information, a case–control study was conducted during 1996–99 in Birmingham and the West Midlands (chosen because of the relatively high prevalence of occupational exposure to metal fume in the local population) [11]. In all, 525 working-aged men of 20–64 years admitted to 11 hospitals with

community-acquired pneumonia were interviewed about their lifetime occupational history, including exposure to metal fume, together with 1122 controls, admitted to the same hospitals under the same medical teams with non-respiratory illness.

Consistent with the mortality data, pneumonia overall was found to be more common among welders and other workers with exposure to metal fume than among workers with non-exposed jobs; and risks were confined to exposures in the previous 12 months (adjusted odds ratio (OR) = 1.6, 95% confidence interval (CI) = 1.1–2.4) and not apparent if the last exposure was more than a year before (OR = 1.1). Also consistent with the mortality data, risks were higher where the X-rays (read blind to occupational history) showed shadowing in a lobar or in a segmental/subsegmental pattern than when the appearance was one of bronchopneumonia (ORs for exposure to any metal fume in the previous 12 months 1.8 and 1.8 respectively, versus 1.3 for bronchopneumonia). Consistent with the iron hypothesis, risks were highest of all when exposure in the past year was to ferrous fumes but not to other metals or alloys (OR for lobar pneumonia = 3.0, 95% CI = 1.4–6.7). Finally, in 43 cases where the pneumonia was confirmed as pneumococcal, by recovery of *S. pneumoniae* from blood and/or sputum, the OR for exposure to metal fume of any kind was 1.8 and for exposure specifically to ferrous fume was 3.1 (95% CI = 1.0–9.5). The findings thus support the hypothesis of a hazard that is reversible following cessation of exposure, which affects the incidence of disease and not just its fatality, and which is linked in particular with recent exposure to ferrous metal fume and with lobar and pneumococcal pneumonia.

Useful though this information is, the study could not tie down precisely the time frame of risk as most workers who were exposed in the previous 12 months had also been exposed in the previous 7 days. Nor did it exclude the possibility that other organisms could sometimes be involved, as in men infected with *Legionella*, *Mycoplasma* or *Haemophilus influenzae* the OR following exposure to ferrous fume was 2.1. Finally, too few men were exposed solely to nonferrous metal fumes to allow confident exclusion of risks from these other sources of exposure.

Further corroboration of the findings came from a study of mortality [12] in a large Swedish cohort of construction workers, including 30 427 men with exposure to metal fumes. Risks of death from pneumonia were elevated 2.3-fold overall and 3.7- and 5.8-fold, respectively, when lobar pneumonia and pneumococcal pneumonia were analysed as subgroups of interest; while the relative risk of infectious pneumonia was only 1.16 in retired workers with former exposure.

Bringing the story up to date are one more analysis of occupational mortality and a survey of patients hospitalized with IPD. In the first of these, Palmer *et al.* [13] published risk estimates from the latest analysis of occupational mortality for the Office for National Statistics (ONS) in England and Wales during 1991–2000. Confirming earlier observations, excesses of mortality were found from pneumococcal and lobar pneumonia (54 deaths versus 27.3 expected) and from pneumonias other than bronchopneumonia (71 versus 52.4), but there were no excesses of mortality from these causes at older ages or from bronchopneumonia at any age. Despite potentially better workplace controls on exposure, the hazard remains manifest in the most recent national statistics. Elsewhere, a study by Wong *et al.* [14], of cases of IPD confirmed at a microbiological reference laboratory in Alberta, Canada, implied a rate among welders of 22.7/100 000 population/year, 2.7 times higher than in the general adult population aged 18–65 years.

Deaths from pneumonia in young adults are rare, as are deaths due to IPD [14,15], but the analysis by Palmer *et al.* [13] found that the attributable mortality from metal fume (45.3 excess deaths) in England and Wales during 1991–2000 was not trivial compared with an estimated 62.6 deaths from occupational asthma over the same period. Using data from various sources, the Health & Safety Executive has since made a similar estimate of attributable mortality [16].

It may be said that, although efforts to control welding fume exposure at source are ongoing, this long-standing hazard has been relatively underappreciated in the UK, especially since the first report by Coggon *et al.* [9] appeared in the *Lancet* in 1994 under the title 'Lobar pneumonia: an occupational disease in welders'. However, in 2001 the Norwegian Labour Inspection Authority (NLIA) issued a warning to Norwegian physicians about the potentially lethal risk of fumes from thermal metal work [17]. The NLIA had received three independent reports of deaths from pneumonia with septicaemia among previously healthy men aged 50–55 years (all three exposed to welding fumes immediately before they fell ill) and had also identified nine cases of non-fatal pneumonia—three workers exposed to fumes from cutting, grinding and welding were hospitalized with lobar pneumonia, and six workers engaged on reconstruction work inside a ship's hull were managed as outpatients [18]. Case reports linking fatal pneumonia in welders and metal fume-exposed occupations with atypical microorganisms also form a part of the record [19].

The NLIA urged physicians to inquire about occupational exposures in working-aged patients with pneumonia, but the more direct and pressing need, to ensure effective controls, has been problematic for several reasons. Although some data suggest that chronic exposure to metal fume blunts responsiveness to inhaled particulate matter (favouring the free radical injury hypothesis) [20], the exact underlying mechanisms remain elusive, and mechanistic chamber experiments are currently in progress (K. T. Palmer, personal communication). In the absence of suitable biomarkers of risk, the dose–response

relationship and the level below which exposures should be controlled have not yet been defined.

## Pneumococcal vaccination

However, the writers of the *Green Book*, the Joint Committee on Vaccination and Immunisation (JCVI), have now acted on available evidence to advise personal protection for workers [3]. Specifically, they advise that 'There is a strong association between welding and the development of pneumococcal disease, particularly lobar pneumonia …. Therefore, welders who have not received the pneumococcal polysaccharide vaccine (PPV23) previously, should be offered a single dose of 0.5 ml of PPV23 vaccine … Employers should ensure that provision is in place for workers to receive PPV23.'

Much is known about the properties and efficacy of this vaccination and about alternative choices [3]. Several vaccines for pneumococcal pneumonia are available worldwide. The vaccine commonly given in childhood in the UK, the pneumococcal conjugate vaccine, prevents infection with seven different serotypes, while the vaccine given in adulthood, PPV23, contains purified capsular polysaccharide from each of 23 capsular types of pneumococcus.

The vaccine is safe, and most healthy adults develop a good antibody response to a single dose of PPV by the third week following immunization. PPV23 will not prevent pneumococcal pneumonia arising from a serotype absent in the vaccine, pneumonias caused by other microorganisms, or pneumonitis secondary to inhalation of metal fume. However, the 23 types included in the vaccine account for 96% of the pneumococcal isolates that cause serious infection in the UK, and PPV has been estimated by a Cochrane review to be 74% effective (95% CI = 56–85%) in preventing IPD, with similar estimates in relation to the prevention of pneumococcal pneumonia [21].

Following a single injection, post-immunization antibody levels usually begin to wane after about 5 years, although the length of protection is not known. Assuming that it lasts at least 10 years and that its efficacy in welders matches that estimated in the Cochrane meta-analysis, the incidence of IPD in welders should fall from the 22.7/100 000/year estimated by Wong *et al.* [14] to <6/100 000/year, and about 588 welders (95% CI = 363–1551) would need to be vaccinated to prevent one case of this disease in 10 years. If the case fatality rate were 12% [1], 4900 welders would need vaccination to avoid one death over the 10-year period. The first ratio looks reasonable compared with the 500 healthy US physicians who would need to take aspirin every year to prevent myocardial infarction (MI) or death over the period, and the 700 patients who would need to take simple anti-hypertensives each year to prevent one stroke, MI or death [22]; while the second can be compared with the roughly 2400 deaths/year [23] prevented by fitting front and rear seat belts to 31 million cars on UK roads (assuming that 31 million × 4 seat belts will prevent 24 000 deaths if cars have a useful life of 10 years, this equates to 5166 seat belt fittings per life saved per decade).

## Whom to vaccinate and when?

The *Green Book* guidance does not specify the types of welding or welder that should be covered, the evidence being of a nature that does not allow clear distinctions to be drawn. Certainly, employees who regard themselves as welders should be offered vaccination with PPV23, but there are many workers who undertake some welding as part of their job, and it would seem prudent to extend the offer of vaccination to this group as well if welding is undertaken on a regular basis.

For other groups, risk assessment will determine whether exposure is improbable, possible or likely. For example, most employees are not exposed to metal fume from well-enclosed automated laser welding and cutting, unless they need to enter the laser welding room shortly after the cessation of laser or hybrid welding; the metal fume produced from high-velocity oxyfuel coating should be removed by the extraction system before an operator re-enters the room; and there should be no concern in relation to plastic, electron beam and friction stir welding, or work on laser metal or powder bed deposition or cold spray technologies. Ultimately, however, as the risk-conferring exposures are not closely defined, there is a case for making offer of a one-off vaccination liberal and inclusive.

No Department of Health funding is available for PPV23 to be given in welders, so employers will need to fund the vaccination programme, which is estimated to cost around £30 per vaccination. The obligation to vaccinate may be seen in the same light as that on hospital managers under the Health and Safety at Work etc. Act to ensure that certain categories of health care worker at higher risk of hepatitis B infection receive the offer of appropriate immunization—it is a necessary cost to the business.

There is current uncertainty regarding the optimum timing of vaccination. An argument can be advanced for offering vaccination to welders only at older ages (e.g. over 50 years). Immunity may last only a few years [3], no booster is presently recommended (because of an increased risk of side-effects) and the incidence of IPD climbs at older ages, being low in young adults [15]. Thus, as absolute risk is higher at older ages, a bigger absolute risk reduction may be anticipated among older welders than among younger ones. Set against this, the act of withholding vaccination would require a judgement about the likelihood a welder would remain exposed at the qualifying older age, and would deny protection in

the interim to those destined to discontinue exposure before then. In view of the uncertainties, the JCVI did not recommend an age restriction. Hopes exist that a polyvalent pneumococcal conjugate vaccine, currently under testing in adults, will provide a more lasting immune memory (A. Hall, personal communication) and could potentially be used for re-vaccination, in which case timing of vaccination will become less important.

## Safety aspects

In the meantime, the uncertain duration of afforded protection serves to remind that prevention at source is paramount. Vaccination should not be seen by employers as an alternative to adequate fume control or by welders as a reason to neglect the controls that employers have provided. Always using appropriate and effective local exhaust ventilation (LEV), keeping the LEV hood near the work-piece, not placing the welder's face in the plume, wearing appropriate personal protective equipment (using an 'improved' rather than a 'standard' helmet), always cleaning the work-piece prior to welding to remove contaminants, undertaking other tasks (e.g. grinding) away from the area in which welding is taking place if possible or at least using an appropriate mask will all help to minimize exposure to welding fume and metal particulates in welders. A recent recommendation by the Dutch welding community (www.5xbeter.nl) to 'count to five' after completing welding before lifting the helmet is also worth following, as this will allow time for agglomeration and aggregation of fume particles, rendering them non-respirable. Ensuring good general ventilation and extraction in laser and electron beam welding and high-velocity oxyfuel coating, and allowing time to pass for fumes to cool before entering the room are all sensible preventive actions.

Finally, as tobacco smoking increases the risk of IPD [24], it is good practice to discourage welders from smoking or exposing their non-smoking co-workers to environmental tobacco smoke.

## Conclusions

On the strength of this review we venture to make five recommendations:

(i) Occupational health providers and employers should offer welders and other employees who are exposed to metal fume a single dose of PPV23.
(ii) Welders and other employees exposed to metal fume should continue to control the amount of fume that they are exposed to by all reasonably possible means.
(iii) Ongoing efforts should be made to encourage welders to discontinue or avoid taking up smoking, not only to reduce their risk of infectious pneumonia but also that of more major and more likely threats to their health from cardiovascular and chronic obstructive pulmonary disease.
(iv) Research should be undertaken into the long-term effectiveness of pneumococcal vaccine (and its optimum timing) in preventing pneumococcal pneumonia and IPD in welders, controlling as appropriate for tobacco smoke exposure, co-morbidity and history of metal fume exposure.
(v) Physicians should monitor periodic updates to the *Green Book* in case a more effective and long-lived vaccine or suitable booster vaccine comes to the fore.

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## Conflicts of interest

None declared.

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# Sydney 2000

The athletic shadow of Millennium Man with his boomerang bursting limbs strides majestically over the city, its five white Olympic rings and the iconic Opera House—a motif echoed in the smoke plume of his torch and repeated on his legs. The blue background mimicking sea and sky is composed of the names of all the competing nations. Sydney 2000 'the athletes' Games' has been acknowledged by many as the best Olympics ever.

Captain Robert Dover opened the first Olimpicks in the Cotswold town of Chipping Campden (1612); Dr William Brookes launched the first Olympian Games in Much Wenlock, Shropshire (1850); and Baron Pierre de Coubertin inaugurated the first Modern Games in Athens (1896). London 2012 will be the XXX Olympiad and will feature 10 500 athletes representing 200 countries in 26 sports. There will be 6250 anti-doping samples, 375 doctors, 150 nurses, 200 000 pairs of gloves and 150 000 condoms. The Games will cost £11.3 billion; be watched by 10 million spectators; and be reported on by 21 000 media personnel. Organizers hope that the Games will leave a 'sustainable legacy of national benefits in culture, sport, volunteering, business and tourism'. Sadly Captain Dover's shin-kicking competition is no longer an Olympic sport.

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