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WOUND BOTULISM IN INJECTORS OF DRUGS: UPSURGE IN CASES IN ENGLAND DURING 2004

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Wound infections due to *Clostridium botulinum* were not recognised in the UK and Republic of Ireland before 2000. *C. botulinum* produces a potent neurotoxin which can cause paralysis and death. In 2000 and 2001, ten cases were clinically recognised, with a further 23 in 2002, 15 in 2003 and 40 cases in 2004. All cases occurred in heroin injectors. Seventy cases occurred in England; the remainder occurred in Scotland (12 cases), Wales (2 cases) and the Republic of Ireland (4 cases). Overall, 40 (45%) of the 88 cases were laboratory confirmed by the detection of botulinum neurotoxin in serum, or by the isolation of *C. botulinum* from wounds. Of the 40 cases in 2004, 36 occurred in England, and of the 12 that were laboratory confirmed, 10 were due to type A. There was some geographical clustering of the cases during 2004, with most cases occurring in London and in the Yorkshire and Humberside region of northeast England.

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Introduction

Heroin, cocaine and amphetamines are among the most widely injected drugs, and complications in injecting drug users (IDUs) resulting in infections are the most frequent reason for admission to hospital in this group of patients [1]. Soft tissue infections caused by spore-forming bacteria in IDUs emerged as a serious problem in the UK in 2000. Cases of infections due to *Clostridium novyi* [2], *Clostridium botulinum* [3,4], *Clostridium tetani* [5], *Clostridium histolyticum* [6], and *Bacillus cereus* [7] were subsequently reported in this patient group. The major risk factors for all these infections was thought to be the availability of higher purity heroin, and 'skin-popping' (subcutaneous injection) or 'muscle-popping' (intramuscular injection) which is sometimes practised by IDUs when access to veins is lost [2,3,5]. A larger amount of an acidulant, such as citric acid, may be needed to make higher purity heroin soluble for injection; this is likely to increase the resulting tissue damage when subcutaneously or intramuscularly injected, and is thus important for the initiation of a wound infection.

Wound botulism occurs when spores of *C. botulinum* contaminate a wound, germinate and produce botulinum neurotoxin in vivo. The symptoms of botulism are caused by the neurotoxin which blocks the release of acetylcholine at the neuromuscular junction, resulting in a descending flaccid paralysis. Patients with botulism typically present with blurred vision, drooping eyelids, slurred speech, difficulty in swallowing, dry mouth, and muscle weakness. Patients usually have no fever or loss of sensation and awareness. If untreated, paralysis may progress to the arms, legs, trunk and respiratory muscles. If onset is very rapid there may be no symptoms before sudden respiratory paralysis [8].

Methods

Cases of wound botulism were defined, as outlined elsewhere [9], as illness resulting from toxin produced by *C. botulinum* that has infected a wound producing symptoms including diplopia, blurred vision,

bulbar weakness and symmetric paralysis. Laboratory confirmation was obtained by the detection of botulinum neurotoxin in serum or wound tissue and/or the isolation of *C. botulinum* from a wound [9].

In the United Kingdom (UK), cases of botulism are reported through national voluntary reporting to the Health Protection Agency (HPA) Centre for Infections (Cfi) and by submission of samples for laboratory confirmation to Cfi, which also receives referred samples from the Republic of Ireland. Laboratory confirmation is achieved as described elsewhere [10,11,12]. Further clinical details from affected patients are obtained by administration of a standard questionnaire to patients by clinicians and microbiologists.

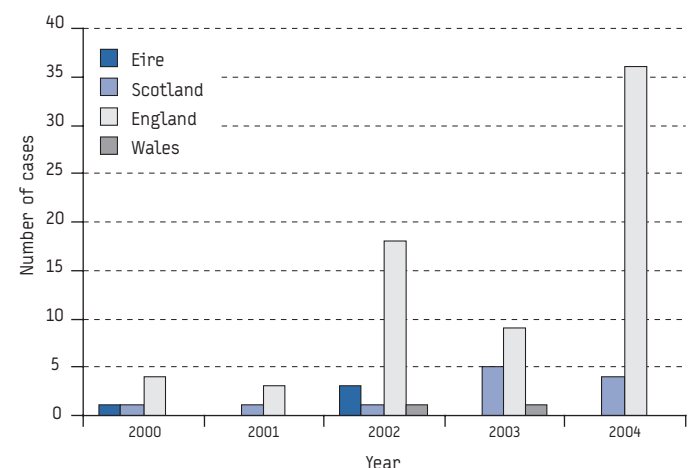
Results

Yearly totals of reports of wound botulism by country in the UK and Republic of Ireland are shown in Figure 1. No cases were recognised before 2000 and a total of 88 cases were reported between 2000 and 2004. Seventy cases were in England, 12 in Scotland, 2 in Wales and the remaining 4 in the Republic of Ireland. No cases were reported from Northern Ireland. All cases occurred in IDUs. The ages were known for 75 of the 88 cases, and the mean age was 34 years (range 22 to 48). Sixty one of the cases were in men and 27 in women; in 2004, where information on gender was provided, 27 were in men and 13 were in women. Details of clinical presentation, outcomes and drug use will be presented elsewhere as data collection is ongoing.

Overall, 40 (45%) of the 88 cases were laboratory confirmed by the detection of botulinum neurotoxin in serum (33 cases), or by the isolation of *C. botulinum* from wounds (25 cases). Neurotoxin was detected in serum together with the isolation of *C. botulinum* from wounds in 18 of the cases. Neurotoxin only was detected in the serum of 15 of the cases, and *C. botulinum* only was isolated from wounds in the remaining seven cases. Based on the neurotoxin detected and/or the *C. botulinum* isolated from the 40 laboratory confirmed cases, 35 were due to type A, three to type B and two to types A and B.

FIGURE 1

Cases of wound botulism in injecting drug users in the UK and Republic of Ireland, 2000-2004



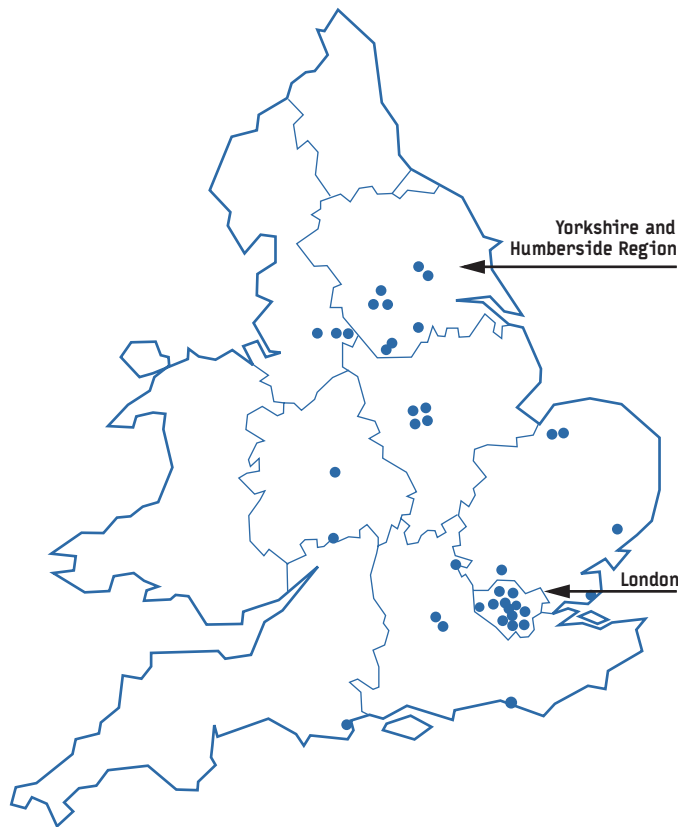
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During 2004, 36 of the 40 cases reported were in England. Twelve of the patients in England were laboratory confirmed, and 10 of these cases were due to type A, one to types A and B, and one to type B. There was some geographical clustering, with cases concentrated in two regions: Yorkshire and Humberside, and London [FIGURE 2].

FIGURE 2

Distribution of wound botulism cases in 2004 by region in England



Discussion

The recognition of wound botulism in injectors of heroin in the UK coincided with increased recognition of soft tissue infections due to other species of endospore forming bacteria [2,5,6,7]. It is not clear if the emergence of these diseases represents the presentation of new diseases in the UK, or is due to ascertainment bias because of diagnosis of diseases not previously recognised. However, the recognition of cases of food and infant botulism together with surveillance systems to capture reports of cases clearly existed in the UK before the detection of the first cases in IDUs in 2000. This suggests that, at least for botulism, these soft tissue infections represent an emerging hazard for this patient group. There was increased recognition of wound botulism in IDUs in California in the mid-1990s [13]. The emergence of wound botulism in IDUs in the United States and the UK may have resulted in part from better recognition of cases and increased medical surveillance of this group, but this is unlikely to be the only explanation for the increase in reported cases. The outbreaks may also have been due to contamination events of specific batches of heroin, or they may reflect changes in drug composition or purity. The availability of 'black tar' heroin in the United States (which differs to that generally used in the UK) was identified as a contributing factor for the Californian outbreak [13]. No explanation could be found for the clustering of the wound botulism cases in 2004. However, this clustering together with an absence of cases in other areas believed to have high prevalence of IDUs (such as Glasgow and the north west of England) supports the hypothesis that there was a causal relationship between the patients. Clustering of cases had not previously occurred in the north east of England.

A small number of wound botulism cases in IDUs has been reported in several other European countries. The first cases were reported in Norway in 1997 [14], followed by at least three further cases [15,16]. Between September 1998 and February 1999, nine cases of wound botulism in IDUs were identified in Switzerland [17-22], and one in Holland [23]. The authors have been unable to locate additional case reports amongst IDUs from other European countries.

Since a major risk factor for all of these soft tissue wound infections is 'skin-' or 'muscle-popping' [2,3,5,13], injection practices in IDUs are likely to be important, and geographic variations in these may explain the absence of a similar increase in cases in other European countries. However, clinicians should suspect botulism in any patient with an afebrile, descending, flaccid paralysis. Botulinum antitoxin is effective in reducing the severity of symptoms for all forms of botulism if administered early in the course of the disease; this should not be delayed until results of microbiological testing are available. In cases of wound botulism, antimicrobial therapy and surgical debridement are important to reduce the organism load and avoid relapse after antitoxin treatment. *C. botulinum* is sensitive to benzyl penicillin and metronidazole. Advice for responding to suspect wound botulism is available on the HPA website [24]. As well as providing information for health professionals, the HPA website gives advice for preventative measures to IDUs including the following:

- Smoke rather than inject heroin;
- If IDUs must inject, inject intravenously and not intramuscularly or subcutaneously;
- Do not share needles, syringes, cookers, or spoons for injection;
- Use as little citric acid as possible;
- If injecting more than one type of drug, inject in separate places;
- If swelling, redness or pain occurs at injection sites, seek medical advice immediately [24].

At the time of writing (July 2005) a further 20 cases of wound botulism in IDUs had been reported in the UK during 2005.

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ORIGINAL ARTICLES

Euroroundup

PNEUMOCOCCAL VACCINATION POLICY IN EUROPE

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Infection due to *Streptococcus pneumoniae* (Pneumococcus) (Pnc) is an important cause of invasive clinical manifestations such as meningitis, septicaemia and pneumonia, particularly in young children and the elderly. A 23-valent polysaccharide Pnc vaccine (PPV) has been available for many years and a 7-valent conjugate Pnc vaccine (PCV) has been licensed since 2001 in Europe. As part of a European Union (EU) funded project on pneumococcal disease (Pnc-EURO), a questionnaire was distributed to all 15 EU member states, Switzerland, Norway and the 10 accession countries in 2003 to ascertain current pneumococcal vaccination policy. Twenty three of the 27 target countries, constituting the current European Union (plus Norway and Switzerland), completed the questionnaire. PPV was licensed in 22 of the 23 responding countries and was in the official recommendations of 21. In all the 20/21 countries for which information was available, risk groups at higher risk of infection were targeted. The number of risk groups targeted ranged from one to 12. At least 17 countries recommend that PPV be administered to all those >65 years of age (in three countries, to those over 60 years of age).

Thirteen countries had developed national recommendations for PCV in 2003. No country recommended mass infant immunisation at that time, but rather targeted specific risk groups (between 1 and 11), particularly children with asplenia (n=13) and HIV infection (n=12). PCV use was restricted to children under two years of age in seven countries, and in four countries to children under five years of age. Future decisions on use of pneumococcal vaccines in Europe will be decided on the basis of several factors including: local disease burden; the predicted impact of any universal programme, particularly the importance of serotype replacement and herd immunity (indirect protection to the unvaccinated population); the effectiveness of reduced dose schedules, and vaccine cost. Indeed, at least one country, Luxembourg, has since implemented a universal infant PCV immunisation policy.

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Introduction

Pneumococcal (Pnc) disease is caused by the bacterium *Streptococcus pneumoniae* of which more than 90 serotypes are now recognised. Pnc is an important cause of morbidity and mortality in Europe [1] – with the observed burden varying geographically, due in part to differences in healthcare factors such as blood culture practice and antibiotic use [2]. With large reductions in the incidence of *Haemophilus influenzae* type b in many European countries, Pnc is now one of the leading causes of meningitis and invasive bacterial disease in children; Pnc is also one of the main aetiological agents for community-acquired pneumonia in adults and for otitis media in children [1]. Furthermore, in recent years antibiotic resistant strains of Pnc have emerged as an increasing problem, with rates of penicillin resistance ranging up to almost 50% of invasive isolates in some European countries [1].

Two types of pneumococcal vaccine are now licensed in Europe, and include a variable number of capsular serotypes: the older 23-valent Pnc polysaccharide vaccine (PPV) and the newer conjugated 7-valent Pnc vaccine (PCV). PPV provides protection against invasive Pnc disease due to 23 serotypes in subjects older than two years [3]. PCV protects against seven serotypes but also in those younger than two years and provides longer lasting immunity against invasive disease. Conjugate vaccine also protects against non-invasive Pnc disease manifestations such as pneumonia [4]. Post-licensure surveillance following introduction of PCV in the United States in 1999 as a universal infant immunisation programme has shown a large reduction in both invasive and non-invasive disease incidence due to vaccine serotypes in both vaccinated and older unvaccinated populations ('herd immunity'). This reduction in disease has also been accompanied by a fall in the rate of penicillin-resistant Pnc [5]. However, a small increase in invasive disease due to non-vaccine serotypes (termed 'serotype replacement') has also been observed [6].

Historically, individuals at higher risk of Pnc infection such as those with immune system impairment, and more recently, the elderly, have been targeted with PPV in Europe. The licensure of the new 7-valent Pnc conjugate vaccine in Europe by the European Medicine Evaluation Agency (EMA) in 2001 has re-ignited interest in pneumococcal disease and the most appropriate vaccination strategy in a European setting. A number of factors have contributed to this decision making, including the potentially preventable disease burden and the cost and effectiveness of alternative intervention programmes. For European countries to be able to design the most appropriate